In February 2013, GlaxoSmithKline (GSK) announced a commitment to further clinical transparency through the public disclosure of GSK Clinical Study Reports (CSRs) on the GSK Clinical Study Register.

The following guiding principles have been applied to the disclosure:

- Information will be excluded in order to protect the privacy of patients and all named persons associated with the study
- Patient data listings will be completely removed* to protect patient privacy. Anonymized data from each patient may be made available subject to an approved research proposal. For further information please see the Patient Level Data section of the GSK Clinical Study Register.
- Aggregate data will be included; with any direct reference to individual patients excluded
*Complete removal of patient data listings may mean that page numbers are no longer consecutively numbered

This study includes documents that were originally reported in a language other than English. All documents that are available in English have been made available via the GSK Clinical Study Register.

## GlaxoSmithKline Biologicals, SA

## Study detailed title

A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy

## Clinical Study Report for Study 116427 (ZOSTER-028)

This report provides immunogenicity and safety results obtained from Dose 1 (Day 0 ) and Dose 2 ( 1 to 2 months after first vaccination) through primary completion (Month 2), and up to the end of study (Month 13, i.e., 12 months after last vaccination).

## Development Phase II/III

IND Number: BB-IND 13879
EUDRACT Number: 2012-002966-11
Name of Investigational Product: GlaxoSmithKline (GSK) Biologicals' lyophilized formulation of the Herpes Zoster (HZ) vaccine (GSK 1437173A)

Indication Studied: Prevention of Herpes Zoster (HZ) and related complications in adults $\geq 50$ years of age and immunocompromised adults $\geq 18$ years of age.

Study initiation date:
Study active phase (Visit 3, Month 2) completion date:
Data lock point (Date of database freeze) active phase:
Study completion date:
Data lock point (Date of database freeze) end of study:
Date of report: Final:

6-March-2013
18-June-2015
15-March-2016
20-May-2016
10-February-2017
03-May-2017

Sponsor Signatory: Lidia Oostvogels,<br>Director, Clinical and Epidemiology Project Leader, Zoster Program.

This study was performed according to the principles of GCP including the archiving of essential documents.

Based on GSK Biologicals'Study Report INS-BIO-CLIN-1010 v05
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## SYNOPSIS

| Name of company: <br> GlaxoSmithKline <br> Biologicals, SA, <br> Rixensart, Belgium | Name of finished product: | Name of active substance: <br> Varicella zoster virus <br> glycoprotein E (VZV gE) |
| :--- | :--- | :--- |
| Study No.: 116427 (ZOSTER-028) |  |  |
| Title of the study: <br> A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the <br> immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when <br> administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid <br> tumours receiving chemotherapy. |  |  |
| Investigator(s) and study centre(s): <br> Multicentre study (with 29 sites recruiting subjects) in 6 countries: Canada, Czech Republic, France, <br> Republic of Korea, Spain and United Kingdom. <br> The principal investigator who reviewed the clinical study report: Dr. Ignacio Delgado Mingorance, H <br> Infanta Cristina, Badajoz, Spain. |  |  |
| Publication (reference): <br> None at the time of this report. |  |  |
| Study period: <br> Study initiation date: $6-M a r c h-2013 ~$ |  |  |
| Study active phase (Visit 3, Month 2) completion date: 18-June-2015 |  |  |
| Data lock point (Date of database freeze) active phase: 15-March-2016 |  |  |
| Study completion date: 20-May-2016 |  |  |
| Data lock point (Date of database freeze) end of study: 10-February-2017 |  |  |
| Indication: Prevention of Herpes Zoster (HZ) and related complications in adults $\geq 50$ years of age and |  |  |
| immunocompromised (IC) adults $\geq 18$ years of age. |  |  |

## Objectives:

## Co-primary:

- To evaluate anti-glycoprotein E (anti-gE) humoral immune responses at Month 2, following a twodose administration of the Herpes Zoster subunit (HZ/su) vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).

Criterion used: The objective is met if the lower limit of the 95\% confidence interval (CI) of the Geometric Mean (GM) ratio (HZ/su PreChemo group over placebo PreChemo group) in anti-gE Enzyme-linked immunosorbent assay (ELISA) antibody (Ab) concentrations is greater than 3.

- To evaluate the safety and reactogenicity following administration of the HZ/su vaccine as compared to placebo up to 30 days post last vaccination in subjects with solid tumours receiving chemotherapy.

Criterion used: This analysis is descriptive, no criterion has been defined.

## Secondary:

- To evaluate vaccine response rate (VRR) in anti-gE humoral immunogenicity responses at Month 2, following a two-dose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).

Criterion used: The objective is met if the lower limit of the 95\% CI of the VRR for anti-gE ELISA Ab concentrations at Month 2 in the HZ/su PreChemo group is at least $60 \%$.

- To evaluate gE-specific CD4+ T-cell immunogenicity responses at Month 2, following a two-dose administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only) (in the cell-mediated immunity [CMI] subcohort).
Name of company:
GlaxoSmithKline
Biologicals, SA,
Rixensart, Belgium

Criterion used: The objective is met if the lower limit of the 95\% CI of the GM ratio (HZ/su PreChemo group over placebo PreChemo group) in gE-specific CD4+ T-cell frequencies at Month 2 is greater than 1.

- To evaluate VRR in gE-specific CD4+ T-cell mediated immunogenicity at Month 2, following a two-dose administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine in subjects with solid tumours receiving chemotherapy (PreChemo Groups only) (in the CMI sub-cohort).
Criterion used: The objective is met if the lower limit of the $95 \%$ CI of the VRR for $g E$-specific CD4 $+T$-cell frequencies at Month 2 in the HZ/su PreChemo group is at least $50 \%$.
- To evaluate the anti-gE humoral immunogenicity response at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (all subjects).

Criterion used: The objective is met if the lower limit of the $95 \%$ CI of the Geometric Mean (GM) ratio (HZ/su group over placebo group) in anti-gE ELISA Ab concentrations is greater than 3.

- To evaluate VRR in anti-gE humoral immunogenicity responses at Month 2, following a two-dose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (all subjects receiving the $\mathrm{HZ} /$ su vaccine).
Criterion used: The objective is met if the lower limit of the $95 \%$ CI of the VRR for anti-gE ELISA Ab concentrations at Month 2 in the HZ/su group is at least $60 \%$.
- To evaluate safety following administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine, as compared to placebo, from 30 days post last vaccination until study end in subjects with solid tumours receiving chemotherapy.
- To characterize anti-gE humoral immunogenicity responses at Month 0, Month 1, Month 2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13 within the $\mathrm{HZ} / \mathrm{su}$ and placebo groups.
- To characterize gE-specific CD4+ T-cell mediated immunogenicity responses at Month 0, Month 1, Month 2, and Month 13 within the HZ/su and placebo groups (PreChemo Groups only) (in the CMI sub-cohort).


## Methodology:

This was a phase II/III, observer-blind randomised, placebo controlled, multi-centre, multi-country study with two parallel groups to assess the immunogenicity and safety of HZ/su when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age (YOA) with solid tumours receiving chemotherapy. The focus of the study was to examine the immunological response to HZ/su, when subjects were immunocompromised (IC) through the use of chemotherapy.

The first vaccination visit at Month 0 (Visit 1) was preceded by a mandatory Pre-vaccination visit that took place from 30 days prior up to the day of Visit 1.
Eligible subjects were randomised to HZ/su vaccine or placebo (1:1 ratio) and to the PreChemo group (first vaccination at least 10 days* (up to 1 month) before the administration of a chemotherapy cycle) or the OnChemo group (first vaccination at the start of a chemotherapy cycle) (PreChemo: OnChemo 4:1 ratio). The overall ratio of these 4 study groups, HZ/su-PreChemo, Placeb-PreChemo, HZ/su-OnChemo, and Placeb-OnChemo, was 4:4:1:1.
The analysis of safety was performed within the TVC on all subjects of the PreChemo and OnChemo groups.
The analysis of humoral immunogenicity and humoral persistence were performed within the applicable According to Protocol (ATP) cohorts on all subjects of the PreChemo and OnChemo groups. The

| Name of company: <br> GlaxoSmithKline <br> Biologicals, SA, <br> Rixensart, Belgium | Name of finished product: | Name of active substance: <br> Varicella zoster virus <br> glycoprotein E (VZV gE) |
| :--- | :--- | :--- |

analyses of CMI and CMI persistence were performed within the applicable ATP cohorts on the CMI sub-cohort, comprised exclusively of subjects from the PreChemo Groups.

Overall, target enrolment was approximately 232 eligible subjects to provide 168 subjects evaluable for immunogenicity ( 84 per treatment group). In the PreChemo group, target enrolment of eligible subjects was 186 , to provide 134 subjects evaluable for immunogenicity ( 67 per treatment group).

The second dose of study vaccine/ placebo was administered between 1 and 2 months after the first vaccination and at the first day (allowing a window of $+/-1$ day) of a subsequent cycle of chemotherapy (Visit 2). Visit 3 occurred approximately one month after the second vaccination.
Visit 4 occurred within Months 4 to 13 at the start of the last cycle of chemotherapy (coincided with the subject's lowest immune status). The timing of this particular visit was variable depending on the subject's chemotherapy schedule and also on when they started vaccination in relation to their chemotherapeutic regimen. Dependent on the timing of Visit 4, it could replace Month 5 or Month 9 phone contacts, or it could coincide with Visit 5 (at Month 13, approximately 12 months after the second dose of study vaccine/placebo). Blood samples were collected from all subjects at Visits 1, 2, 3, 4 and 5 to assess humoral immune responses, and from a sub-cohort (CMI sub-cohort) of subjects at Visits 1, 2, 3 and 5 to assess CMI responses.

Study staff provided subjects a diary card after each vaccination for daily recording of solicited symptoms (Days 0 to 6 ) and unsolicited symptoms (Days 0 to 29). Serious adverse events (SAEs), potential immune-mediated diseases (pIMDs), pregnancies, and intercurrent medical conditions such as the occurrence of herpes zoster (HZ) were reported from Month 0 to study end.

Per GSK process, blinded review of safety data was performed by the safety review team. An internal safety review committee of GSK was assigned to provide additional oversight by reviewing unblinded safety data.

A first analysis and an end of study analysis were performed. The first analysis was performed when all data up to and including Month 2/Visit 3 ( 30 days post dose 2 : active phase) were available. The confirmatory objectives were assessed at first analysis. The end of study analysis was performed when all data up to and including Month 13 were available.

* For analysis purposes, taking into account the actual clinical experience, the 'PreChemo' sub-group was allowed as' first vaccination at least 8 days (up to 1 month) before the administration of chemotherapy'.

Study vaccine, dose, mode of administration, lot no.:

## Vaccination schedule /site:

HZ/su group subjects received 2 doses of HZ/su (blinded to dosing): the first dose at Visit 1 and the second dose at Visit 2 ( 1 to 2 months after the first dose) through intramuscular injection into the deltoid muscle, preferably of non-dominant arm, but in the other arm when clinically indicated.

| Name of company: GlaxoSmithKline Biologicals, SA, Rixensart, Belgium |  | Name of finished product:$\mathrm{HZ} / \mathrm{su}$ |  |  | Name of active substance: Varicella zoster virus glycoprotein E (VZV gE) |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Vaccine composition /dose /lot number: |  |  |  |  |  |  |
| Treatment name | Product |  | Formulation | Presentation | Volume to be administered | Lot numbers |
| HZ/su | VZV gE |  | $50 \mu \mathrm{~g} \mathrm{~g}$ per 0.5 mL of reconstituted vaccine | Lyophilised pellet in a monodose vial | 0.5 mL | $\begin{aligned} & \text { DVZVA00 } \\ & \text { 7B } \end{aligned}$ |
|  | AS01B |  | MPL, QS21 and liposome ( $50 \mu \mathrm{~g} \mathrm{MPL}$ and $50 \mu \mathrm{~g}$ QS21) per 0.5 mL of reconstituted vaccine | Liquid in a monodose vial |  | $\begin{aligned} & \text { DA01A050 } \\ & \text { A } \end{aligned}$ |

*Components of the reconstituted study vaccine HZ/su.
HZ/su: Herpes Zoster subunit vaccine
VZV gE: Varicella Zoster Virus recombinant purified glycoprotein E
AS01b: Adjuvant System
MPL: 3-O-desacyl-4'-monophosphoryl lipid A
QS-21: QS-21 (Quillaja saponaria Molina, fraction 21) (Licensed by GSK from Antigenics Inc, a wholly owned subsidiary of Agenus Inc., a Delaware, USA corporation)
$\mu \mathrm{g}$ : microgram; mL: millilitre

## Reference vaccine /Comparator, dose and mode of administration, lot no.:

## Vaccination schedule /site:

Placebo group subjects received 2 doses of placebo (blinded to dosing): the first dose at Visit 1 and the second dose at Visit 2 ( 1 to 2 months after the first dose) through intramuscular injection into the deltoid muscle, preferably of non-dominant arm, but in the other arm when clinically indicated.
Vaccine composition /dose /lot number:

| Treatment <br> name | Product name* | Formulation | Presentation | Volume to be <br> administered | Lot <br> numbers |
| :--- | :--- | :--- | :--- | :--- | :--- |
| Placebo | Lyophilised <br> sucrose cake | 20 mg sucrose per 0.5 <br> mL of reconstituted <br> placebo | lyophilised pellet <br> in a monodose <br> vial | 0.5 mL | PVZVA005 <br> A |
|  | Saline $(\mathrm{NaCl})$ <br> solution for <br> reconstitution | 150 mM NaCl solution <br> (water for injection) | Liquid in a <br> monodose vial |  | DD 02 A 011 <br> A |

*Components of the reconstituted placebo
NaCl : Sodium Chloride

## Study Population:

Male and female subjects at least 18 years old (and having reached the age of local legal consent) at the time of study entry, who had provided informed consent, had been diagnosed with one or more solid tumours (defined as a solid malignancy, i.e., not a blood element malignancy) and would receive or were receiving a cytotoxic or immunosuppressive chemotherapy (such that investigational product could be administered no later than the start of the second cycle of chemotherapy).
Female subjects were to be of non-childbearing potential or were to practice adequate contraception for a minimum of 30 days prior to vaccination to be continued through two months post study vaccinations and to have a negative pregnancy test before each vaccination dose.

Subjects who received a previous chemotherapy course within one month of first study vaccination were excluded; as were subjects receiving only newer, more targeted therapies (e.g. trastuzumab) without a classical immunocompromising chemotherapy. Subjects having a varicella or HZ episode or a varicella or HZ vaccination within 12 months of first study vaccination were excluded.

| Name of company: <br> GlaxoSmithKline <br> Biologicals, SA, <br> Rixensart, Belgium | Name of finished product: | Name of active substance: <br> Varicella zoster virus <br> glycoprotein E (VZV gE) |
| :--- | :--- | :--- |

## Duration of treatment:

The total duration of the study for each subject was expected to be approximately 14 months including the pre-vaccination visit, 5 other study site visits and 2 phone contacts.

## Criteria for evaluations:

## Primary endpoints:

- Anti-gE humoral immunogenicity with respect to components of the study/investigational vaccine.
- Anti-gE Ab concentrations as determined by ELISA at Month 2.
- Occurrence of solicited local and general symptoms.
- Occurrence, intensity and duration of each solicited local symptom within 7 days (Days 0-6) after each vaccination.
- Occurrence, intensity, duration and relationship to vaccination of each solicited general symptom within 7 days (Days $0-6$ ) after each vaccination.
- Occurrence of unsolicited adverse events (AEs).
- Occurrence, intensity and relationship to vaccination of unsolicited AEs during 30 days (Days 0-29) after each vaccination, according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence of SAEs.
- Occurrence and relationship to vaccination of SAEs up to 30 days post last vaccination.
- Occurrence of AEs of specific interest.
- Occurrence and relationship to vaccination of any pIMDs up to 30 days post last vaccination.


## Secondary endpoints:

- For immunogenicity with respect to components of the study/investigational vaccine.
- Anti-gE Ab concentrations as determined by ELISA at Month 0, Month 1, Month 2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13.
- Vaccine response for anti-gE Abs at Month 1, Month 2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13.
- Frequencies of gE-specific CD4+ T-cells, expressing at least 2 activation markers (from among IFN- $\gamma$, IL-2, TNF- $\alpha$ and CD40 L*), as determined by in vitro intracellular cytokine staining (ICS), at Month 0 , Month 1, Month 2, and Month 13.
- Vaccine response for gE-specific CD4+ T-cells expressing at least 2 activation markers (from among IFN- $\gamma$, IL-2, TNF- $\alpha$ and CD40L*), as determined by in vitro ICS, at Month 1, Month 2 and Month 13.
- Occurrence of SAEs.
- Occurrence and relationship to vaccination of SAEs during the period starting after 30 days post last vaccination until study end.
- Occurrence of AEs of specific interest.
- Occurrence of any pIMDs during the period starting after 30 days post last vaccination until study end.
* Interferon gamma, interleukin-2, tumour necrosis factor alpha and CD40 ligand

| Name of company: <br> GlaxoSmithKline <br> Biologicals, SA, <br> Rixensart, Belgium | Name of finished product: | Name of active substance: <br> Varicella zoster virus |
| :--- | :--- | :--- |
|  |  | glycoprotein E (VZV gE) |

## Statistical methods:

This section of statistical methods is restricted to support the analyses presented in the synopsis section.

## Analysis of demographics and other baseline characteristics

Demographic characteristics (age at first study vaccination, gender, geographic ancestry and ethnicity), and withdrawal status were summarised using descriptive statistics.

## Analysis of immunogenicity

## Humoral immunogenicity

The primary analysis of humoral immunogenicity at Month 0,1 and 2 was based on the According to Protocol (ATP) cohort for Humoral immunogenicity. Whereas, the analyses at Month 6 and 13 were based on ATP cohort for Humoral persistence.

## Within group assessment

- VRR at Months 1, 2, 6 and 13 with exact $95 \%$ CI.

VRR defined as percentage of subjects with vaccine response:

- For seronegative subjects, Ab concentration at Month $2 \geq 4$-fold the cut-off for anti-gE ( 4 x 97 $\mathrm{mIU} / \mathrm{mL}$ ).
- For seropositive subjects, Ab concentration at Month $2 \geq 4$-fold the pre-vaccination Ab concentration.


## Between group assessment

To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine, as compared to placebo, a repeated measurement modelling integrating Month 1 and Month 2 data and based on a likelihood based approach was used to assess the GM fold increase over placebo. The pre-vaccination log-transformed Ab concentration (Month 0 ) was included as a continuous covariate. The fixed-effect model included the means for all levels of the visit by treatment interaction effect. The 2 levels of the first vaccination schedule (OnChemo/PreChemo) were included in the model for the analysis that included all data. Adjusted GM ratio of HZ/su over Placebo groups for anti-gE Ab ELISA concentrations at Month 2 was calculated and tabulated.

## CMI

The primary analysis at Month 0,1 and 2 was based on the ATP cohort for CMI immunogenicity. Whereas, the primary analysis at Month 13 was based on the ATP cohort for CMI persistence.

## Within groups assessment

- VRR in the gE-specific CD4[2+] T-cell frequencies at Months 1,2 and 13 with exact $95 \%$ CI.

VRR defined as percentage of subjects with vaccine response:

- For initially subjects with pre-vaccination T-cell frequencies below the threshold, at least a 2fold increase as compared to the threshold ( $2 \times 320$ Events $/ 10^{6}$ CD4+ T-cells).
- For initially subjects with pre-vaccination T-cell frequencies above the threshold, at least a 2fold increase as compared to pre-vaccination T -cell frequencies.


## Between groups assessment

The evaluation of the CMI responses at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only), was performed in terms of gE-specific CD4[2+] T-cells.

| Name of company: <br> GlaxoSmithKline <br> Biologicals, SA, <br> Rixensart, Belgium | Name of finished product: | Name of active substance: <br> Varicella zoster virus <br> glycoprotein E (VZV gE) |
| :--- | :--- | :--- |

A likelihood-based approach with Repeated Measurement model was used to analyse the logtransformed ratio between induction frequency and background frequency of CD4[2+] T-cells. The fixed-effect included all levels of the treatment effect by visits interaction. The continuous covariates included the pre-vaccination log-transformed CD4[2+] T-cell frequency following induction with gE (Month 0 ) and the post-vaccination log-transformed CD4[2+] T-cell frequency under the background condition. Least-square means and difference of least-squares means were back-transformed and used to provide estimates for the frequency difference divided by background ([induction - background] / background). The log-transformation of the ratios of these estimates between treatments was calculated. The CI for the ratio of gE-specific CD4[2+] T-cell frequencies was calculated using the Delta method.

## Analysis of safety

The primary analysis for safety was based on the TVC.

## Within group assessment

The results for the analysis of safety were tabulated as:

- The percentage of subjects reporting each individual solicited local and general AE during the solicited 7-day-follow-up period were tabulated with exact 95\% CI.
- For all solicited symptoms, the same tabulation was performed for grade 3 solicited AEs and for solicited general AEs with relationship to vaccination.
- The proportion of subjects with at least one report of unsolicited AEs (all unsolicited AEs/ grade 3 unsolicited AEs / unsolicited AEs with relationship to vaccination) classified by MedDRA Preferred Term and reported up to 30 days after each vaccination was tabulated with exact 95\% CI.
- Number/percentage of subjects with pIMDs/SAEs was tabulated.
- Number/percentage of subjects with fatal outcome was tabulated.

| Synopsis Table 1 Study population (Total Vaccinated Cohort) | Placebo |  |
| :--- | :--- | :--- |
| Number of subjects | 116 | 116 |
| Planned, N | 117 | 115 |
| Randomised, N (Total Vaccinated Cohort) | $90(76.9)$ | $90(78.3)$ |
| Completed, $\mathrm{n}(\%)$ | HZ/su | Placebo |
| Demographics | 117 | 115 |
| N (Total Vaccinated Cohort) | $70: 47$ | $69: 46$ |
| Females:Males | $57.1(10.8)$ | $58.5(11.7)$ |
| Mean Age, years (SD) | $57(35,85)$ | $59(31,87)$ |
| Median Age, years (minimum, maximum) | $92(78.6)$ | $88(76.5)$ |
| White - Caucasian / European Heritage, $\mathrm{n}(\%)$ | $11(9.4)$ | $14(12.2)$ |
| Asian - East Asian Heritage, $\mathrm{n}(\%)$ | $9(7.7)$ | $8(7.0)$ |
| Missing race, $\mathrm{n}(\%)$ |  |  |
| HZ/su |  |  |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
In regards to 'Missing race', this data was purposely not collected secondary to local laws prohibiting the collection of race data and therefore is missing.

| Name of company: | Name of finished product: | Name of active substance: <br> Garicella zoster virus <br> GiosmithKline <br> Biologicals, SA, <br> Rixensart, Belgium |
| :--- | :--- | :--- | HZ/su $\quad$|  |
| :--- |

## Summary:

## Immunogenicity results:

## Assessment of confirmatory objectives

Results of confirmatory humoral immunogenicity objectives assessed on the ATP cohort for Humoral immunogenicity, and confirmatory CMI objectives assessed on the ATP cohort for CMI, are presented.

The confirmatory objectives were assessed sequentially in order of ascending rank. The objectives were assessed until an objective was not met. At this point, a descriptive analysis of the remaining endpoints was conducted. The assessment of the confirmatory objectives was conducted on active phase data and referred to as a "first analysis" in this CSR. The immunogenicity tables and figures were generated on active phase data at first analysis and end of study analysis using the respective clinical database. The active phase results on humoral immunogenicity generated at first analysis and at end of study analysis were the same, the tabulations and figures generated at end of study analysis are presented in this report.

The active phase results on CMI generated at first analysis and at end of study were not the same, as a result of changes in the laboratory CMI data release definitions allowing for more CMI data to be released, even so, there was no impact on study conclusions.

Regarding the CMI-related confirmatory secondary objectives, the results obtained at first analysis (i.e. Synopsis Table 4A and 5A) and end of study analysis (i.e. Synopsis Table 4B and 5B) are both presented in this report. In these cases, the tabulations from the first analysis have 'first analysis' added in the table title.

- The confirmatory primary objective of the study was met as the lower limit of the $95 \% \mathrm{CI}$ of the GM ratio (HZ/su PreChemo Group over Placebo PreChemo group) in anti-gE Ab concentrations at Month 2 (post second vaccination) was 17.9. Therefore, the success criterion (greater than 3 ) was demonstrated. The adjusted GM ratio was 23.2 ( $95 \% \mathrm{CI}: 17.9-30.0 ; \mathrm{P}<0.0001$ ) (Synopsis Table 2).
- The first confirmatory secondary objective of the study was met as the lower limit of the $95 \%$ CI of the VRR for anti-gE Ab concentrations in the HZ/su PreChemo group (at Month 2 (post second vaccination) was $85.0 \%$. Therefore, the success criterion (at least $60 \%$ ) was demonstrated. The VRR was $93.8 \%$ ( $95 \%$ CI: 85.0 - 98.3) (Synopsis Table 3).
- The second confirmatory secondary objective of the study was met as the lower limit of the 95\% CI of the GM ratio (HZ/su PreChemo group over Placebo PreChemo group) in gE-specific CD4[2+] T-cell frequencies) at Month 2 (post second vaccination) was 3.79. Therefore, the success criterion (greater than 1) was demonstrated. The observed GM ratio was 13.67 ( $95 \% \mathrm{CI}: 3.79-49.38$; $\mathrm{P}=0.0002$ ) (Synopsis Table 4A).
Descriptive results obtained with the end of study analysis: the observed GM ratio at Month 2 was 9.94 ( $95 \%$ CI: 3.63 - 27.19) (Synopsis Table 4B).
- The third confirmatory secondary objective of the study was not met as the lower limit of the $95 \%$ CI of the VRR for gE-specific CD4[2+] T-cell frequencies in the HZ/su PreChemo group (at Month 2 (post second vaccination) was $33.5 \%$. Therefore, the success criterion (at least $50 \%$ ) was not demonstrated. The observed VRR was $57.9 \%$ ( $95 \%$ CI: 33.5 - 79.7) (Synopsis Table 5A). Descriptive results obtained with the end of study analysis: the observed VRR at Month 2 was 50.0\% (95\% CI: 28.2 - 71.8) (Synopsis Table 5B).

| Name of company: <br> GlaxoSmithKline <br> Biologicals, SA, <br> Rixensart, Belgium | Name of finished product: | Name of active substance: <br> Varicella zoster virus <br> glycoprotein E (VZV gE) |
| :--- | :--- | :--- |

According to the hierarchical procedure applied, the confirmatory objectives were assessed sequentially in order of ascending rank until an objective was not met. Therefore, the following objectives were analysed descriptively.

- Regarding the anti-gE humoral immune response at Month 2 (post second vaccination) in the $\mathrm{HZ} /$ su group compared to the Placebo group (all subjects), the observed adjusted GM ratio was 14.4 ( $95 \%$ CI: 10.7 - 19.5) (Synopsis Table 6).
- The VRR in anti-gE humoral immune response at Month 2 (post second vaccination) in the HZ/su group (all subjects) was 86.2 \% ( $95 \%$ CI: 77.1-92.7) (Synopsis Table 7).
Synopsis Table 2 Adjusted geometric means and ratio of HZ/su over placebo for anti-gE antibody ELISA concentrations at Month 2 in PreChemo Groups only (ATP cohort for Humoral immunogenicity)

|  |  |  | Adjusted geometric mean |  |  | Adjusted geometric mean ratio |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Timing | Group | N | Value | LL | UL | Value | LL | UL | P- <br> val <br> ue <br> for <br> the <br> rati |
| PlI(M2) | HZ/su | 65 | 24501.57 | 19051.99 | 31509.94 | 23.2 | 17.9 | 30.0 | $\begin{aligned} & <.0 \\ & 001 \end{aligned}$ |
|  | Placebo | 76 | 1056.77 | 990.37 | 1127.62 | . | . | . |  |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval
Confidence Interval (CI) were back transformed to original units
The $p$-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)
Synopsis Table 3 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 2 in PreChemo Groups only (ATP cohort for Humoral immunogenicity)

|  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |
| Test description | Group | N | n | \% | LL | U |
| VZV.gE Ab.IgG | HZ/su | 65 | 61 | 93.8 | 85.0 | 98 .3 |
|  | Placebo | 76 | 0 | 0.0 | 0.0 | 4. 7 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at Month $2 \geq 4$ fold the cut-off for Anti-gE ( $4 \times 97 \mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at Month $2 \geq 4$ fold the pre-vaccination antibody concentration
$N=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
$95 \% \mathrm{Cl}=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

| Name of company: <br> GlaxoSmithKline <br> Biologicals, SA, <br> Rixensart, Belgium | Name of finished product: |
| :--- | :--- |
|  |  |

Name of active substance: Varicella zoster virus glycoprotein E (VZV gE)

Synopsis Table 4A Adjusted geometric means and ratio of HZ/su over placebo for gE-specific CD4[2+] Tcells frequencies at Month 2 in PreChemo Groups only (ATP cohort for CMI immunogenicity) (First analysis)

|  |  |  | Adjusted geometric mean |  |  | Adjusted geometric mean ratio |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Timing | Group | N | Value | LL | UL | Value | LL | UL | P- <br> val <br> ue <br> for <br> the <br> rati <br> 0 |
| PII(M2) | HZ/su | 19 | 923.7 | 616.4 | 1346.8 | 13.67 | 3.79 | 49.38 | $\begin{aligned} & 0.0 \\ & 002 \end{aligned}$ |
|  | Placebo | 20 | 67.6 | -3.4 | 164.2 | . | . | . | . |

## HZ/su = Herpes Zoster sub-unit vaccine group

Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval
Confidence Interval (CI) were back transformed to original units
The $p$-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)
Synopsis Table 4B Adjusted geometric means and ratio of HZ/su over placebo for gE-specific CD4[2+] Tcells frequencies at Month 2 in PreChemo Groups only (ATP cohort for CMI immunogenicity)

|  |  |  | Adjusted geometric mean |  |  | Adjusted geometric mean ratio |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | \% CI |  |  | \% CI |  |
| Timing | Group | $N$ | Value | LL | UL | Value | LL | UL | P-value for the ratio |
| PlI(M2) | HZ/su | 22 | 781.8 | 535.2 | 1110.4 | 9.94 | 3.63 | 27.19 | <. 0001 |
|  | Placebo | 27 | 78.7 | 13.7 | 162.9 |  |  |  |  |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval
Confidence Interval (CI) were back transformed to original units
The $p$-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)

| Name of company: GlaxoSmithKline Biologicals, SA, Rixensart, Belgium | Name of finished product:$\mathrm{HZ} / \mathbf{s u}$ |  | Name of active substance: Varicella zoster virus glycoprotein E (VZV gE) |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Synopsis Table 5A Vaccine response rates for gE-specific CD4[2+] T-cells frequencies at Month 2 in PreChemo Groups only (ATP cohort for CMI immunogenicity) (First analysis) |  |  |  |  |  |  |
|  |  |  | Vaccine response |  |  |  |
|  |  |  |  |  | 95\% CI |  |
| Test description |  | N | n | \% | LL | UL |
| CD4[2+] | HZ/su | 19 | 11 | 57.9 | 33.5 | $79 .$ $7$ |
|  | Placebo | 20 | 0 | 0.0 | 0.0 | $\begin{aligned} & 16 . \\ & 8 \end{aligned}$ |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as:
For initially subjects with pre-vaccination T cell frequencies below the threshold, at least a 2 -fold increase as compared to the threshold ( $2 \times 320$ Events/10E6 CD4+ T cells)
For initially subjects with pre-vaccination $T$ cell frequencies above the threshold, at least a 2-fold increase as compared to pre-vaccination $T$ cell frequencies
$N=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
$95 \% \mathrm{Cl}=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
Synopsis Table 5B Vaccine response rates for gE-specific CD4[2+] T-cells frequencies at Month 2 in PreChemo Groups only (ATP cohort for CMI immunogenicity)

|  |  |  |  | Vacc | respo |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | CI |
| Test description | Group | N | n | \% | LL | UL |
| CD4[2+] | HZ/su | 22 | 11 | 50.0 | 28.2 | 71.8 |
|  | Placebo | 27 | 0 | 0.0 | 0.0 | 12.8 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially subjects with pre-vaccination $T$ cell frequencies below the threshold, at least a 2 -fold increase as compared to the threshold ( $2 x<320>$ Events/10E6 CD4+ T cells)
For initially subjects with pre-vaccination $T$ cell frequencies above the threshold, at least a 2 -fold increase as compared to pre-vaccination $T$ cell frequencies
$\mathrm{N}=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

| Name of company: GlaxoSmithKline Biologicals, SA, Rixensart, Belgium |  | Name of finished product:$\mathrm{HZ} / \mathbf{s u}$ |  |  |  | Name of active substance: Varicella zoster virus glycoprotein E (VZV gE) |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Synopsis Table 6 Adjusted geometric means and ratio of HZ/su over placebo for anti-gE antibody ELISA concentrations at Month 2 in all subjects (ATP cohort for Humoral immunogenicity) |  |  |  |  |  |  |  |  |  |
|  |  |  | Adjusted geometric mean |  |  | Adjusted geometric mean ratio |  |  |  |
|  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Timing | Group | N | Value | LL | UL | Value | LL | UL | P- <br> value <br> for <br> the <br> ratio |
| PII(M2) | HZ/su | 87 | 14781.59 | 11028.12 | 19812.56 | 14.4 | 10.7 | 19.5 | $\begin{aligned} & <.000 \\ & 1 \end{aligned}$ |
|  | Placebo | 94 | 1025.71 | 954.82 | 1101.87 | . | . | . | . |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval
Confidence Interval (CI) were back transformed to original units
The $p$-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)
Synopsis Table 7 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 2 in all subjects (ATP cohort for Humoral immunogenicity)

|  |  |  | Vaccine response |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| Test description | Group | N | n | $\%$ | LL $95 \%$ CI |  |
| VZV.gE Ab.lgG | HZ/su | 87 | 75 | 86.2 | 77.1 | 92.7 |
|  | Placebo | 94 | 0 | 0.0 | 0.0 | 3.8 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at Month $2 \geq 4$ fold the cut-off for Anti-gE ( $4 \times 97 \mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at Month $2 \geq 4$ fold the pre-vaccination antibody concentration
$N=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit PII(M2) = Post-vaccination Dose II (Month 2)

| Name of company: <br> GlaxoSmithKline <br> Biologicals, SA, <br> Rixensart, Belgium | Name of finished product: | Name of active substance: <br> Varicella zoster virus <br> glycoprotein E (VZV gE) |
| :--- | :--- | :--- |

## Results of descriptive analysis <br> Humoral immunogenicity overall <br> Results obtained for all subjects are presented for the ATP cohort for Humoral immunogenicity/Humoral persistence

- Anti-gE humoral immune responses relative to pre-vaccination levels were observed in the HZ/su group at 1 month following the first and second dose and persisted up to 1 year post-dose 2 , relative to the pre-vaccination level.
- Pre-vaccination anti-gE Ab GMCs were 1049.8 ( $95 \% \mathrm{CI}$ : 865.8 - 1273.0) and 1116.7 ( $95 \%$ CI: $918.4-1358.0$ ) $\mathrm{mIU} / \mathrm{mL}$ respectively for $\mathrm{HZ} / \mathrm{su}$ and Placebo groups. Post-vaccination, anti-gE Ab GMCs at Months 1 (post first vaccination) and Month 2 (post second vaccination) were 24793.1 ( $95 \%$ CI: 18747.8 - 32787.6 ) and 18291.7 ( $95 \%$ CI: 14432.1 - 23183.5 ) $\mathrm{mIU} / \mathrm{mL}$ respectively for the HZ/su group. Anti-gE Ab GMC at Month 13 was 4477.3 ( $95 \%$ CI: $3482.4-5756.3$ ) $\mathrm{mIU} / \mathrm{mL}$ for the HZ/su group. The post-vaccination anti-gE Ab GMCs in the Placebo group remained near pre-vaccination level.
- VRRs in the HZ/su group at Month 1 (post first vaccination) and Month 2 (post second vaccination) were $85.9 \%$ ( $95 \% \mathrm{CI}$ : $76.6-92.5$ ) and $86.2 \%$ ( $95 \%$ CI: $77.1-92.7$ ) respectively, and at Month $13,51.5 \%$ ( $95 \% \mathrm{CI}: 39.0-63.8$ ). In the Placebo group, there were no subjects meeting the definition of responder at Months 1, 2 and 13.


## Results obtained for the PreChemo and OnChemo groups are presented for the ATP cohort for Humoral immunogenicity/Humoral persistence.

- Anti-gE humoral immune responses were observed in the HZ/su PreChemo and HZ/su OnChemo groups 1 month post first vaccination and 1 month post second vaccination. Persistence of humoral immunogenicity at 1 year post second vaccination was also observed in HZ/su subjects and appeared to be similar for PreChemo and OnChemo groups despite the different administration schedules of each group. Secondary to the small number of subjects included in the OnChemo group (per stratification factor at randomisation), results obtained for the OnChemo group need to be interpreted with caution.
- In the PreChemo group, pre-vaccination anti-gE Ab GMCs were 1032.3 (95\% CI: 821.0 1298.0) and 1185.4 ( $95 \% \mathrm{CI}$ : $959.3-1464.7$ ) $\mathrm{mIU} / \mathrm{mL}$ respectively for $\mathrm{HZ} / \mathrm{su}$ and Placebo groups. Post-vaccination, anti-gE Ab GMCs at Month 1 (post first vaccination) and Month 2 (post second vaccination) were 34729.8 ( $95 \%$ CI: $27485.9-43882.8$ ) and 22974.3 ( $95 \% \mathrm{CI}$ : $19080.0-27663.5$ ) $\mathrm{mIU} / \mathrm{mL}$ respectively, and at Month 13, 4563.0 ( $95 \% \mathrm{CI}: 3532.8$ - 5893.7 ) $\mathrm{mIU} / \mathrm{mL}$ for the HZ/su PreChemo group. The post-vaccination anti-gE Ab GMCs in the Placebo PreChemo group remained near pre-vaccination level.
- In the OnChemo group, pre-vaccination anti-gE Ab GMCs were 1103.4 (95\% CI: 753.4 1616.0) and 868.2 ( $95 \% \mathrm{CI}$ : $512.9-1469.7$ ) $\mathrm{mIU} / \mathrm{mL}$ respectively for $\mathrm{HZ} / \mathrm{su}$ and Placebo groups. Post-vaccination, anti-gE Ab GMCs at Months 1 (post first vaccination), and Month 2 (post second vaccination) were 8876.6 ( $95 \% \mathrm{CI}$ : $4134.3-19058.6$ ) and 9328.0 ( $95 \% \mathrm{CI}$ : 4492.5 - 19368.2) mIU/mL respectively, and at Month 13, 4229.5 ( $95 \% \mathrm{CI}$ : 2073.8 - 8626.0) $\mathrm{mIU} / \mathrm{mL}$ for the $\mathrm{HZ} / \mathrm{su}$ group. The post-vaccination anti-gE Ab GMCs in the Placebo OnChemo group remained near pre-vaccination level.
- In the PreChemo group, VRRs in the HZ/su group at Month 1 (post first vaccination) and Month 2 (post second vaccination) were $93.8 \%$ ( $95 \% \mathrm{CI}: 84.8-98.3$ ) and $93.8 \%$ ( $95 \% \mathrm{CI}$ : $85.0-98.3$ ) respectively, and at Month $13,52.9 \%$ ( $95 \%$ CI: $38.5-67.1$ ). In the Placebo group, there were no subjects meeting the definition of responder at any time point.
- In the OnChemo group, VRRs in the HZ/su group at Month 1 (post first vaccination) and Month 2 (post second vaccination) were $61.9 \%$ ( $95 \% \mathrm{CI}: 38.4-81.9$ ) and $63.6 \%(95 \% \mathrm{CI}$ :
- $40.7-82.8$ ) respectively, and at Month 13, $47.1 \%$ ( $95 \%$ CI: $23.0-72.2$ ). In the Placebo group, there were no subjects meeting the definition of responder at Month 1, 2 and 13.

| Name of company: <br> GlaxoSmithKline <br> Biologicals, SA, <br> Rixensart, Belgium | Name of finished product: | Name of active substance: <br> Varicella zoster virus <br> glycoprotein E (VZV gE) |
| :--- | :--- | :--- |
| CMI |  |  |

## CMI

Results obtained for the CMI sub-cohort are presented for the ATP cohort for CMI immunogenicity/ CMI persistence

- gE-specific CMI responses to HZ/su in the PreChemo group were above pre-vaccination levels 1 month after the first vaccination; stronger immune responses were observed 1 month after the second dose. Additionally, the persistence of gE-specific CMI at 1 year post-dose 2 in PreChemo $\mathrm{HZ} / \mathrm{su}$ subjects was observed. However secondary to the small number of subjects with evaluable CMI results, these results need to be interpreted with caution.
- In the HZ/su group, the observed median (min - max) frequency of gE-specific CD4[2+] T-cells (per $10^{6}$ total CD4+ T-cells) was 127.3 (1.0-662.4), 391.9 (1.0-3276.6) and 778.8 (1.0-4835.8) at Months 0 (pre-vaccination), 1 (post first vaccination) and 2 (post second vaccination) respectively, and $332.9(1.0-2416.0)$ at Month 13. In the Placebo group, the observed median frequency of gE-specific CD4[2+] T-cells (point estimate) was $104.8,50.0$ and 61.8 at Month 0,1 and 2 respectively, and 51.2 at Month 13.
- In the HZ/su group, the VRR in the frequency of gE-specific CD4[2+] T-cells was $20.0 \%$ ( $95 \%$ CI: $6.8-40.7$ ) and $50.0 \% ~(95 \%$ CI: $28.2-71.8$ ) at Month 1 and Month 2 and $17.6 \%$ ( $95 \%$ CI: $3.8-43.4$ ) at Month 13. In the Placebo group, there were no subjects meeting the definition of responder at any timepoint.

Analysis by age strata (18-49 years of age [YOA] and $\geq 50 \mathrm{YOA}$ ) in the PreChemo group (anti-gE humoral immunogenicity and gE-specific CMI); and in all subjects (anti-gE humoral immunogenicity).

Comparable immune responses for both age strata were observed 1 month post first and 1 month post second vaccination up to 1 year post dose 2 .

- Secondary to the small number of subjects included in the 18-49 YOA stratum (miminisation procedure applied at randomisation), results obtained for the 18-49 YOA stratum need to be interpreted with caution.


## Safety results:

The primary analysis for safety was based on the TVC.A descriptive summary of safety data obtained at end of study analysis for the TVC is provided in this section. No safety concern was identified.

## All subjects

Results obtained for all subjects with solid tumours receiving chemotherapy included in the TVC are presented. A total of $90.5 \%$ of subjects in the TVC received the second dose.

| Name of company: <br> GlaxoSmithKline <br> Biologicals, SA, <br> Rixensart, Belgium | Name of finished product: | Name of active substance: <br> Varicella zoster virus <br> glycoprotein E (VZV gE) |
| :--- | :--- | :--- |

## Solicited symptoms

A higher percentage of subjects reported solicited local and general AEs (any grade, grade 3) during the 7-day post-vaccination period in the HZ/su group compared to the Placebo group. In the HZ/su group, the most frequent solicited local symptom observed was pain; the most frequent solicited general symptom was fatigue, followed by myalgia. In the Placebo group, the percentage of subjects with general symptoms was also high. Of note, the HZ/su and placebo subjects in this study had an underlying disease and were to receive/ received chemotherapy. Note that the following data will be "overall per subject (dose 1 and dose considered)" unless otherwise indicated.

- Any AE during the 7-day (Days 0-6) post-vaccination period:
- At least one solicited or unsolicited AE (local or general) (any grade) was reported for $93.2 \%$ and $80.0 \%$ of subjects in the $\mathrm{HZ} / \mathrm{su}$ and Placebo group, respectively.

At least one local AE (solicited or unsolicited) was reported for $80.3 \%$ and $7.8 \%$ of subjects in the $\mathrm{HZ} /$ su and Placebo group, respectively. At least one general AE (solicited or unsolicited) was reported for $84.6 \%$ and $80.0 \%$ of subjects in the HZ/su and Placebo group, respectively.

- $\quad$ Solicited local symptoms during the 7-day (Days 0-6) post-vaccination period:
- At least one solicited local symptom was reported for $83.9 \%$ and $6.4 \%$ of subjects in the $\mathrm{HZ} / \mathrm{su}$ and Placebo group, respectively.

The most frequently reported solicited local symptom in the HZ/zu group was pain (any grade: $80.4 \%$ in the $\mathrm{HZ} /$ su group versus $6.4 \%$ in the Placebo group) (Synopsis Table 8).After dose 1 and dose 2, respectively, at least one solicited local symptom was reported for $78.6 \%$ and $57.1 \%$ of subjects in the $\mathrm{HZ} /$ su group, and for $2.7 \%$ and $4.8 \%$ of subjects in the Placebo group.

- At least one grade 3 solicited local symptom was reported for $11.6 \%$ and $0.0 \%$ of subjects in the HZ/su and Placebo group, respectively.

Grade 3 pain was reported for $9.8 \%$ and $0.0 \%$ of subjects in the $\mathrm{HZ} /$ su group and Placebo group, respectively (Synopsis Table 8).
After dose 1 and dose 2, respectively, at least one grade 3 solicited local symptom was reported for $8.9 \%$ and $4.1 \%$ of subjects in the $\mathrm{HZ} /$ su group, and for none of the subjects in the Placebo group.

- Solicited general symptoms during the 7-day (Days 0-6) post-vaccination period:
- At least one solicited general symptom was reported for $81.3 \%$ and $66.4 \%$ of subjects in the $\mathrm{HZ} /$ su and Placebo group, respectively.

The most frequently reported solicited general symptoms in the HZ/su group were fatigue (any grade: $69.6 \%$ in $\mathrm{HZ} /$ su group versus $61.8 \%$ in Placebo group) and myalgia (any grade, overall/subject: 53.6\% in HZ/su group versus $28.2 \%$ in Placebo group).

Fatigue assessed by the investigator as related to vaccination, was reported for $17.0 \%$ and $12.7 \%$ of subjects in the HZ/su group and Placebo group, respectively. Myalgia assessed by the investigator as related to vaccination was reported for $26.8 \%$ and $4.5 \%$ of subjects in the $\mathrm{HZ} /$ su group and the Placebo group, respectively (Synopsis Table 9).

| Name of company: <br> GlaxoSmithKline <br> Biologicals, SA, <br> Rixensart, Belgium | Name of finished product: | Name of active substance: <br> Varicella zoster virus <br> glycoprotein E (VZV gE) |
| :--- | :--- | :--- |

After dose 1 and dose 2, respectively, at least one solicited general symptom was reported for $71.4 \%$ and $69.1 \%$ of subjects in the HZ/su group, and for $47.3 \%$ and $57.7 \%$ of subjects in the Placebo group.

- At least one grade 3 solicited general symptom was reported for $22.3 \%$ and $15.5 \%$ of subjects in the HZ/su and Placebo group, respectively. Grade 3 fatigue was reported for $14.3 \%$ and $7.3 \%$ of subjects in the HZ/su group and Placebo group, respectively.

Grade 3 myalgia was reported for $10.7 \%$ and $3.6 \%$ of subjects in the HZ/su group and the Placebo group, respectively. Grade 3 fatigue assessed by the investigator as related to vaccination, was reported for $2.7 \%$ and $0.9 \%$ of subjects in the $\mathrm{HZ} /$ su group and Placebo group, respectively. Grade 3 myalgia assessed by the investigator as related to vaccination was reported for $6.3 \%$ and $0.0 \%$ of subjects in the HZ/su group and the Placebo group, respectively. It is noted that grade 3 shivering assessed by the investigator as related to vaccination was reported for $3.6 \%$ and $0.0 \%$ in the $\mathrm{HZ} / \mathrm{su}$ and Placebo group, respectively (Synopsis Table 9).
After dose 1 and dose 2, respectively, at least one grade 3 solicited general symptom was reported for $13.4 \%$ and $16.5 \%$ of subjects in the $\mathrm{HZ} /$ su group, and for $10.0 \%$ and $9.6 \%$ of subjects in the Placebo group.
Synopsis Table 8 Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-
vaccination period overall subjects and overall doses (Total Vaccinated Cohort)

|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 210 | 135 | 64.3 | 57.4 | 70.8 | 215 | 7 | 3.3 | 1.3 | 6.6 |
|  | Grade 3 | 210 | 12 | 5.7 | 3.0 | 9.8 | 215 | 0 | 0.0 | 0.0 | 1.7 |
| Redness (mm) | All | 210 | 53 | 25.2 | 19.5 | 31.7 | 215 | 0 | 0.0 | 0.0 | 1.7 |
|  | >100 | 210 | 2 | 1.0 | 0.1 | 3.4 | 215 | 0 | 0.0 | 0.0 | 1.7 |
| Swelling (mm) | All | 210 | 23 | 11.0 | 7.1 | 16.0 | 215 | 1 | 0.5 | 0.0 | 2.6 |
|  | >100 | 210 | 0 | 0.0 | 0.0 | 1.7 | 215 | 0 | 0.0 | 0.0 | 1.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 112 | 90 | 80.4 | 71.8 | 87.3 | 110 | 7 | 6.4 | 2.6 | $12 .$ |
|  | Grade 3 | 112 | 11 | 9.8 | 5.0 | 16.9 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Redness (mm) | All | 112 | 40 | 35.7 | 26.9 | 45.3 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >100 | 112 | 2 | 1.8 | 0.2 | 6.3 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Swelling (mm) | All | 112 | 18 | 16.1 | 9.8 | 24.2 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | >100 | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit

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| Name of company: <br> GlaxoSmithKline Biologicals, <br> SA, Rixensart, Belgium | Name of finished product: | Name of active <br> substance: <br> Varicella zoster virus <br> glycoprotein E (VZV <br> gE) |
| :--- | :--- | :--- |

Synopsis Table 9 Incidence of solicited general symptoms reported during the 7-day (Days 0-6) postvaccination period overall subjects and overall doses (Total Vaccinated Cohort)

|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 209 | 113 | 54.1 | 47.1 | 61.0 | 214 | 101 | 47.2 | 40.4 | 54.1 |
|  | Grade 3 | 209 | 19 | 9.1 | 5.6 | 13.8 | 214 | 9 | 4.2 | 1.9 | 7.8 |
|  | Related | 209 | 21 | 10.0 | 6.3 | 14.9 | 214 | 18 | 8.4 | 5.1 | 13.0 |
|  | Grade 3 Related | 209 | 3 | 1.4 | 0.3 | 4.1 | 214 | 1 | 0.5 | 0.0 | 2.6 |
| Gastrointestinal symptoms | All | 209 | 73 | 34.9 | 28.5 | 41.8 | 214 | 60 | 28.0 | 22.1 | 34.6 |
|  | Grade 3 | 209 | 7 | 3.3 | 1.4 | 6.8 | 214 | 8 | 3.7 | 1.6 | 7.2 |
|  | Related | 209 | 15 | 7.2 | 4.1 | 11.6 | 214 | 4 | 1.9 | 0.5 | 4.7 |
|  | Grade 3 Related | 209 | 1 | 0.5 | 0.0 | 2.6 | 214 | 1 | 0.5 | 0.0 | 2.6 |
| Headache | All | 209 | 57 | 27.3 | 21.4 | 33.8 | 214 | 49 | 22.9 | 17.4 | 29.1 |
|  | Grade 3 | 209 | 6 | 2.9 | 1.1 | 6.1 | 214 | 3 | 1.4 | 0.3 | 4.0 |
|  | Related | 209 | 17 | 8.1 | 4.8 | 12.7 | 214 | 6 | 2.8 | 1.0 | 6.0 |
|  | Grade 3 Related | 209 | 2 | 1.0 | 0.1 | 3.4 | 214 | 0 | 0.0 | 0.0 | 1.7 |
| Myalgia | All | 209 | 82 | 39.2 | 32.6 | 46.2 | 214 | 40 | 18.7 | 13.7 | 24.6 |
|  | Grade 3 | 209 | 12 | 5.7 | 3.0 | 9.8 | 214 | 4 | 1.9 | 0.5 | 4.7 |
|  | Related | 209 | 38 | 18.2 | 13.2 | 24.1 | 214 | 7 | 3.3 | 1.3 | 6.6 |
|  | Grade 3 Related | 209 | 7 | 3.3 | 1.4 | 6.8 | 214 | 0 | 0.0 | 0.0 | 1.7 |
| Shivering | All | 209 | 47 | 22.5 | 17.0 | 28.8 | 214 | 30 | 14.0 | 9.7 | 19.4 |
|  | Grade 3 | 209 | 8 | 3.8 | 1.7 | 7.4 | 214 | 3 | 1.4 | 0.3 | 4.0 |
|  | Related | 209 | 18 | 8.6 | 5.2 | 13.3 | 214 | 8 | 3.7 | 1.6 | 7.2 |
|  | Grade 3 Related | 209 | 5 | 2.4 | 0.8 | 5.5 | 214 | 0 | 0.0 | 0.0 | 1.7 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 209 | 21 | 10.0 | 6.3 | 14.9 | 214 | 5 | 2.3 | 0.8 | 5.4 |
|  | >39.0 | 209 | 0 | 0.0 | 0.0 | 1.7 | 214 | 0 | 0.0 | 0.0 | 1.7 |
|  | Related | 209 | 15 | 7.2 | 4.1 | 11.6 | 214 | 1 | 0.5 | 0.0 | 2.6 |
|  | >39.0 Related | 209 | 0 | 0.0 | 0.0 | 1.7 | 214 | 0 | 0.0 | 0.0 | 1.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 112 | 78 | 69.6 | 60.2 | 78.0 | 110 | 68 | 61.8 | 52.1 | 70.9 |
|  | Grade 3 | 112 | 16 | 14.3 | 8.4 | 22.2 | 110 | 8 | 7.3 | 3.2 | 13.8 |
|  | Related | 112 | 19 | 17.0 | 10.5 | 25.2 | 110 | 14 | 12.7 | 7.1 | 20.4 |
|  | Grade 3 Related | 112 | 3 | 2.7 | 0.6 | 7.6 | 110 | 1 | 0.9 | 0.0 | 5.0 |
| Gastrointestinal symptoms | All | 112 | 51 | 45.5 | 36.1 | 55.2 | 110 | 49 | 44.5 | 35.1 | 54.3 |
|  | Grade 3 | 112 | 6 | 5.4 | 2.0 | 11.3 | 110 | 7 | 6.4 | 2.6 | 12.7 |
|  | Related | 112 | 11 | 9.8 | 5.0 | 16.9 | 110 | 3 | 2.7 | 0.6 | 7.8 |
|  | Grade 3 Related | 112 | 1 | 0.9 | 0.0 | 4.9 | 110 | 1 | 0.9 | 0.0 | 5.0 |
| Headache | All | 112 | 43 | 38.4 | 29.4 | 48.1 | 110 | 40 | 36.4 | 27.4 | 46.1 |
|  | Grade 3 | 112 | 6 | 5.4 | 2.0 | 11.3 | 110 | 3 | 2.7 | 0.6 | 7.8 |
|  | Related | 112 | 16 | 14.3 | 8.4 | 22.2 | 110 | 6 | 5.5 | 2.0 | 11.5 |
|  | Grade 3 Related | 112 | 2 | 1.8 | 0.2 | 6.3 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Myalgia | All | 112 | 60 | 53.6 | 43.9 | 63.0 | 110 | 31 | 28.2 | 20.0 | 37.6 |
|  | Grade 3 | 112 | 12 | 10.7 | 5.7 | 18.0 | 110 | 4 | 3.6 | 1.0 | 9.0 |
|  | Related | 112 | 30 | 26.8 | 18.9 | 36.0 | 110 | 5 | 4.5 | 1.5 | 10.3 |
|  | Grade 3 Related | 112 | 7 | 6.3 | 2.5 | 12.5 | 110 | 0 | 0.0 | 0.0 | 3.3 |



| Name of company: <br> GlaxoSmithKline <br> Biologicals, SA, <br> Rixensart, Belgium | Name of finished product: | Name of active substance: <br> Varicella zoster virus <br> glycoprotein E (VZV gE) |
| :--- | :--- | :--- |

## Unsolicited AEs

Numbers and percentages of subjects with unsolicited AEs were overall balanced between HZ/su and Placebo groups.

- Unsolicited AEs during the 30-day (Days 0-29) post-vaccination period:
- Overall, 100 ( $85.5 \%$ ) subjects in the HZ/su group and 103 (89.6\%) subjects in the Placebo group reported at least one unsolicited AE. Overall per subject, the most frequent unsolicited AEs within 30 days post vaccination were nausea ( 31 subjects or $26.5 \%$ ) and asthenia ( 30 subjects or $25.6 \%$ ) for the $\mathrm{HZ} /$ su group, and also nausea and asthenia (both at 28 subjects or $24.3 \%$ ) for the Placebo group.
- Overall, $18(15.4 \%)$ subjects in the HZ/su group and 15 ( $13.0 \%$ ) subjects in the Placebo group reported at least one grade 3 unsolicited AE. Overall per subject, the most frequent grade 3 unsolicited AEs within 30 days post vaccination were febrile neutropenia ( 4 subjects or $3.4 \%$ ) and neutropenia ( 3 subjects or $2.6 \%$ ) for the HZ/su group, and neutropenia ( 3 subjects or $2.6 \%$ ), febrile neutropenia ( 2 subjects or $1.7 \%$ ) and acute kidney injury ( 2 subjects or $1.7 \%$ ) for the Placebo group.
- Overall, $10(8.5 \%)$ subjects in the HZ/su group and 9 (7.8\%) subjects in the Placebo group reported at least one unsolicited AE with causal relationship to vaccination as per investigator assessment.
- Overall, there was 1 subject ( $0.9 \%$ ) in the HZ/su group with at least one grade 3 unsolicited AE with causal relationship to vaccination as per investigator assessment; the unsolicited AE reported was gastroenteritis. There were no subjects in the Placebo group with at least one grade 3 unsolicited AE with causal relationship to vaccination as per investigator assessment.
- Overall, 31 (26.5\%) subjects in the HZ/su group and 33 (28.7\%) subjects in the Placebo group reported at least one unsolicited AE with medically attended visit.


## SAEs, (S)AEs leading to withdrawal, pIMDs

Numbers and percentages of subjects with fatalities, SAEs, (S)AEs leading to withdrawal from study and pIMDs were overall balanced between $\mathrm{HZ} /$ su and Placebo group.

- SAEs:
- From the first vaccination up to study end, the number (\%) of subjects with fatal outcome reported was $12(10.3 \%)$ in the HZ/su group and $11(9.6 \%)$ in the Placebo group. None of the fatalities were considered causally related to vaccination as per investigator assessment.
- From the first vaccination up to 30 days post last vaccination, the number (\%) of subjects with at least one SAE reported was $16(13.7 \%)$ in the $\mathrm{HZ} /$ su group and $14(12.2 \%)$ in the Placebo group. From 30 days post last vaccination up to study end, the number (\%) of subjects with at least one SAE reported was $30(25.6 \%)$ in the HZ/su group and $31(27.0 \%)$ in the Placebo group. From first vaccination up to study end, the number (\%) of subjects with at least one SAE reported was $36(30.8 \%)$ in the HZ/su group and $42(36.5 \%)$ in the Placebo group. During the study, no subjects were reported with SAEs with causal relationship to vaccination as per investigator assessment.
- SAEs, AEs leading to withdrawal:
- Up to the Month 2 visit (Visit 3), 3 subjects in the HZ/su group and 2 subjects in the Placebo group were withdrawn from the study due to an SAE, no subjects were withdrawn from the study due to a non-serious AE.

| Name of company: <br> GlaxoSmithKline Biologicals, <br> SA, Rixensart, Belgium | Name of finished product: | Name of active <br> substance: <br> Varicella zoster virus <br> glycoprotein E (VZV <br> gE) |
| :--- | :--- | :--- |

- Up to study end, 13 subjects in the HZ/su group and 12 subjects in the Placebo group were withdrawn from the study due to an SAE, of which 12 and 11 subjects respectively were withdrawn due to fatalities. No subjects were withdrawn from the study due to a non-serious AE.
- pIMDs:
- From first vaccination up to 30 days post last vaccination, no subjects with pIMDs were reported.
- From 30 days post last vaccination up to study end, and from first vaccination up to study end, there was 1 pIMD (autoimmune thyroiditis), considered as serious per investigator assessment, in a subject from the Placebo group..


## Pregnancies:

- No pregnancies were reported.


## Subjects in the PreChemo and OnChemo groups

Results were obtained for subjects included in the PreChemo and OnChemo groups, respectively. It is noted that the results obtained for the OnChemo group represent data from a relatively small number of subjects compared to the PreChemo group (according to the stratification ratio PreChemo/OnChemo 4:1).

## Solicited symptoms

Results regarding solicited local symptoms (any grade, grade 3) reported during the 7-day (Days 0-6) post-vaccination period in the PreChemo and OnChemo groups were generally consistent with the results obtained for all subjects.

Results regarding solicited general symptoms (any grade, grade 3) in the PreChemo and OnChemo groups were generally consistent with the results obtained for all subjects.

## Unsolicited AEs

Results regarding unsolicited AEs reported during the 30-day (Days 0-29) post-vaccination period in the PreChemo and OnChemo groups were generally consistent with the results obtained for all subjects.

## SAEs, (S)AEs leading to withdrawal, pIMDs

Results regarding SAEs and (S)AEs leading to withdrawal in the PreChemo and OnChemo groups reported during the study were generally consistent with the results obtained for all subjects. One pIMD, assessed as serious by investigator, occurred in a Placebo OnChemo subject.

## Subjects in the 18-49 YOA and $\geq \mathbf{5 0}$ YOA strata

Results were obtained for subjects included in the $18-49 \mathrm{YOA}$ and $\geq 50 \mathrm{YOA}$ strata, respectively. It is noted that the results obtained for the 18-49 YOA stratum represent data from a relatively small number of subjects compared to the $\geq 50 \mathrm{YOA}$ stratum.

## Solicited symptoms

Results regarding solicited local symptoms (any grade, grade 3) reported during the 7-day (Days 0-6) post-vaccination period in the $18-49 \mathrm{YOA}$ and $\geq 50 \mathrm{YOA}$ strata were generally consistent with results obtained for all subjects.

Results regarding solicited general symptoms (any grade, grade 3 ) in the $18-49 \mathrm{YOA}$ and $\geq 50 \mathrm{YOA}$ strata were generally consistent with results obtained for all subjects.

| Name of company: <br> GlaxoSmithKline Biologicals, <br> SA, Rixensart, Belgium | Name of finished product: | Name of active <br> substance: <br> Varicella zoster virus <br> glycoprotein E (VZV <br> gE) |
| :--- | :--- | :--- |
| Hnsolicited $A E s$ |  | su |

Results regarding unsolicited AEs reported during the 30-day (Days 0-29) post-vaccination period in the 18-49 YOA and $\geq 50$ YOA strata were generally consistent with results obtained for all subjects.

SAEs, (S)AEs leading to withdrawal, pIMDs
Results regarding SAEs and (S)AEs leading to withdrawal in the $18-49$ YOA and $\geq 50$ YOA strata reported during the study were generally consistent with results obtained for all subjects. One pIMD, assessed as serious by investigator, occurred in a Placebo OnChemo subject in the $\geq 50 \mathrm{YOA}$ stratum.

## Important safety information received after the data lock point (database freeze date):

No relevant additional safety information was available after the data lock point.

## Conclusion:

This study in subjects with solid tumours receiving/to receive chemotherapy evaluated the HZ/su vaccine in terms of immunogenicity and safety.

## Immunogenicity

The focus of the study was to examine the immunological response to $\mathrm{HZ} /$ su given in different immunisation schedules to subjects receiving/to receive chemotherapy which would compromise their immune systems. The confirmatory immunogenicity objectives were assessed sequentially in order of ascending rank until an objective was not met. The confirmatory objectives were assessed at the first analysis step. The active phase results on CMI were different at end of study analysis compared to first analysis. Even so, there was no impact on study conclusions.

- The confirmatory primary objective of the study was met as the lower limit of the $95 \% \mathrm{CI}$ of the GM ratio (HZ/su PreChemo Group over Placebo PreChemo group) in anti-gE Ab concentrations at Month 2 (post second vaccination) was 3. Therefore the success criterion (greater than 3) was demonstrated. The adjusted GM ratio was 23.2 ( $95 \% \mathrm{CI}: 17.9-30.0$; $\mathrm{P}<0.0001$ ).
- The first confirmatory secondary objective of the study was met as the lower limit of the $95 \%$ CI of the VRR for anti-gE Ab concentrations in the HZ/su PreChemo group at Month 2 (post second vaccination) was $85.0 \%$. Therefore the success criterion (at least $60 \%$ ) was demonstrated. The VRR was $93.8 \%$ ( $95 \%$ CI: $85.0-98.3$ ).
- The second confirmatory secondary objective of the study was met as the lower limit of the $95 \%$ CI of the GM ratio (HZ/su PreChemo group over Placebo PreChemo group) in gE-specific CD4[2+] T-cell frequencies at Month 2 (post second vaccination) was 3.79. Therefore the success criterion (greater than 1) was demonstrated. The observed GM ratio was 13.67 ( $95 \%$ CI: $3.79-49.38$; $\mathrm{P}=0.0002$ ).

| Name of company: <br> GlaxoSmithKline Biologicals, <br> SA, Rixensart, Belgium | Name of finished product: | Name of active <br> substance: <br> Varicella zoster virus <br> glycoprotein E (VZV <br> gE) |
| :--- | :--- | :--- |

Descriptive results obtained with the end of study analysis: the observed GM ratio at Month 2 was 9.94 ( $95 \%$ CI: 3.63 - 27.19).

- The third confirmatory secondary objective of the study was not met as the lower limit of the $95 \%$ CI of the VRR for gE-specific CD4[2+] T-cell frequencies in the HZ/su PreChemo group (33.5\%) at Month 2 (post second vaccination) was $33.5 \%$. Therefore the success criterion (at least $50 \%$ ) was not demonstrated. The observed VRR was 57.9\% (95\% CI: 33.5 - 79.7).
Descriptive results obtained with the end of study analysis: the observed VRR at Month 2 was $50.0 \%$ ( $95 \%$ CI: 28.2 - 71.8).

Results from descriptive analyses showed in HZ/su subjects (overall, and in the PreChemo and OnChemo groups) humoral immune responses 1 month post first vaccination and 1 month post second vaccination. Persistence of 12 month post second vaccination humoral response was also observed.

Results from descriptive analyses in the PreChemo group showed that CMI responses to HZ/su were above the pre-vaccination level 1 month post first vaccination; a stronger immune response was observed 1 month post second vaccination. Additionally, the persistence of gE-specific CMI at 1 year post second vaccination in PreChemo HZ/su subjects was observed.

## Safety

Results from descriptive analyses did not reveal a safety concern.
In subjects with solid tumours receiving chemotherapy, a higher percentage of subjects reported solicited local and general AEs (any grade, grade 3) during the 7 -day post-vaccination period in the HZ/su group compared to the Placebo group. In the Placebo group, the percentage of subjects with solicited general symptoms was also high. Numbers and percentages of subjects with unsolicited AEs reported during the 30-day post-vaccination period and numbers and percentages of subjects with respectively fatalities, SAEs and (S)AEs leading to study withdrawal reported during the study were generally well balanced between HZ/su and Placebo group. During the study, no subjects were reported with SAEs with causal relationship to vaccination as per investigator assessment. There was 1 pIMD , considered as serious per investigator assessment, in a subject from the Placebo group..

Reactogenicity and safety results obtained for the Prechemo and OnChemo groups and for the 18-49 YOA and $\geq 50$ YOA strata were generally consistent with the overall results for all subjects in this study.

Date of report: Final: 03-May-2017.

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## LIST OF ABBREVIATIONS

| Ab: | Antibody |
| :---: | :---: |
| AE: | Adverse Event |
| AS01 $_{\text {B }}$ : | MPL, QS21, liposome based Adjuvant System [50 $\mu \mathrm{g}$ MPL and $50 \mu \mathrm{~g}$ QS21] |
| ATP: | According-To-Protocol |
| CD40 L: | CD40 Ligand |
| CDC: | Centres for Disease Control |
| CDP: | Clinical Development Plan |
| CDQA: | Clinical Development Quality Assurance |
| CEPL: | Clinical and Epidemiology Project Leader |
| CI: | Confidence Interval |
| CLS: | Clinical Laboratory Sciences |
| CMI: | Cell-Mediated Immunity |
| CRDL: | Clinical Research and Development Leader |
| CSR: | Clinical Study Report |
| DNA: | Deoxyribonucleic Acid |
| ECOG: | Eastern Cooperative Oncology Group |
| eCRF: | electronic Case Report Form |
| ELISA: | Enzyme-Linked Immunosorbent Assay |
| FDA: | Food and Drug Administration, United States of America |
| GCP: | Good Clinical Practice |
| gE: | Glycoprotein E |
| GM: | Geometric Mean |
| GMC: | Geometric Mean Concentration |
| GQC: | Global Quality Compliance |


| GSK: | GlaxoSmithKline |
| :---: | :---: |
| GVCL: | Global Vaccines Clinical Laboratories |
| HCG: | Human Chorionic Gonadotropin |
| HCT: | Haematopoietic stem Cell Transplant |
| HIV: | Human Immunodeficiency Virus |
| HZ: | Herpes Zoster |
| HZ/su: | Herpes Zoster subunit vaccine [gE[50 ug]/AS01 ${ }_{\mathrm{B}}$ ] |
| IC: | immunocompromised |
| ICF: | Informed Consent Form |
| ICH: | International Conference on Harmonisation |
| ICS: | Intracellular Cytokine Staining |
| IEC: | Independent Ethics Committee |
| IFN- $\gamma$ : | Interferon Gamma |
| IgG: | Immunoglobulin class G |
| IL-2: | Interleukin-2 |
| IM: | Intramuscular |
| IND: | Investigational New Drug |
| IRB: | Institutional Review Board |
| iSRC: | internal Safety Review Committee |
| $\log 10:$ | Decimal Logarithm |
| MAR: | Missing At Random |
| MCAR: | Missing Completely at Random |
| MedDRA: | Medical Dictionary for Regulatory Activities |
| Mg: | Milligram |
| MGI: | Mean Geometric Increase |


| Min: | Minimum |
| :---: | :---: |
| Max: | Maximum |
| mIU: | Milli-International Unit |
| mL: | Millilitre |
| MPL: | 3-O-desacyl-4'-Monophosphoryl Lipid A |
| $\mu \mathrm{g}:$ | Microgram |
| NaCl : | Sodium Chloride |
| PBMC: | Peripheral Blood Mononuclear Cells |
| PCR: | Polymerase Chain Reaction |
| PHN: | Postherpetic Neuralgia |
| pIMD: | Potential Immune-Mediated Disease |
| QS21: | Quillaja saponaria Molina, fraction 21 (purified saponin extract from the South American tree) |
| SAE: | Serious Adverse Event |
| SAS: | Statistical Analysis Software |
| SBIR: | Randomisation System on Internet |
| SD: | Standard Deviation |
| SOP: | Standard Operating Procedure |
| TNF- $\alpha$ : | Tumour Necrosis Factor Alpha |
| TVC: | Total Vaccinated Cohort |
| US: | United States (of America) |
| VRR: | Vaccine Response Rate |
| VZV: | Varicella Zoster Virus |
| YOA: | Years of Age |

## GLOSSARY OF TERMS

Adapted ATP cohort for Humoral immunogenicity / Adapted ATP cohort for CMI immunogenicity

## Adequate contraception:

'Adapted ATP* cohort for Humoral immunogenicity’ and 'Adapted ATP cohort for CMI**immunogenicity' was used to denote that for each phase, the corresponding ATP cohort was used.

More specifically,

- The analyses on the active phase timepoints Months 0,1 and 2 were based on the ATP cohort for Humoral immunogenicity/ CMI immunogenicity;
- The analyses on the persistence timepoints Months 6 (for Humoral immunogenicity only) and 13 were based on the ATP cohort for Humoral persistence/ CMI persistence.
* ATP: According-To-Protocol
** CMI: Cell-mediated Immunogenicity
Adequate contraception was defined as a contraceptive method with failure rate of less than $1 \%$ per year when used consistently and correctly and when applicable, in accordance with the product label for example:
- abstinence from penile-vaginal intercourse, when this was their preferred and usual lifestyle,
- oral contraceptives, either combined or progestogen alone,
- injectable progestogen,
- implants of etenogestrel or levonorgestrel,
- estrogenic vaginal ring,
- percutaneous contraceptive patches,
- intrauterine device or intrauterine system,
- male partner sterilisation prior to the female subject's entry into the study, and this male was the sole partner for that subject,

The information on the male sterility could come from the site personnel's review of the subject's medical records; or interview with the subject on her medical history.

- male condom combined with a vaginal spermicide (foam, gel, film, cream or suppository),
- male condom combined with a female diaphragm, either
with or without a vaginal spermicide (foam, gel, film, cream, or suppository).

Adequate contraception did not apply to subjects of child bearing potential with same sex partners, when this was their preferred and usual lifestyle.
$\left.\begin{array}{ll}\text { Adverse event: } & \begin{array}{l}\text { Any untoward medical occurrence in a patient or clinical } \\ \text { investigation subject, temporally associated with the use of a } \\ \text { medicinal product, whether or not considered related to the } \\ \text { medicinal product. }\end{array} \\ & \text { An adverse event (AE) could therefore be any unfavourable } \\ \text { and unintended sign (including an abnormal laboratory } \\ \text { finding), symptom, or disease (new or exacerbated) } \\ \text { temporally associated with the use of a medicinal product. } \\ & \text { For marketed medicinal products, this also included failure } \\ \text { to produce expected benefits (i.e., lack of efficacy), abuse or } \\ \text { misuse. } \\ \text { Blinding: } & \begin{array}{l}\text { A procedure in which one or more parties to the trial were } \\ \text { kept unaware of the treatment assignment in order to reduce }\end{array} \\ \text { the risk of biased study outcomes. The level of blinding was } \\ \text { maintained throughout the conduct of the trial, and only } \\ \text { when the data were cleaned to an acceptable level of quality }\end{array}\right\}$
$\left.\begin{array}{ll}\begin{array}{l}\text { ECOG performance } \\ \text { status: }\end{array} & \begin{array}{l}\text { A scale used by doctors and researchers to assess how a } \\ \text { patient's disease is progressing, assess how the disease } \\ \text { affects the daily living abilities of the patient and determines } \\ \text { appropriate treatment and prognosis. }\end{array} \\ \text { Eligible: } & \begin{array}{l}\text { Qualified for enrolment into the study based upon strict } \\ \text { adherence to inclusion/exclusion criteria. }\end{array} \\ \text { Epoch: } & \begin{array}{l}\text { An epoch was a self-contained set of consecutive timepoints } \\ \text { or a single timepoint from a single protocol. Self-contained } \\ \text { meant that data collected for all subjects at all timepoints }\end{array} \\ \text { eTrack: } & \begin{array}{l}\text { within that epoch allowed to draw a complete conclusion to } \\ \text { define or precise the targeted label of the product. }\end{array} \\ \text { Evaluable: } & \begin{array}{l}\text { GSK's tracking tool for clinical trials. }\end{array} \\ \text { Immunological } & \begin{array}{l}\text { Meeting all eligibility criteria, complying with the } \\ \text { procedures defined in the protocol, and, therefore, included } \\ \text { in the according-to-protocol (ATP) analysis. }\end{array} \\ \text { correlate of } & \begin{array}{l}\text { The defined immune response above which there is a high } \\ \text { protection: }\end{array} \\ \text { likelihood of protection in the absence of any host factors } \\ \text { that might increase susceptibility to the infectious agent. }\end{array}\right\}$
OnChemo:
Potential Immune-
Mediated Disease:

Primary completion date:

PreChemo: Mediated Disease:

OnChemo refers to the administration of first dose of HZ/su vaccine or placebo simultaneous with a chemotherapeutic cycle (+/-1day), i.e. vaccination is 'on' top of the next chemotherapeutic cycle.

Potential immune-mediated diseases (pIMDs) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology.

PreChemo refers to the administration of first dose of HZ/su vaccine or placebo at least 10 days* prior to a chemotherapeutic cycle, i.e. vaccination is 'pre' the next chemotherapeutic cycle.

* At least 8 days were allowed for analysis purposes

The date that the final subject was examined or received an intervention for the purpose of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated.

Protocol amendment: The International Conference on Harmonisation (ICH) defines a protocol amendment as: 'A written description of a change(s) to or formal clarification of a protocol.' GSK Biologicals further details this to include a change to an approved protocol that affects the safety of subjects, scope of the investigation, study design, or scientific integrity of the study.

Randomisation: Process of random attribution of treatment to subjects in order to reduce bias of selection.

## Self-contained study:

Solicited adverse event:

Sub-cohort:

## Subject:

Study with objectives not linked to the data of another study.
AEs to be recorded as endpoints in the clinical study. The presence/occurrence/intensity of these events was actively solicited from the subject or an observer during a specified post-vaccination follow-up period.

A group of subjects for whom specific study procedures were planned as compared to other subjects.

Term used to denote an individual who had been contacted in order to participate or participates in the clinical study, either as a recipient of the vaccine(s)/product(s) or as a control.

| Subject number: | A unique number identifying a subject, assigned to each <br> subject consenting to participate in the study. |
| :--- | :--- |
| Treatment: | Term used throughout the clinical study to denote a set of <br> investigational product(s) or marketed product(s) or placeb <br> intended to be administered to a subject, identified by a <br> unique number, according to the study randomisation or <br> treatment allocation. |
| Treatment number: | A number identifying a treatment to a subject, according to <br> the study randomisation or treatment allocation. |
| Unsolicited adverse | Any AE reported in addition to those solicited during the <br> clinical study. Also any 'solicited' symptom with onset <br> eutside the specified period of follow-up for solicited <br> symptoms was to be reported as an unsolicited AE. |

## TRADEMARKS

The following trademark is used in the present report.
Note: In the body of the Study Report, the names of the vaccines/products and/or medications will be written without the superscript symbol ${ }^{\mathrm{TM}}$ or $\circledR^{\circledR}$ and in italics.

| Trademarks not owned by the <br> GlaxoSmithKline group of companies |
| :---: |
| Zostavax ${ }^{\text {TM }}$ (Merck \& Co., Inc.) |


| Generic description |
| :--- |
| Herpes zoster vaccine consisting of high- <br> titre live attenuated varicella-zoster virus <br> (Oka strain) |

## 1. ETHICS

### 1.1. Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

The study protocol, any amendments, the informed consent, and other information that required pre-approval were reviewed and approved by a national, regional, or investigational centre IEC or IRB.

### 1.2. Ethical conduct of the study

Overall this study was conducted in accordance with ethical principles that have their origins in the Declaration of Helsinki, the principles of "good clinical practice" (GCP) and all applicable regulatory requirements.

During the course of the study, whenever potential issues with regard to the conduct of the study were identified, either via site monitoring activities or brought to GlaxoSmithKline (GSK) Biologicals' attention by other active oversight mechanisms, these issues were thoroughly investigated and appropriate corrective actions and, where possible, preventive actions were taken (see Section 5.10).

### 1.3. Subject information and consent

Written informed consent was to be obtained from each subject prior to the performance of any study-specific procedures. If a separate Pre-vaccination visit occurred, informed consent was reconfirmed at Visit 1, if needed per local requirements (see Table 4).

Refer to Section 6.3.2 for information regarding deviations noted in the informed consent process for individual subjects.

## 2. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

This multicentre study, sponsored by GSK Biologicals, was conducted in 6 countries: Canada, Czech Republic, France, Republic of Korea, Spain and United Kingdom. There were 29 sites recruiting subjects.

The following Principal Investigator reviewed the Clinical Study Report (CSR): Dr. Ignacio Delgado Mingorance, H Infanta Cristina, Badajoz, Spain.

GSK Biologicals sponsored the study and was responsible for coordinating activities for manufacturing of the Herpes Zoster subunit vaccine (HZ/su), initiating and conducting the study, including clinical trial supply management, monitoring, randomisation, data management and statistical analyses.

Per GSK process, blinded review of safety data was performed by the safety review team (SRT).

Additonal safety reviews were performed by an internal safety review committee (iSRC). This iSRC included as core members a GSK Biologicals' Safety Physician, a Clinical Research \& Development Lead and a Biostatistician, that were not otherwise involved in the conduct of the project, to maintain the observer-blind amongst project-related personnel. During the enrolment and the vaccination phase, the iSRC reviewed the unblinded safety data and assessed any potential findings that could have had an impact on the safety of the subjects. The main target of the reviews was to be able to stop the recruitment in case of an unexpected safety issue. Operational details for iSRC were provided in the iSRC Charter, Version 1, 18 March 2013, on file at GSK Biologicals.

GSK Biologicals Global Vaccines Clinical Laboratories (GVCL) [Clinical Laboratory Sciences (CLS)], Rixensart, Belgium performed humoral immunogenicity testing.

The Contract Reseach Organisation (CRO), Center for Vaccinology (CEVAC), Ghent University, Gent, Belgium, performed Cell-Mediated Immunity (CMI) testing.

The CROs 4Clinics, Waterloo, Belgium, and S-Clinica, Brussels, Belgium, were involved in statistical analyses by an independent statistician for iSRC reviews, and in the statistical analyses for the first analysis and end of study analysis step.

Study monitoring at the country level, and management of the country monitoring study file were performed by local CROs and/or by GSK Local Operating Companies (GSK LOCs).

## 3. INTRODUCTION

Varicella-Zoster Virus (VZV) causes two distinct diseases. Varicella (chickenpox) occurs shortly after primary VZV infection and is characterized by systemic illness and a widely disseminated rash. Herpes Zoster (shingles) occurs when VZV reactivates from latency and typically manifests as a localised, dermatomal rash.

The typical HZ rash usually lasts 2 to 4 weeks and is usually accompanied by pain that is often described as burning, shooting, or stabbing. In some patients, even touching the affected area lightly may cause pain, a phenomenon known as allodynia. This HZassociated pain may be severe, and pruritus, which can also be severe, may be as common as pain.

Although age is the most common risk factor for developing HZ, an increased incidence of HZ is also associated with immune suppression caused by haematologic malignancies (such as lymphoma), certain solid tumours, iatrogenic immunosuppression, human immunodeficiency virus (HIV) infection and some autoimmune diseases [Rusthoven, 1988; Feller, 2007; Kim, 2008; Rogers, 2011; Hata, 2011]. In a retrospective cohort study of over 55,000 hospital patients using Cox proportional hazards models, it was found that patients with diseases such as brain, breast, oesophageal, gastric, colorectal or gynecologic cancers, and malignant lymphoma displayed a 1.8-8.4-fold increased risk of

HZ events, compared to patients in this cohort with none of these diseases [Hata, 2011]. Notable in this study is that these patients at increased risk of HZ were not compared to healthy individuals but instead emerged through the analysis of patients with other underlying diseases within this hospitalized cohort. The increase in HZ within these populations is likely due to their immunocompromised (IC) state and indicates that there is a medical need to vaccinate these patients to reduce the morbidity associated with HZ . The increased cumulative incidence rate of HZ following diagnosis of malignant neoplasm, relative to the general population, is in part attributed to impaired immunity due to chemotherapy and radiotherapy [Rusthoven, 1988]. Patients with solid tumours receiving chemotherapy are at increased risk of HZ on the basis of debility and malnutrition and may also be at high HZ risk due to immunosuppressive therapy for their underlying disease [Tong, 2007; Gopalan, 2012].

A live attenuated VZV vaccine, Zostavax (Merck \& Co, Inc), is licensed in the United States (US), the European Union and elsewhere to prevent HZ in people $\geq 50$ years of age (YOA) [Zostavax Prescribing Information, 2016; Zostavax, Summary of Product Characteristics, 2016]. This vaccine, however, is contraindicated in immunosuppressed or immunodeficient individuals [Kroger, 2011]. There is currently no licensed vaccine for the prevention of HZ in IC populations.

GSK Biologicals' candidate vaccine for the prevention of HZ is a recombinant subunit (su) vaccine consisting of the VZV glycoprotein E (gE) antigen and an Adjuvant System ( $\mathrm{AS} 01_{\mathrm{B}}$ ). It has been evaluated in several studies in adults $\geq 50 \mathrm{YOA}$ and was shown to elicit strong cellular and humoral immune responses. The safety and reactogenicity profile of this candidate vaccine was also acceptable. Based on phase II data from the antigen dose-ranging study, ZOSTER-003 [Chlibek, 2014], and the adjuvant dose comparison study, ZOSTER-010 [Chlibek, 2013], a gE antigen dose of $50 \mu \mathrm{~g}$ and the Adjuvant System AS01 b were selected as the final vaccine formulation. Henceforth, the final vaccine formulation of GSK Biologicals' candidate HZ vaccine was referred to as HZ/su.

In one arm of the clinical development plan (CDP), the vaccine is being studied in subjects $\geq 50$ YOA. Within this older subject development arm, the results of two large Phase III safety and efficacy studies, which started recruitment in 2010, became available and were reported while ZOSTER-028 study was under conduct. Results from one of these studies (ZOSTER-006/ZOE-50) have shown that the HZ/su vaccine significantly reduced the risk of HZ in subjects $\geq 50 \mathrm{YOA}$ with high efficacy that was consistent across the ages studied [Lal, 2015]. Results of the other large study in adults aged $\geq 70 \mathrm{YOA}$ (ZOSTER-022/ZOE-70), confirmed these high efficacy results, and pooled results over both studies additionally showed a significant reduction in the risk of postherpetic neuralgia (PHN) in subjects $\geq 70$ YOA [Cunningham, 2016]. In both studies HZ/su had an acceptable safety profile in these populations.

In the other arm of the CDP, $\mathrm{HZ} / \mathrm{su}$ is evaluated for the prevention of HZ and related complications in adults with selected immunocompromising conditions, such as Haematopoietic stem Cell Transplant (HCT) recipients, HIV-infected individuals, solid organ transplants recipients, malignant haematologic patients and solid tumours patients.

ZOSTER-028 study was designed to specifically study HZ/su in patients with solid tumours receiving/who will receive chemotherapy.

As part of the immunocompromised populations CDP, an initial phase I/IIa study, ZOSTER-001, was conducted to evaluate the safety and immunogenicity of HZ/su in autologous HCT recipients $\geq 18 \mathrm{YOA}$ [Stadtmauer, 2014]. The primary endpoint data from this study showed that gE-specific CMI responses to HZ/su administered on schedules of 0,1 and 3 months, or 1 and 3 months (with Month 0 defined as 50-70 days following autologous HCT), were significantly higher than in placebo recipients. The post-dose 2 responses were comparable with both schedules: 0,1 months (of 0,1 and 3 months) and land 3 months. Also, the safety profile of HZ/su was acceptable in this study. Therefore, the results of study ZOSTER-001 supported the further evaluation of $\mathrm{HZ} /$ su in phase II/III studies for the prevention of HZ in autologous HCT and other IC populations such as patients with solid tumours receiving/ who will receive chemotherapy.

Although immunisation is the optimal way to prevent infection, IC patients may be unable to mount a protective immune response post-vaccination. Data in the literature on their immune responses to vaccination are sparse and sometimes contradictory. It is also unclear what the optimal vaccine dosing schedule is for patients receiving chemotherapy. However publications on vaccination against the H1N1 influenza virus showed that cancer patients, even if under chemotherapy, were able to mount a reasonably robust immune response [Mackay, 2011; Hottinger, 2012; Kotton, 2012; Rousseau, 2012; Xu, 2012]. Furthermore, immunization of highly IC persons with live virus vaccines may result in uncontrolled proliferation of attenuated strains [Center for Disease Control (CDC), 1993]. Thus, patients with solid tumours receiving chemotherapy comprise an IC population that may benefit from vaccination with a non-replicating vaccine such as HZ/su.

The purpose of study ZOSTER-028 was to assess the immunogenicity and safety of $\mathrm{HZ} /$ su when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ YOA with solid tumours receiving/who will receive chemotherapy. The focus of the study was to examine the immunological response to $\mathrm{HZ} / \mathrm{su}$, when subjects were IC through the use of chemotherapy. As such, the planned administration of immunocompromising chemotherapy was a pre-requisite for subject inclusion and the use of chemotherapy was a requirement for enrolement (regardless of their study arm) to assure they were IC (see Section 5.1.1). Subjects receiving only newer, more targeted therapies (e.g. trastuzumab) without aclassical immunocompromising chemotherapy were not to be included in the study (see Section 5.3.3).

This study report includes all the final immunogenicity and safety data.

## 4. STUDY OBJECTIVES

### 4.1. Primary objectives

- To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).
Criteria to be used:
The objective is met if the lower limit of the $95 \%$ confidence interval (CI) of the Geometric Mean (GM) ratio (HZ/su PreChemo group over placebo PreChemo group) in anti-gE enzyme-linked immunosorbent assay (ELISA) antibody (Ab) concentrations is greater than 3 .
- To evaluate the safety and reactogenicity following administration of the HZ/su vaccine as compared to placebo up to 30 days post last vaccination in subjects with solid tumours receiving chemotherapy.
Criteria to be used:
This analysis is descriptive, no criterion has been defined.
Refer to Section 5.9.1 for the definition of the primary endpoints.


### 4.2. Secondary objectives

- To evaluate vaccine response rate (VRR) in anti-gE humoral immunogenicity responses at Month 2, following a two-dose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).

Criteria to be used:
The objective is met if the lower limit of the $95 \%$ CI of the VRR for anti-gE ELISA Ab concentrations at Month 2 in the HZ/su PreChemo group is at least $60 \%$.

- To evaluate gE-specific CD4+T-cell immunogenicity responses at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only) (in the CMI sub-cohort).


## Criteria to be used:

The objective is met if the lower limit of the $95 \%$ CI of the GM ratio (HZ/su PreChemo group over placebo PreChemo group) in gE-specific CD4+ T-cell frequencies at Month 2 is greater than 1.

- To evaluate VRR in gE-specific CD4+ T-cell mediated immunogenicity at Month 2, following a two-dose administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine in subjects with solid tumours receiving chemotherapy (PreChemo Groups only) (in the CMI sub-cohort).

Criteria to be used:
The objective is met if the lower limit of the $95 \%$ CI of the VRR for gE-specific CD4+ T-cell frequencies at Month 2 in the HZ/su PreChemo group is at least 50\%.

- To evaluate the anti-gE humoral immunogenicity response at Month 2, following a two-dose administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (all subjects).


## Criteria to be used:

The objective is met if the lower limit of the $95 \%$ CI of the GM ratio (HZ/su group over placebo group) in anti-gE ELISA Ab concentrations is greater than 3 .

- To evaluate VRR in anti-gE humoral immunogenicity responses at Month 2, following a two-dose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (all subjects receiving the HZ/su vaccine).
Criteria to be used:
The objective is met if the lower limit of the $95 \%$ CI of the VRR for anti-gE ELISA Ab concentrations at Month 2 in the HZ/su group is at least $60 \%$.
- To evaluate safety following administration of the HZ/su vaccine, as compared to placebo, from 30 days post last vaccination until study end in subjects with solid tumours receiving chemotherapy.
- To characterize anti-gE humoral immunogenicity responses at Month 0, Month 1, Month 2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13 within the HZ/su and placebo groups.
- To characterize gE-specific CD4+ T-cell mediated immunogenicity responses at Month 0, Month 1, Month 2, and Month 13 within the HZ/su and placebo groups (PreChemo Groups only) (in the CMI sub-cohort).

Refer to Section 5.9.2 for the definition of the secondary endpoints.

## 5. INVESTIGATIONAL PLAN

### 5.1. Study design

### 5.1.1. Overall study design - Description



* The first dose of vaccine/ placebo was administered to the groups in relation to a chemotherapy cycle. The Dose 1 scheduling windows for the study groups are indicated below:
- HZ/su-PreChemo and Placeb-PreChemo Groups - within a maximum of 1 month to a minimum of 10 days before the start of a chemotherapy cycle.
- $\mathrm{HZ} /$ su-OnChemo and Placeb-OnChemo Groups - at the first day (allowing a window of $+/-1$ day) of a chemotherapy cycle.
*The second dose of study vaccine/ placebo was administered between 1 and 2 months after the first vaccination AND at the first day (allowing a window of $+/-1$ day) of a subsequent cycle of chemotherapy.
"* Visit 3 occurred approximately one month after the second vaccination.
$\dagger$ Visit 4 occurred within Months 4 to 13 for a Blood Sampling at the start of the last cycle of chemotherapy (if at least two months after the previous Blood Sampling (V3/M2)). Thus, the timing of this particular visit was variable depending on the subject's chemotherapy schedule and also on when they started vaccination in relation to their chemotherapeutic regimen. This visit was coincided with the subject's lowest immune status.
$\ddagger$ Should Visit 4 have coincided with Month 5 or Month 9, it replaced the Month 5 or the Month 9 Phone Contact, respectively (see Table 4).
${ }^{\Delta}$ Should Visit 4 have coincided with Month 13, the Visit 5 procedures were conducted (including a Blood Sampling for CMI).
* Blood samples ( $\sim 8 \mathrm{~mL}$ ) were collected from all subjects at Visit $1,2,3$, first day of last chemotherapy cycle at Visit 4 and Visit 5 to evaluate humoral immune responses.
§ Blood samples ( $\sim 30 \mathrm{~mL}$ ) were collected from a sub-cohort of subjects at Visit 1, 2, 3 and 5 to evaluate cell-mediated immune responses (CMI sub-cohort).
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb $=$ Placebo; Vacc = Vaccination
Protocol waivers or exemptions were not allowed with the exception of immediate safety concerns. Therefore, adherence to the study design requirements, including those specified in the outline of study procedures (Section 5.2.3) were essential and required for study conduct.
- Experimental design:

Phase II/III, observer-blind randomised, placebo controlled, multi-centre, multicountry study with two parallel groups.

- Duration of the study:

Each subject was followed at least until he/she completed Visit 5 (i.e., until Month 13 , approximately 12 months after the second dose of study vaccine/ placebo). The first vaccination visit at Month 0 (Visit 1) was preceded by a mandatory Prevaccination visit that was to take place from 30 days prior to Visit 1 up to the day of Visit 1 (the Pre-vaccination visit could occur on the same day as Visit 1).

- Epoch 001: Primary starting from the Pre-vaccination visit (up to -30 days) and ending at Visit 5 (Month 13). The study end took place when all subjects had completed their 12 month post-dose 2 follow-up visit (at Month 13, Visit 5). The total duration of the study for each subject was expected to be approximately 14 months including the Pre-vaccination visit.
- Study groups:

Table 1 Study groups and epochs foreseen in the study

| Study groups | Number of subjects | Age (Min.)* | Epoch |
| :--- | :---: | :---: | :---: |
|  |  |  |  |
| HZ/su-PreChemo | 93 | 18 years | $\bullet$ |
| Placeb-PreChemo | 93 | 18 years | $\bullet$ |
| HZ/su-OnChemo | 23 | 18 years | $\bullet$ |
| Placeb-OnChemo | 23 | 18 years | $\bullet$ |

HZ/su = Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb = Placebo; Min. = Minimum

* And above the legal age of consent (see Protocol, Section 11.1)

Table 2 Study groups and treatment foreseen in the study

| Treatment <br> name | Vaccine/ <br> Product name | PreChemo Study Groups |  | OnChemo Study Groups |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | $\mathrm{HZ} / \mathrm{su}$ | HZ/su- <br> PreChemo | Placeb- <br> PreChemo | HZ/su- <br> OnChemo | Placeb- <br> OnChemo |
| Placebo | VZV gE | $\bullet$ |  | $\bullet$ |  |
|  | AS01B | $\bullet$ |  | $\bullet$ |  |
|  | Lyophilised sucrose cake |  | $\bullet$ |  | $\bullet$ |

HZ/su = Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb = Placebo; VZV = Varicella Zoster Virus; gE
$=$ recombinant purified Glycoprotein E; AS01 ${ }_{\mathrm{B}}=$ Adjuvant System AS01 ${ }_{\mathrm{B}} ; \mathrm{NaCl}=$ sodium chloride

- Control: placebo control [Lyophilised sucrose reconstituted with saline $(\mathrm{NaCl})$ solution].
- Vaccination schedule: 0, 1-2 Month
- Treatment allocation:

Eligible subjects were randomised to two treatment groups: investigational HZ/su vaccine or placebo (HZ/su or placebo, 1:1); and to two vaccination strata: PreChemo Group, first vaccination at least 10 days before the start of a chemotherapy cycle, or OnChemo Group, first vaccination at the start of a chemotherapy cycle (PreChemo or OnChemo, 4:1). The overall ratio of these 4 study groups, HZ/su-PreChemo, Placeb-PreChemo, HZ/su-OnChemo, and Placebo-OnChemo, was 4:4:1:1 (see Table 7).

Note:
The analysis of safety was performed within the Total Vaccinated Cohort (TVC) on all subjects of the PreChemo and OnChemo groups (see Sections 5.9.4.1 and 5.9.9).
The analysis of humoral immunogenicity and humoral persistence were performed within the applicable According to Protocol (ATP) cohorts on all subjects of the PreChemo and OnChemo groups. The analysis of CMI and CMI persistence were performed within the applicable ATP cohorts on the CMI sub-cohort, comprised exclusively of subjects from the PreChemo Groups (see Sections 5.9.4.4, 5.9.4.5, 5.9.4.6, 5.9.4.7 and 5.9.8).

- Blinding:

Observer-blind for study vaccine administered (HZ/su versus placebo), but not blinded in regards time of vaccination relative to chemotherapy (PreChemo vs OnChemo).

Table 3 Blinding of study epochs

| Study Epoch | Blinding |
| :--- | :--- |
| Epoch 001 | observer-blind* |

* Beyond Visit 3 (Month 2), the investigator could be unexpectedly unblinded with respect to individual subjects. For details, please refer to Section 5.11.2).

Refer to Section 5.5 for details of the blinding procedure.

- Biological samples to be collected:
- A urine specimen was collected from all female subjects of childbearing potential at the Pre-vaccination Visit, Visit 1 and Visit 2. If a serum pregnancy test instead of a urine pregnancy test was required by country, local or ethics committee regulations, a blood sample was collected from women of childbearing potential at Visit 1 and Visit 2 and used for the test as per local guidance.
- Blood samples (approximately 8 mL ) were collected from all subjects at Visits 1 , 2, 3, 4 and 5 . Blood samples were used to assess humoral immune responses with respect to the study/investigational vaccine in all subjects.
- Blood samples (approximately 30 mL ) were collected from a sub-cohort of subjects at Visits 1, 2, 3 and 5 to assess CMI responses (CMI sub-cohort).
- Type of study: self-contained.
- Data collection: Standardised electronic Case Report Form (eCRF).
- Safety monitoring:

Per GSK process, blinded review of safety data was performed annually by the SRT. An iSRC of GSK was assigned to provide additional oversight by reviewing unblinded safety data (see Section 2).

### 5.1.2. Discussion of study design

Study ZOSTER-028 was conducted to evaluate the immunogenicity and safety of HZ/su in patients $\geq 18$ YOA diagnosed with one or more solid tumours and receiving chemotherapy. The results of studies in healthy adults and from the active phase of ZOSTER-001 (in autologous HCT patients) supported the selection of a 2-dose vaccine schedule. Studies in healthy adults demonstrated strong vaccine-induced immune responses following vaccine administration at 0 and 2 months. In addition, the results of ZOSTER-001 demonstrated comparably strong immune responses following vaccine administration at months 0 and 1 . Therefore, in the present study, the window for administration of the second vaccine dose was $30-60$ days after the first dose giving some flexibility to the patient and the investigators for the safe administration of $\mathrm{HZ} / \mathrm{su}$ while dealing with chemotherapy cycles.

Subjects in the ZOSTER-028 study were initially randomised into two groups based on the vaccination schedule in relation to the start of a chemotherapy cycle. The OnChemo group received their first $\mathrm{HZ} / \mathrm{su}$ vaccination at the start of a chemotherapy cycle, while the PreChemo group was planned to receive their first $\mathrm{HZ} /$ su vaccination at least 10 days before the start of a chemotherapy cycle (see Section 5.9.6). Unpublished data with other GSK candidate vaccines indicated that vaccination simultaneous with the administration of chemotherapy can lead to a decreased/suppressed immune response, possibly due to steroids used concomitantly in high doses to prevent nausea and vomiting. Therefore, the primary objective linked to immunogenicity was assessed in the PreChemo groups only. For this reason, the study groups were allocated 4:1 (186/46) PreChemo:OnChemo.

Two statistical analyses were performed: a first analysis with data up to Month 2 (active phase data) and an end of study analysis with all data up to Month 13. Analyses previously performed at first analysis were repeated at end of study analysis using the final cleaned database (see Section 5.9.12).

### 5.1.3. Rationale for the use of placebo

A lyophilised sucrose cake reconstituted with saline ( NaCl ) solution was included as a negative control (placebo) for this study, evaluating the immunogenicity and safety profile of the candidate $\mathrm{HZ} /$ su vaccine in this study population. The use of the placebo control, observer-blind and randomisation allowed controling for potential biases in the conduct of the study.

### 5.2. Study procedures

### 5.2.1. General study aspects: suspected HZ cases

Suspected HZ was defined as onset of a rash characteristic of HZ (i.e., unilateral, dermatomal and accompanied by pain broadly defined to include allodynia, pruritus or other sensations), or a vesicular rash suggestive of VZV infection regardless of the dermatomal distribution, and without alternative diagnosis. Additionally, sometimes HZ cases do not present with the characteristic HZ or VZV rash, but have a clinical presentation and specific laboratory tests ${ }^{1}$ suggestive of VZV infection. These cases were also to be considered as occurrences of HZ . Complications of HZ were to include, but were not limited to, PHN, HZ vasculitis, disseminated disease, ophthalmic disease, neurologic disease, and visceral disease.

The occurrence of HZ and/or HZ complications constituted an $\mathrm{AE} / \mathrm{SAE}$ as appropriate. The occurrence of HZ was defined as an intercurrent medical condition (see Section 5.3.4.5). The reporting period for cases of HZ was from Month 0 to study end. The standard reporting period as specified in Sections 5.8.1 and 5.8.2 for AE/SAE was to be used for HZ complications.

At Visit 1, all subjects were informed of the signs and symptoms of typical HZ.

### 5.2.2. Diary cards completion

Any supplied diary cards should have been preferably completed by the subjects themselves. In case of illiterate subjects or subjects having difficulty in self-completion of the diary cards, a trained and designated person (such as a family member, care provider or field worker) who was not involved in the study, could have provided assistance with reading the questions (verbatim) and/or transcribing the subject's responses on the diary cards. Thus the possibility of assistance by a trained and designated person in case of illiterate subjects or subjects requiring assistance was to be taken into account for all study procedures related to the completion of diary cards, and training of the designated person was to be given for this by the study staff at the first study visit. This assistance was to be given 'in real time', when the subject had to complete the diary card, and not retrospectively. The process needed to be documented by an internal operational procedure. When the completed diary cards were returned to the study staff, the study staff would ask the subject (at the time of return or at subsequent contact) if he/she had received any assistance in completing the diary card. In case diary cards were completed at the study site, study staff could assist in reading the questions (verbatim).

[^0]
### 5.2.3. Outline of study procedures

Table 4 summarises the list of study procedures followed during the study visits and contacts.
Table $4 \quad$ Outline of study procedures

| Epoch | Epoch 001 |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of contact | Pre- vaccination Visit $t$ | Visit ${ }^{*}$ | Visit 2** | Visit 3 | Visit 4** | Month 5 <br> Phone <br> Contact | Month 9 <br> Phone <br> Contact | Visit ${ }^{\text {a }}$ |
| Timepoints | $\begin{gathered} \text { Up to }-30 \\ \text { to }-10 \text { days } \end{gathered}$ | Month 0 | Month 1 | Month 2 | Month 6 (Months 4 to 13) | Month 5 | Month 9 | Month 13 |
| Sampling timepoints |  | Pre-Vacc | Post-Vacc 1 | Post-Vacc 2 | Post-Vacc 2 |  |  | Post-Vacc 2 |
| Informed consent | $\bullet$ | 0 a |  |  |  |  |  |  |
| Check inclusion criteria ${ }^{\text {b }}$ | $\bullet$ | $\bullet$ |  |  |  |  |  |  |
| Check exclusion criteria b | $\bullet$ | $\bullet$ |  |  |  |  |  |  |
| Record demographic data | $\bullet$ |  |  |  |  |  |  |  |
| Randomisation | $\bullet$ |  |  |  |  |  |  |  |
| Pre-vaccination visit conclusion | $\bullet$ |  |  |  |  |  |  |  |
| Medical history |  | $\bullet$ |  |  |  |  |  |  |
| Specific subject characteristics ${ }^{\text {c }}$ |  | $\bullet$ |  |  |  |  |  |  |
| Check contraindications |  | $\bullet$ | $\bullet$ |  |  |  |  |  |
| History directed physical examination |  | 0 |  |  |  |  |  |  |
| Training on self-reporting by subjects ${ }^{\text {d }}$ | 0 | 0 | 0 | 0 | 0 |  |  |  |
| HCG pregnancy test if applicable e | - ${ }^{\text {e }}$ | $\bullet$ | $\bullet$ |  |  |  |  |  |
| Pre-vaccination body temperature |  | $\bullet$ | $\bullet$ |  |  |  |  |  |
| Blood sampling (approximately 8 mL ) for humoral immune response from all subjects |  | $\bullet$ | $\bullet$ | - | $\bullet$ |  |  | $\bullet$ |
| Blood sampling (approximately 30 mL ) for CMI response in CMI sub-cohort subjects only |  | $\bullet$ | - | $\bullet$ |  |  |  | $\bullet$ |
| Assignment/recording of treatment number |  | $\bullet$ | $\bullet$ |  |  |  |  |  |
| Vaccination |  | $\bullet$ | - ${ }^{\text {f }}$ |  |  |  |  |  |
| Training on completion of diary cards |  | 0 | 0 |  |  |  |  |  |
| Dispensing of a diary card for solicited AEs and for unsolicited AEs and concomitant medication/vaccination to the subjects |  | 0 | 0 |  |  |  |  |  |


| Epoch | Epoch 001 |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of contact | Prevaccination Visit $t$ | Visit ${ }^{*}$ | Visit 2** | Visit 3 | Visit 4*** | Month 5 Phone Contact | Month 9 Phone Contact | Visit $5^{\Delta}$ |
| Timepoints | $\begin{aligned} & \text { Up to }-30 \\ & \text { to }-10 \text { days } \end{aligned}$ | Month 0 | Month 1 | Month 2 | Month 6 (Months 4 to 13) | Month 5 | Month 9 | Month 13 |
| Sampling timepoints |  | Pre-Vacc | Post-Vacc 1 | Post-Vacc 2 | Post-Vacc 2 |  |  | Post-Vacc 2 |
| Daily post-vaccination recording of solicited adverse events (Days 0-6) by subjects on diary card 9 |  | 0 | 0 | 0 |  |  |  |  |
| Return of diary cards (for solicited and unsolicited symptoms) |  |  | 0 | 0 |  |  |  |  |
| Transcription of the diary card for solicited symptoms, unsolicited AE and concomitant medication and vaccination by study staff/investigator 9 |  |  | $\bullet$ | $\bullet$ |  |  |  |  |
| Recording of any concomitant medication//product/vaccine/treatment which could impact the immune response or is part of a chemotherapy |  | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Recording of non-serious adverse events within 30 days (Days 0-29) post-vaccination, by investigator |  | $\bullet$ | $\bullet$ | $\bullet$ |  |  |  |  |
| Reporting of intercurrent medical conditions including HZ h |  | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Reporting of serious adverse events (SAEs)g |  | - ${ }^{i}$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Reporting of SAEs related to study participation or to a concurrent GSK medication/vaccine 9 | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Reporting of pregnancies |  | - ${ }^{i}$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Reporting of potential immune-mediated diseases (pIMDs) ${ }^{g}$ |  | - ${ }^{i}$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Study analysis |  |  |  | 0 |  |  |  | 0 |
| Study conclusion |  |  |  |  |  |  |  | $\bullet$ |

Note: The double-line border following Month 2 indicates the analyses which were performed on all data (i.e., data that were as clean as possible) obtained after completion of Visit 3.
Vacc = vaccination; HCG = Human Chorionic Gonadotropin; pIMDs = potential Immune-Mediated Diseases; GSK = GlaxoSmithKline; CMI = Cell-Mediated Immunity; HZ = Herpes Zoster.

- is used to indicate a study procedure that required documentation in the individual eCRF.
$\circ$ is used to indicate a study procedure that did not require documentation in the individual eCRF.
${ }^{\dagger}$ The Pre-vaccination visit was mandatory and could occur on the same day as Visit 1 . If the Pre-vaccination visit occurred on the same day as Visit 1 , all procedures indicated under the Pre-vaccination visit were performed and recorded in the eCRF at Visit 1.
* Visit 1 was the day of first vaccination.
${ }^{* *}$ Visit 2 (the second dose of study vaccine/ placebo administration) was 1 to 2 months after the first vaccination AND was planned to occur at the first day (allowing a window of $+/-1$ day) of a subsequent cycle of chemotherapy.
*** Visit 4 was to occurr within Months 4 to 13 for a Blood Sampling at the start of the last cycle of chemotherapy (if at least two months after the previous Blood Sampling (V3/M2)).
Thus, the timing of this particular visit was variable depending on the subject's chemotherapy schedule and also on when they started vaccination in relation to their chemotherapeutic regimen (see Table 5). This visit coincided with the subject's lowest immune status.
${ }^{\Delta}$ Should Visit 4 have coincided with Month 13, it was recorded as Visit 5 in the eCRF, i.e., the Visit 5 procedures were conducted (including a Blood Sampling for CMI) and Visit 5 was to be the visit recorded using the special Visit 5 tick-box in the eCRF indicating that Visit 5 had superseded Visit 4.
a If a Pre-vaccination visit occurred, informed consent was reconfirmed at Visit 1 , if needed per local requirements.
${ }^{\text {b }}$ If study entry occurred at the Pre-vaccination visit, eligibility criteria, medical history and demographic characteristics were checked at this visit (otherwise these were checked at Visit 1). A check for any changes compared to the Pre-vaccination Visit was performed at Visit 1 and recorded in the Pre-vaccination section of the eCRF. In case the subject was no longer eligible at Visit 1, the subject was withdrawn from the study. The reason for this was recorded in the Pre-vaccination section of the eCRF.
c The following subject characteristics were recorded in the eCRF for each subject at the time of enrolment:

1. Diagnosis for solid tumour malignancy;
2. Previous varicella and HZ vaccination status;
3. Evidence of prior VZV infection: when readily available, serological evidence of prior VZV infection, or else by medical history;
4. History of current and previous hospitalisations/surgery(s)/chemotherapy (based on readily available admissions and discharge for the solid tumour for which the subject was included in the study). Notes:
a. Number and dates of chemotherapy courses and cycles, and chemotherapeutic regimens;
b. Number and dates of radiotherapy courses and treatments;
c. Number and dates of surgeries.
5. ECOG performance status (Eastern Cooperative Oncology Group, PPD M.D., Group Chair) [Oken, 1982]
${ }^{\mathrm{d}}$ Subjects were instructed to contact their study site immediately if the subject developed any symptoms suggestive of HZ , if the subject manifested any symptoms he/she perceived as serious and, in case of pregnancy for women of childbearing potential.
${ }^{e}$ Only for women of childbearing potential. Pregnancy testing was to be performed with a urine or serum sample. Serum test were only to be considered, instead of a urine pregnancy test, if required by country, local or ethics committee regulations. In case, a serum pregnancy test was required, a blood sample was to be collected and testing performed per local guidance. The results of the applicable test were recorded in the eCRF. Pregnancy testing at the Pre-vaccination visit was done only using urine samples.
${ }^{\text {f }}$ Any subject with a HZ episode between Visit 1 and Visit 2 was not to receive the second dose.
9 For each solicited and unsolicited symptom the subject experienced, the subject was asked if he/she received medical attention defined as hospitalisation, an emergency room visit or a visit to or from medical personnel (medical doctor) for any reason and this information was recorded in the eCRF. Any concomitant medication/product/vaccine/treatment which could have interfered with the immune response or was part of a chemotherapy was recorded throughout the entire study (see Section 5.6.1).
${ }^{\mathrm{h}}$ Refer to Section 5.3.4.5 for details regarding intercurrent medical conditions. The occurrence of HZ was an intercurrent medical condition. At Visit 1 , all subjects were informed of the signs and symptoms of typical HZ.
${ }^{\text {I }}$ Study procedure was assessed only after administration of vaccine at Visit 1.

Time intervals between study visits/contacts and study procedures performed are presented in Table 5.

Table $5 \quad$ Intervals between study visits

| Interval between visits ${ }^{1}$ | Optimal length of interval ${ }^{2}$ | Allowed interval ${ }^{3}$ (range in days) |
| :---: | :---: | :---: |
| Pre-vaccination visit ${ }^{4} \rightarrow$ Visit 1 | Up to 30 to 10 days | Maximally 30 days and minimally 10 days before Visit 1 |
| Visit $1 \rightarrow$ Visit 2 (1 month) | 1-2 months ${ }^{5}$ | 30-60 |
| Visit $2 \rightarrow$ Visit 3 (1 month) | 1 month | 30-48 |
| Visit $1 \rightarrow$ Visit 4 (between Month 4, and Month 13) ${ }^{7}$ | 4-13 months, Variable ${ }^{6}$ | Minimally $\sim 120$ days after Visit 1 <br> Maximally $\sim 335$ days after Visit 1 |
| Visit $3 \rightarrow$ Month 5 Phone Contact ${ }^{7}$ | 3 months ${ }^{8}$ | 80-110 |
| Month 5 Phone Contact $\rightarrow$ Month 9 Phone Contact ${ }^{7}$ (Visit $3 \rightarrow$ Month 9 Phone Contact) | 4 months ${ }^{9}$ <br> (7 months) | $\begin{aligned} & 110-150 \\ & (190-260) \\ & \hline \end{aligned}$ |
| Visit $2 \rightarrow$ Visit 5 (12 months) | 12 months $^{10}$ | 335-425 |

${ }^{1}$ Unless otherwise specified, Visit 1 was taken as a reference to determine the applicable allowed interval between
Visits 2 and 4; and Visit 2 was taken as a reference to determine the applicable allowed interval between Visits 3, and 5.
2 Whenever possible the investigator was to arrange study visits within this interval.
${ }^{3}$ Whenever subject's clinical conditions necessitated a visit outside the optimal interval lenght the investigator was to arrange study visits within this interval. Subjects might not be eligible for inclusion in the ATP cohort if they made the study visit or contact outside any of these intervals (see Section 5.9.4, also regarding allowed intervals defined for ATP analysis of immunogenicity).
${ }^{4}$ The Pre-vaccination visit could occur on the same day as Visit 1.
${ }^{5}$ The second dose of study vaccine/ placebo was to be administered between 1 and 2 months after the first vaccination AND was planned to be at the first day (allowing a window of $+/-1$ day) of a subsequent cycle of chemotherapy.
${ }^{6}$ Visit 4 occurred within Months 4 to 13 for a Blood Sampling at the start of the last cycle of chemotherapy (if at least two months after the previous Blood Sampling (V3/M2)). Thus, the timing of this particular visit was variable depending on the subject's chemotherapy schedule and also on when they started vaccination in relation to their chemotherapeutic regimen (refer to Section 5.1.1). This visit coincided with the subject's lowest immune status.
${ }^{7}$ Should Visit 4 have coincided with Month 5 or Month 9, it was to replace the Month 5 or the Month 9 Phone Contact, respectively.
${ }^{8}$ Visit 3 was taken here as reference to determine the applicable allowed interval up to the Month 5 Phone Contact.
${ }^{9}$ The Month 5 Phone Contact was taken here as reference to determine the applicable allowed interval up to the Month 9 Phone Contact (If Visit 4 coincided with the Month 5 Phone Contact, the date of Visit 3 was to be used as a reference instead of Month 5).
${ }^{10}$ Visit 5 occurred approximately 12 months after the second vaccination.

### 5.3. Selection of study population

### 5.3.1. Number of subjects

Target enrolment was approximately 232 eligible adults diagnosed with solid tumours who would be receiving chemotherapy. Details regarding the actual number of subjects screened and the number of subjects included in the Total Vaccinated Cohort (TVC) is presented in Section 6.2.

See Section 5.9.3.1 for a description of the criteria used in the determination of sample size. Refer to Sections 5.3.2 and 5.3.3 for eligibility criteria.

The sub-cohort foreseen for CMI analyses is described in Table 6. Refer to Section 5.9.3 for details regarding the estimation of its sample size.

Table 6 Sub-cohorts

| Sub-cohort name | Description | Estimated number of <br> enrolled subjects |
| :--- | :--- | :--- |
| CMI sub-cohort* | Blood samples (approximately 30 mL ) collected at Visits <br> $1,2,3$ and 5 will be analysed to assess CMI response | 76 |

* This CMI sub-cohort was comprised exclusively of subjects from the PreChemo Groups. $\mathrm{mL}=$ Millilitre; CMI = Cell-mediated Immunity
- Overview of the recruitment plan:

Study ZOSTER-028 was planned to be conducted at sites in different countries worldwide. The number of eligible subjects required for enrolment for the study groups and within the CMI Sub-cohort is indicated in Table 7. The actual number of subjects included in the CMI Sub-cohort is indicated in Section 6.3.1.2. The CMI sub-cohort was comprised exclusively of subjects from the PreChemo Groups.

Table $7 \quad$ Number of subjects required for enrolment

| Vaccination Start stratum | Study groups | Estimated number of subjects |  |
| :--- | :--- | :--- | :--- |
|  |  | Overall <br> $\mathbf{N}$ | CMI sub-cohort <br> $\mathbf{N}$ |
|  | HZ/su-PreChemo | 93 | 38 |
| First Vaccination <br> at the start of a chemotherapy cycle | Placeb-PreChemo | 93 | 38 |
|  | HZ/su-OnChemo | 23 | 0 |
|  | Placeb-OnChemo | 23 | 0 |

HZ/su = Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb = Placebo
The enrolment period was estimated to be approximately 6 months after the first subject had been enrolled depending on the enrolment rate. Refer to Section 5.9.3 for a description of the assumptions used in the estimation of sample size. Enrolment target numbers per region, country and sub-cohort were assigned at the study start and could be adjusted during the study. The recruitment rate was monitored using a study-specific central randomisation system on the Internet (SBIR).

Transfer of supplies was tracked by the central randomisation system. Monitoring visit frequency was to be adapted to the pace of enrolment. Vaccine doses were distributed to each study site respecting the randomisation block size.

### 5.3.2. Inclusion criteria for enrolment

Deviations from inclusion criteria were not allowed because they could potentially jeopardize the scientific integrity of the study, regulatory acceptability or subject safety. Therefore, adherence to the criteria as specified in the protocol was essential.

All subjects were to satisfy ALL the following criteria at study entry:
Study entry occurred at the Pre-vaccination visit. Inclusion criteria were checked at the Pre-vaccination visit, and a check for any changes compared to the Pre-vaccination visit was performed at Visit 1 and recorded in the Pre-vaccination Section of the eCRF.

- Subjects who, in the opinion of the investigator, could and would comply with the requirements of the protocol (e.g., completion of the diary cards, return for follow-up visits, ability to have scheduled contacts to allow evaluation during the study);
- Written informed consent obtained from the subject;
- A male or female aged 18 years or older (and has reached the age of local legal consent) at the time of study entry (i.e., when informed consent is signed). Refer to Protocol Section 11.1 for country-specific age of legal consent;
- Subject who had been diagnosed with one or more solid tumours (defined as a solid malignancy, i.e., not a blood element malignancy);
- Subjects who were receiving or were to receive a cytotoxic or immunosuppressive chemotherapy (such that the study vaccine could be administered at the latest at the start of the second cycle of chemotherapy).
- Life expectancy of greater than one year;
- Female subjects of non-childbearing potential could be enrolled in the study;

Non-childbearing potential was defined as pre-menarche, current tubal ligation, hysterectomy, ovariectomy or post-menopause;

- Female subjects of childbearing potential could be enrolled in the study, if the subject:
- had practiced adequate contraception for 30 days prior to vaccination, and
- had a negative pregnancy test on the day of vaccination, and
- had agreed to continue adequate contraception during the entire treatment period and for 2 months after completion of the vaccination series.


### 5.3.3. Exclusion criteria

Deviations from exclusion criteria were not allowed because they could potentially jeopardize the scientific integrity of the study, regulatory acceptability or subject safety. Therefore, adherence to the criteria as specified in the protocol was essential.

The following criteria were to be checked at the time of study entry. If ANY exclusion criterion applied, the subject was not to be included in the study:

Study entry occurred at the Pre-vaccination visit. Exclusion criteria were checked at the Pre-vaccination visit, and a check for any changes compared to the Pre-vaccination visit was to be performed at Visit 1 and recorded in the Pre-vaccination section of the eCRF.

- Subjects receiving only newer, more targeted therapies (e.g., trastuzumab) if not taken together with a classical chemotherapy (since these new more targeted therapies were not considered immunosuppressant);
- Chronic administration and/or planned administration of systemic glucocorticoids (defined as prednisone $\geq 20 \mathrm{mg} /$ day, or equivalent, for more than 14 consecutive days in total) within one month prior to the first vaccine dose and up to Visit 3 (Month 2). Inhaled, intra-articularly injected, and topical steroids were allowed;
- Previous vaccination against HZ or varicella within 12 months preceding the first dose of study vaccine/ placebo;
- Planned administration during the study of a HZ vaccine (including an investigational or non-registered vaccine) other than the study vaccine;
- Previous chemotherapy course less than 28 days before first study vaccination (refer to Section 5.11.2 for a clarification regarding this exclusion criterion);
- Occurrence of a varicella or HZ episode by clinical history within the 12 months preceding the first dose of study vaccine/ placebo;
- History of allergic disease or reactions likely to be exacerbated by any component of the vaccine or study material and equipment;
- Administration or planned administration of a live vaccine in the period starting 30 days before the first dose of study vaccine and ending 30 days after the last dose of study vaccine, or, administration or planned administration of a non-replicating vaccine* within 8 days prior to or within 14 days after either dose of study vaccine.
-     * E.g., inactivated and subunit vaccines, including inactivated and subunit influenza vaccines and pneumococcal conjugate vaccines;
- HIV infection by clinical history;
- Acute disease and/or fever at the time of vaccination. Acute disease was defined as the presence of a moderate or severe illness with or without fever, but excluded the underlying malignancy, as well as the expected symptoms/signs associated with that disease or its treatment;
- Fever was defined as temperature $\geq 37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ on oral, axillary or tympanic setting, or $\geq 38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$ on rectal setting. The preferred route for recording temperature in this study was oral.
- Subjects with a minor illness (such as mild diarrhoea, mild upper respiratory infection) without fever, could receive the first dose of study vaccine/ placebo at the discretion of the investigator.
- Any condition which, in the judgment of the investigator would have made intramuscular (IM) injection unsafe;
- Pregnant or lactating female;
- Female planning to become pregnant or planning to discontinue contraceptive precautions (if of childbearing potential) before Month 3 (i.e., 2 months after the last dose of study vaccine/ placebo).


### 5.3.4. Withdrawal criteria

### 5.3.4.1. Subject completion

A subject, who returned for the concluding visit/was available for the concluding contact foreseen in the protocol, was considered to have completed the study.

### 5.3.4.2. Subject withdrawal from the study

Only subjects withdrawn at the Pre vaccination visit and who were no longer eligible at Visit 1 were to be replaced. All the other withdrawals were not to be replaced.

From an analysis perspective, a 'withdrawal' from the study referred to any subject who did not come back for the concluding visit/was not available for the concluding contact foreseen in the protocol.

All data collected until the date of withdrawal/last contact of the subject were used for the analysis.

A subject was considered a 'withdrawal' from the study when no study procedure had occurred, no follow-up had been performed and no further information had been collected for this subject from the date of withdrawal/last contact.

Investigators were to make an attempt to contact those subjects who did not return for scheduled visits or follow-up.

Information relative to the withdrawal was documented in the eCRF. The investigator documented whether the decision to withdraw a subject from the study was made by the subject himself/herself, or by the investigator, as well as which of the following possible reasons was responsible for withdrawal:

- SAE.
- Non-serious AE.
- Protocol violation (specify).
- Consent withdrawal, not due to an $\mathrm{AE}^{*}$.
- Moved from the study area.
- Lost to follow-up.
- Other (specify).
*In case a subject was withdrawn from the study because he/she had withdrawn consent, the investigator documented the reason for withdrawal of consent, if specified by the subject, in the CRF.

Subjects who were withdrawn from the study because of SAEs/AEs were to be clearly distinguished from subjects who were withdrawn for other reasons. Investigators were to follow subjects who were withdrawn from the study as result of a SAE/AE until resolution of the event (see Section 5.8.1.6.2).

### 5.3.4.3. Subject withdrawal from investigational vaccine/product

A 'withdrawal' from the investigational vaccine/ placebo referred to any subject who did not receive the complete treatment, i.e. when no further planned dose was administered from the date of withdrawal. A subject withdrawn from the investigational vaccine/ placebo was not necessarily to be withdrawn from the study as further study procedures or follow-up could be performed (safety or immunogenicity) as planned in the study protocol.

Information relative to premature discontinuation of the investigational vaccine/ placebo was documented on the Vaccine Administration page/screen of the eCRF. The investigator documented whether the decision to discontinue further vaccination/treatment was made by the subject himself/herself, or by the investigator, as well as which of the following possible reasons was responsible for withdrawal:

- SAE.
- Non-serious AE.
- Other (specify).


### 5.3.4.4. Contraindications to subsequent vaccination

The following events constituted absolute contraindications to further administration of $\mathrm{HZ} / \mathrm{su}$ study vaccine or placebo. If any of these events occurred during the study, the subject was not to receive additional doses of vaccine but could continue other study procedures at the discretion of the investigator (see Section 5.3.4.3).

- Anaphylaxis following the administration of vaccine.
- Pregnancy (see Section 5.8.4).
- If the subject experienced an SAE judged to be vaccine-related by the investigator.

The following events constituted contraindications to administration of HZ/su study vaccine or placebo at that point in time; if any of these events occurred at the time scheduled for vaccination, the subject could be vaccinated at a later date, within the time window specified in the protocol (see Section 5.2.3), or the subject could be withdrawn at the discretion of the investigator (see Section 5.3.4.2).

- Acute disease at the time of vaccination. Acute disease was defined as the presence of a moderate or severe illness with or without fever, but excluded the underlying malignancy for which the subject was included in the present study as well as the expected symptoms/signs associated with that disease or its treatment.
- Any condition which, in the judgment of the investigator would have made IM injection unsafe.
- All vaccines could be administered to persons with a minor illness such as diarrhoea, mild upper respiratory infection with or without low-grade febrile illness, i.e., oral temperature $<37.5^{\circ} \mathrm{C}\left(99.5^{\circ} \mathrm{F}\right) /$ axillary temperature $<37.5^{\circ} \mathrm{C}\left(99.5^{\circ} \mathrm{F}\right)$.

Note: Any subject with an event of HZ between Visit 1 and Visit 2 was not to receive the second dose.

### 5.3.4.5. Intercurrent medical conditions that may have led to elimination of a subject from According-To-Protocol (ATP) analyses

At each study visit subsequent to the first vaccination visit, it was verified whether the subject had experienced or was experiencing any intercurrent medical condition. If it was the case, the condition(s) were to be recorded in the eCRF. Intercurrent medical conditions were recorded in AE/SAE screens as appropriate.

Intercurrent medical conditions were clinical events during the course of the study which might have altered or confounded the interpretation of the immunologic (not safety) assessments of the protocol. In regards to humoral gE assessments, this included any clinical event that might have increased or decreased the measurement of anti-gE antibodies, such as protein losing conditions in which the loss of gammaglobulin or total proteins might have underestimated the subject's gE response (e.g. protein losing enteropathy, proteinuria, or cachexia). Additional examples would be conditions that would cause the administration of exogenous $g E$ antibodies, resulting in an overestimate of the subject's anti-gE Ab response to HZ/su vaccination, such as conditions requiring the use of intravenous immunoglobulin or blood products. The occurrence of HZ was an intercurrent medical condition, as the anti-gE Ab formed in response to active shingles could not be distinguished from the anti-gE Ab formed in response to vaccination. The reporting period for cases of HZ was from Month 0 to study end.

For the CMI sub-cohort, in regards to measuring their cellular immunity, intercurrent medical conditions were active viral infections that might have altered CD4+ T-cell counts and/or responses. Examples, not exhaustive, of such acute viral infections would include acute Hepatitis A, acute Hepatitis B, new onset HIV, and potentially acute cytomegalovirus and/or Epstein Barr virus infections.

Subjects might be eliminated from the ATP cohort for immunogenicity if, during the study, they incurred a condition that has the capability of confounding their immune response to the study vaccine or its interpretation (e.g., cases of HZ up to study end).

Refer to Section 5.6.2 for concomitant medications/ vaccines that may have led to the elimination of a subject from ATP analyses.

### 5.4. Composition and administration of vaccines

### 5.4.1. Description of study vaccine/ placebo

The Quality Control Standards and Requirements for the candidate vaccine were described in separate Quality Assurance documents (e.g. release protocols, certificate of analysis) and the required approvals had been obtained.

The vaccines were labelled and packed according to applicable regulatory requirements.
The characteristics of the study vaccine $\mathrm{HZ} /$ su and placebo are as detailed in Table 8.

## Table 8 Study vaccine/ placebo

| Treatment name | Product name* | Formulation | Presentation | Volume to be administered | Number of doses | Lot numbers |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| HZ/su | VZV gE | $50 \mu \mathrm{~g} \mathrm{gE}$ per 0.5 mL of reconstituted vaccine | Lyophilised pellet in a monodose vial |  |  | DVZVA007B |
|  | $A^{\text {AS01 }}$ | MPL, QS21 <br> and liposome <br> ( $50 \mu \mathrm{~g} \mathrm{MPL}$ <br> and $50 \mu \mathrm{~g}$ <br> QS21) per 0.5 <br> mL of <br> reconstituted <br> vaccine | Liquid in a monodose vial | 0.5 mL | 2 | DA01A050A |
| Placebo | Lyophilised sucrose cake | 20 mg sucrose per 0.5 mL of reconstituted placebo | lyophilised pellet in a monodose vial | 0.5 mL | 2 | PVZVA005A |
|  | Saline ( NaCl ) solution for reconstitution | 150 mM NaCl solution (water for injection) | Liquid in a monodose vial |  |  | DD02A011A |

*Components of the reconstituted study vaccine HZ/su, and Placebo, respectively HZ/su: Herpes Zoster subunit vaccine
VZV gE: Varicella Zoster Virus recombinant purified glycoprotein E
AS01b: Adjuvant System
MPL: 3-O-desacyl-4'-monophosphoryl lipid A
QS-21: Quillaja saponaria Molina, fraction 21 (Licensed by GSK from Antigenics Inc, a wholly owned subsidiary of Agenus Inc., a Delaware, USA corporation)
$\mu \mathrm{g}$ : microgram; mL: milliliter
There was a slight difference in appearance between the diluents used for the vaccine and placebo ( $\mathrm{ASO1}{ }_{\mathrm{B}}$ and saline solution) as well as between the reconstituted vaccine and placebo and therefore this study was conducted in an observer-blind manner.

### 5.4.2. Dosage and administration of study vaccine/placebo

Vaccine/placebo was administered as indicated in Table 9.
The reconstituted vaccine or placebo $(0.5 \mathrm{~mL})$ was to be administered by IM injection into the deltoid muscle of the non-dominant arm using a standard aseptic technique. In rare situations when there was no alternative, the injection could be given in the other arm.

Notes:

- In case of contraindication to the administration in the non-dominant arm (e.g., arm radiotherapy for breast cancer) the dominant arm was to be used.
- In case of bleeding risk(s), the vaccine was only to be administered, if according to the investigator, it could be with reasonable safety by this route. A fine adapted needle was to be used for the vaccination and firm pressure applied to the site, without rubbing, for $\geq 2$ minutes. The subject was to be informed concerning the risk for haematoma from the injection.

Table 9 Dosage and administration

| Type of contact and timepoint | Study group | Treatment name | Volume to be administered | Route ${ }^{1}$ | Site | Side |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Visit 1 (Day 0) |  | HZ/su | 0.5 mL | IM | Deltoid | Nondominant |
| Visit 2 (Month 1) | HZsu-PreChemo | HZsu |  |  |  |  |
| Visit 1 Day 0) | Placeb-PreChemo | Placebo |  |  |  |  |
| Visit 2 (Month 1) |  |  |  |  |  |  |
| Visit 1 (Day 0) | HZ/su-OnChemo | HZ/su |  |  |  |  |
| Visit 2 (Month 1) |  |  |  |  |  |  |
| Visit 1 (Day 0) | Placeb-OnChemo | Placebo |  |  |  |  |
| Visit 2 (Month 1) |  |  |  |  |  |  |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster subunit vaccine; Chemo $=$ Chemotherapy; Placeb $=$ Placebo; $\mathrm{mL}=$ millilitre, ${ }^{1} 1$ ntramuscular (IM)

The vaccine/placebo recipients were to be observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccine/placebo.

The contraindications to vaccination were specified in the protocol (see protocol for details).

### 5.4.2.1. Replacement of unusable vaccine/ placebo doses

In addition to the vaccine/ placebo doses provided for the planned number of subjects (including over-randomisation when applicable), at least $5 \%$ additional vaccine/placebo doses were supplied to replace those that were unusable (i.e., cracked, broken).

The investigator used SBIR to obtain a new treatment number that was used as a replacement. The replacement numbers were allocated by dose. The system ensured, in a blinded manner, that the replacement vials matched the formulation the subject was assigned to by randomisation.

### 5.4.3. Treatment allocation and randomisation

### 5.4.3.1. Subject identification

Subject numbers were assigned sequentially to subjects consenting to participate in the study, according to the range of subject numbers allocated to each study centre.

### 5.4.3.2. Randomisation of treatment

### 5.4.3.2.1. Randomisation of supplies

The randomisation was performed at GSK Biologicals, Belgium, using MATEX, a program developed for use in Statistical Analysis Systems (SAS) (Cary, NC, United States [US]) by GSK Biologicals.

To allow GSK Biologicals to take advantage of greater rates of recruitment than anticipated at individual centres in this multicentre study, and to thus reduce the overall study recruitment period, an over-randomization of supplies was prepared.

The vaccine/placebo doses were distributed to each study centre, respecting the randomization block size.

### 5.4.3.2.2. Treatment allocation to the subject

The treatment allocation at the investigator site was performed using SBIR. The treatment numbers were allocated by dose. Eligible subjects were randomised to the investigational $\mathrm{HZ} / \mathrm{su}$ vaccine or placebo (1:1).

When SBIR was not available, reference was made to the SBIR user guide or the Study Procedures Manual for specific instructions.

After having checked the eligibility of the subject and obtaining the informed consent form (ICF), the site staff in charge of the vaccination accessed SBIR. Upon providing the subject identification number, the randomisation system used the minimisation algorithm to determine the treatment number to be used for the subject. Each treatment number was recorded in the eCRF on the Vaccine Administration screen.

## Study group and treatment number allocation

Target enrolment was approximately 232 eligible adults diagnosed with solid tumours receiving chemotherapy. During the Pre-vaccination visit eligible subjects were randomised to the investigational $\mathrm{HZ} / \mathrm{su}$ vaccine or placebo according to a $1: 1$ ratio (vaccine:placebo), and stratified to PreChemo Group, first vaccination at least 10 days before the start of a chemotherapy cycle or OnChemo Group, first vaccination at the start of a chemotherapy cycle (PreChemo:OnChemo, 4:1). The overall ratio of these 4 study groups (HZ/su-PreChemo, Placeb-PreChemo, HZ/su-OnChemo, and Placeb-OnChemo) was 4:4:1:1 (see Section 5.1.1 for target enrolment of eligible subjects by group).

Allocation of the subject to a study group at the investigator site was performed using SBIR. The randomisation algorithm used a minimisation procedure accounting for age (18-49 YOA and $\geq 50 \mathrm{YOA}$ ), centre, country and gender (Male and Female).

After obtaining the signed and dated ICF from the subject and having checked the eligibility of the subject, the site staff in charge of the vaccine administration accessed SBIR. Upon providing the subject identification number, the randomisation system determined the study group and provided the treatment number to be used for each dose.

The number of each administered treatment was recorded in the eCRF on the Vaccine Administration screen.

## Treatment number allocation for subsequent doses

For each dose subsequent to the first dose, the study staff in charge of the vaccine administration accessed SBIR, provided the subject identification number, and the system provided a treatment number consistent with the allocated group.

The number of each administered treatment was recorded in the eCRF on the Vaccine Administration screen.

### 5.4.3.3. Allocation of subjects to assay subsets (CMI sub-cohort)

The CMI analyses were performed at specified timepoints for subjects included in the CMI sub-cohort (Refer to Table 6). This CMI sub-cohort was comprised exclusively of subjects from the PreChemo Groups. This was a subgroup of the subjects in the study in selected countries at designated sites that had access to a peripheral blood mononuclear cells (PBMC) processing facility within the acceptable time window from sample collection to PBMC processing.

The target number for the CMI sub-cohort was 76 subjects ( 30 evaluable subjects per treatment group). A randomization algorithm was used to attribute the subjects to the subcohorts at the designated sites (see Table 7).

### 5.5. Blinding

Data were collected in an observer-blind manner. By observer-blind, it was meant that during the course of the study, the vaccine recipient and those responsible for the evaluation of any study endpoint (e.g., safety and reactogenicity) were all unaware of which vaccine was administered. To do so, vaccine preparation and administration was done by authorised medical personnel who did not participate in any of the study clinical evaluation assays.

From study start until Month 13 (Visit 5, study end), the study staff remained blinded and study-related procedures and observations performed at the study sites continued to be conducted in an observer-blind manner (see Section 5.11.2).

The subjects continued to be blinded and access to unblinded individual subject treatment assignments was restricted to GSK personnel only on an as-needed basis. The individual data listings and subject treatment assignments were not provided to the investigators until after the conclusion of the study, following the completion of Month 13 (Visit 5, study end).

The laboratory in charge of the laboratory testing was blinded to the treatment, and codes were used to link the subject and study (without any link to the treatment attributed to the subject) to each sample.

GSK Biologicals' policy (incorporating International Conference on Harmonisation [ICH] E2A guidance, European Clinical Trial Directive and Federal Regulations) is to unblind any SAE report associated with the use of the investigational product, which is unexpected and attributable/suspected, prior to regulatory reporting.

Also, unblinding of a subject's individual treatment code occurred only in the case of a medical emergency, or in the event of a serious medical condition, when knowledge of the study treatment was essential for the clinical management or welfare of the subject, as judged by the investigator. Refer to the protocol for details.

### 5.6. Prior and concomitant medication /vaccinations

At each study visit/contact, the investigator questioned the subject about any medication/product taken and vaccination received by the subject.

### 5.6.1. Recording of concomitant medications/products and concomitant vaccination

The following concomitant medications/ vaccines were recorded in the eCRF if administered during the indicated recording period:

- Previous HZ vaccination.
- All concomitant medications, except vitamins and dietary supplements, administered at any time during the period starting with the administration of each dose of study vaccine/ placebo and ending 30 days (Days $0-29$ ) after each dose of study vaccine/placebo.
- Prophylactic medication (i.e. medication administered in the absence of ANY symptom and in anticipation of a reaction to the vaccination).
E.g., an anti-pyretic was considered to be prophylactic when it was given in the absence of fever and any other symptom, to prevent fever from occurring [fever was defined as temperature $\geq 37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ on oral, axillary or tympanic setting, or $\geq$ $38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$ on rectal setting].
- Any concomitant medication/product/vaccine listed in Section 5.6.2.
- Any concomitant medication/product/vaccine relevant to a SAE* or administered at any time during the study period for the treatment of a SAE*.
* SAEs that were required to be reported per protocol.
- Any concomitant medication/product/vaccine/treatment which could interfere with the immune response was to be recorded during the entire study period.
- Any concomitant medication/ product/vaccine/treatment as part of a chemotherapy was to be recorded during the entire study period.


### 5.6.2. Concomitant medications/ vaccines that may have led to the elimination of a subject from ATP analyses

The use of the following concomitant medications/products/vaccines did not require withdrawal of the subject from the study but could determine a subject's evaluability in the ATP analysis for a specific timepoint. See Section 5.9.4 for study cohorts/ data sets analysed.

- Chronic administration and/or planned administration of systemic glucocorticoids (defined as prednisone $\geq 20 \mathrm{mg} /$ day, or equivalent, for more than 14 consecutive days in total) within one month prior to the first vaccine dose and up to Visit 3 (Month 2); and one month prior to subsequent blood sampling at Visits 4 and 5. Inhaled, intra-articularly injected, and topical steroids were allowed.
- Administration of any vaccine against varicella or HZ other than the study vaccine during the study period;
- Administration of a vaccine not foreseen by the study protocol starting 30 days before the first dose of study vaccine until 30 days after the last dose of study vaccine. However, licensed non-replicating vaccines (e.g., inactivated and subunit vaccines, including inactivated and subunit influenza vaccines, and pneumococcal conjugate vaccines) could be administered within 8 days prior to or within 14 days after either dose of study vaccine;
A detailed, comprehensive list of reasons for elimination from ATP analyses were established at the time of data cleaning.


### 5.7. Assessment of immunogenicity variables

### 5.7.1. Biological samples

The different biological samples collected in the study, the quantities needed, the units and the timepoints are described in Table 10. Samples were not labelled with information that directly identifies the subject but were coded with the identification number for the subject (subject number).

## Table 10 Biological samples

| Sample type | Quantity <br> (approximate vol.) | Unit | Timepoint | Sub-cohort Name* |
| :--- | :--- | :--- | :--- | :--- |
| Blood (Humoral immunity) | 8 | mL | Visit 1, 2, 3, 4 and 5 | All subjects |
| Blood (Cell-mediated immunity) | 30 | mL | Visit 1, 2, 3 and 5 | CMI sub-cohort |

*Refer to Section 5.3.1 for sub-cohort description / Refer to Section 5.4.3.3 for subset description.

Collected samples could be used in other assays, for test improvement or development of analytical methods related to the study vaccine and its constituents or the disease under study to achieve a more reliable measurement of the vaccine response. Under these circumstances, additional testing on the samples might have been performed by GSK Biologicals outside the scope of this protocol.

Collected samples could also be used for purposes related to the quality assurance of data generated linked to the study vaccine or the disease under study, such as for maintenance of assays described in this protocol and comparison between analytical methods and/or laboratories.

All sample testing was done in line with the consent of the individual subject.

### 5.7.2. Laboratory assays

Laboratory assays, which were used in this study, are summarised in Table 11 (Humoral Immunity) and Table 12 (CMI), respectively.

Table 11 Humoral Immunity (Ab determination)

| System | Component | Method | Kit $/$ <br> Manufacturer | Unit | Cut-off | Laboratory |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| Serum | Varicella Zoster <br> Virus.Glycoprotein E <br> Ab.lgG | ELISA | NA | $\mathrm{mlU} / \mathrm{mL}$ | 97 | GSK <br> Biologicals* |

* GSK Biologicals laboratory refers to the Global Vaccines Clinical Laboratories (GVCL [CLS], Rue de I'Institut, 89 - B-

1330 Rixensart - Belgium.
$\mathrm{gE}=$ Glycoprotein $\mathrm{E} ; \mathrm{Ab}=$ Antibody; IgG = Immunoglobulin class G; ELISA = Enzyme-linked Immunosorbent Assay;
NA = Not applicable; mL = millilitre; mIU = milli international unit.

## Description of the assay to test humoral immunity:

Anti-gE ELISA: Anti-gE Ab concentrations were measured using an anti-gE ELISA. Diluted blood serum samples of study subjects were added to microtitre wells pre-coated with $g E$ antigen. Secondary peroxidase-conjugated anti-human Abs were added, which bound to the primary human anti-gE Abs. After incubation of the microtitre wells with a chromogen substrate solution, the enzymatic reaction was stopped. Optical densities were recorded and anti-gE Ab concentrations were calculated from a standard curve. The assay cut-off was $97 \mathrm{mIU} / \mathrm{mL}$.
Table 12 Cell-Mediated Immunity (CMI)

| System | Component | Challenge | Method | Unit | Cut-off | Laboratory |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| PBMC | CD4.polypositives <br> CD40L+IL2+TNFa+IF <br> $N g^{*}$ | gE | ICS | Events | N/A | CEVAC** |

* CD4.polypositives CD40L+IL2+TNFa+IFNg = CD4+ T-cells expressing at least 2 activation markers (from among

IFN- $\gamma$, IL-2, TNF- $\alpha$ and CD40L)
** University of Ghent, De Pintelaan, 185 Ghent - Belgium
PBMC = Peripheral blood mononuclear cells
$\mathrm{gE}=$ Glycoprotein E; ICS = Intracellular cytokine staining

## Description of the assay to test CMI:

## Intracellular cytokine staining (ICS)

CMI responses were performed by CEVAC-Ghent on thawed PBMCs by ICS. The assay was performed on samples collected during the course of the study. This assay provided information on the frequency of CD4+ T-cells responding to culture medium or antigens (gE peptide pool) by secreting cytokine molecules involved in immunity such as IFN- $\gamma$, IL-2, TNF- $\alpha$, and CD40L ${ }^{2}$. Briefly, PBMC collected from the subjects were stimulated for two hours using culture medium (for evaluation of the non-specific response) or with a pool of overlapping peptides covering the entire sequence of the vaccine antigen gE (for evaluation of the gE -specific response). Then, an intracellular block (brefeldin A) was added to inhibit cytokine secretion for a subsequent overnight incubation. Cells were then harvested, stained for surface markers (CD3, CD4 and CD8) and fixed. The fixed cells were then permeabilised and stained with anti-cytokine Abs, washed and analysed by cytofluorometry. The results of ICS assays were expressed as the frequency of specific CD4+ T-cells per million total CD4+ T-cells.

The GSK Biologicals' clinical laboratories have established a Quality System supported by procedures. The activities of GSK Biologicals' clinical laboratories are audited regularly for quality assessment by an internal (sponsor-dependent) but laboratoryindependent Quality Department.

Refer to Section 5.5 for details regarding measures to maintain blinding during the study.

### 5.7.3. Biological samples evaluation

### 5.7.3.1. Immunological read-outs

The plan for immunogenicity testing on samples obtained is shown in Table 13. For all subjects, anti-gE Abs were measured by ELISA at specified timepoints.

For subjects included in the CMI sub-cohort, the gE-specific CMI response was measured at specified timepoints.

[^1]Table 13 Immunological read-outs

| Blood sampling timepoint |  |  | Sub-cohort/Subset Name | Marker |
| :---: | :---: | :---: | :---: | :---: |
| Visit no | Timing | Month |  |  |
| Visit 1 | Pre-Vacc | 0 | Humoral immune response (all subjects) | Ab gE ELISA |
|  |  |  | CMI sub-cohort | ICS gE |
| Visit 2 | Post-Vacc 1 | 1 | Humoral immune response (all subjects) | Ab gE ELISA |
|  |  |  | CMI sub-cohort | ICS gE |
| Visit 3 | Post-Vacc 2 | 2 | Humoral immune response (all subjects) | Ab gE ELISA |
|  |  |  | CMI sub-cohort | ICS gE |
| Visit 4* | Post-Vacc 2 | $\begin{array}{\|l\|} \hline 6 \\ \text { (Months } 4 \text { to 13) } \\ \hline \end{array}$ | Humoral immune response (applicable subjects**) | Ab gE ELISA |
| Visit 5 | Post-Vacc 2 | 13 | Humoral immune response (all subjects) | Ab gE ELISA |
|  |  |  | CMI sub-cohort | ICS gE |

* Visit 4 occurred within Months 4 to 13 for a blood Sampling at the start of the last cycle of chemotherapy. This visit coincided with the subject's lowest immune status.
** Applicable subjects were eligible for Visit 4 if their last cycle of chemotherapy was at least two months after the previous Blood Sampling (V3/M2).
Vacc = Vaccination; CMI = Cell-Mediated Immunity; Ab = Antibody; gE = Glycoprotein E;
ELISA = Enzyme-linked Immunosorbent Assay; ICS = Intracellular cytokine staining
No other assays than those stipulated in this section were performed at the time of this report.


### 5.7.4. Immunological correlates of protection

No generally accepted immunological correlate of protection has been demonstrated as of this report date for the gE antigen used in HZ/su.

### 5.8. Assessment of safety variables

The description of the assessment of safety events is provided in the subsections 5.8.1, 5.8.2, 5.8.3, 5.8.4 and 5.8.5. Details of procedures to report events to GSK are provided in the protocol.

During the active phase of the study, an iSRC performed safety data monitoring (see Section 2).

### 5.8.1. Adverse events

The standard definition for AE was provided in the protocol.
The investigator or site staff was/were responsible for the detection, documentation and reporting of events meeting the criteria and definition of an AE or serious SAE as provided in this protocol.

Each subject was instructed to contact the investigator immediately should they manifest any signs or symptoms they perceived as serious.

As a consistent method of collecting AEs, the subject was asked a non-leading question such as:
'Have you felt different in any way since receiving the vaccine or since the previous visit?'

When an AE/SAE occurred, it was the responsibility of the investigator to review all documentation (e.g. hospital progress notes, laboratory, and diagnostics reports) relative to the event. The investigator then recorded all relevant information regarding an AE/SAE on the eCRF or SAE screens as applicable. The investigator attempted to establish a diagnosis pertaining to the event based on signs, symptoms, and/or other clinical information. In such cases, the diagnosis was documented as the AE/SAE and not the individual signs/symptoms.

After each vaccination, a diary card was provided to the subjects by study staff/investigator for daily recording of:

- solicited symptoms from Days 0 to 6 after each vaccination;
- unsolicited symptoms from Days 0 to 29 after each vaccination;
- any medication/vaccination taken from Days 0 to 29 after each vaccination.

The subjects were trained on how to complete the diary cards (refer for Section 5.2.2 for details on process in case of illiterate subjects or subjects having difficulty in selfcompletion of diary cards).

The local (injection-site) AEs described in Table 14 were solicited.

## Table 14 Solicited local adverse events

## Solicited local AEs

Pain at injection site
Redness at injection site
Swelling at injection site

### 5.8.1.1. Solicited general adverse events

The general AEs described in Table 15 were solicited.
Table 15 Solicited general adverse events

| Solicited general AEs |
| :--- |
| Fever |
| Headache |
| Fatigue |
| Myalgia |
| Gastrointestinal symptoms ${ }^{\dagger}$ |
| Shivering |
| $\dagger$ Gastrointestinal symptoms include nausea, vomiting, diarrhoea and/or abdominal pain. |

Note: Temperature was recorded in the evening. Should additional temperature measurements have been performed at other times of day, the highest temperature was to be recorded in the eCRF.

All AEs other than the solicited AEs were to be recorded as UNSOLICITED AEs.

Intercurrent medical conditions (see Section 5.3.4.5) were recorded from Month 0 until study end. Intercurrent medical conditions were recorded in AE/SAE screens as appropriate.

The occurrence of HZ constituted an $\mathrm{AE} / \mathrm{SAE}$ as appropriate. The reporting period for cases of HZ was from Month 0 to study end.

Refer to Sections 5.8.1.3 and 5.8.3 for assessment of SAEs and potential immunemediated diseases (pIMDs), respectively.

### 5.8.1.2. Assessment of intensity

The intensity of the following solicited AEs was assessed as described in Table 16.
Table 16 Intensity scales for solicited symptoms

| Adverse Event | Intensity grade | Parameter |
| :---: | :---: | :---: |
| Pain at injection site | 0 | None |
|  | 1 | Mild: Any pain neither interfering with nor preventing normal every day activities |
|  | 2 | Moderate: Painful when limb was moved and interferes with every day activities |
|  | 3 | Severe: Significant pain at rest. Prevents normal every day activities |
| Redness at injection site |  | Greatest surface diameter in mm recorded |
| Swelling at injection site |  | Greatest surface diameter in mm recorded |
| Fever* |  | Temperature in ${ }^{\circ} \mathrm{C} /{ }^{\circ} \mathrm{F}$ recorded |
| Headache | 0 | Normal |
|  | 1 | Mild: Headache that was easily tolerated |
|  | 2 | Moderate: Headache that interfered with normal activity |
|  | 3 | Severe: Headache that prevented normal activity |
| Fatigue | 0 | Normal |
|  | 1 | Mild: Fatigue that was easily tolerated |
|  | 2 | Moderate: Fatigue that interfered with normal activity |
|  | 3 | Severe: Fatigue that prevented normal activity |
| Gastrointestinal symptoms (nausea, vomiting, diarrhoea and/or abdominal pain) | 0 | Gastrointestinal symptoms normal |
|  | 1 | Mild: Gastrointestinal symptoms that were easily tolerated |
|  | 2 | Moderate: Gastrointestinal symptoms that interfered with normal activity |
|  | 3 | Severe: Gastrointestinal symptoms that prevented normal activity |
| Myalgia | 0 | Normal |
|  | 1 | Mild: Myalgia that was easily tolerated |
|  | 2 | Moderate: Myalgia that interfered with normal activity |
|  | 3 | Severe: Myalgia that prevented normal activity |
| Shivering | 0 | None |
|  | 1 | Shivering that was easily tolerated |
|  | 2 | Shivering that interfered with normal activity |
|  | 3 | Shivering that prevented normal activity |

${ }^{*}$ Fever was defined as temperature $\geq 37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ on oral, axillary or tympanic setting, or $\geq 38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$ on rectal setting. The preferred route for recording temperature in this study was oral.
For this study, no temperature grading was used except for the solicited pooled analyses. For solicited pooled analyses the standard GSK rule temperature (measured by oral, axillary or tympanic route) was scored as follows: $0:<37.5^{\circ} \mathrm{C} ; 1: 37.5^{\circ} \mathrm{C}$ to $38.0^{\circ} \mathrm{C} ; 2: 38.1^{\circ} \mathrm{C}$ to $39.0^{\circ} \mathrm{C} ; 3:>39.0^{\circ} \mathrm{C}$.

The maximum intensity of local injection site redness/swelling was scored at GSK Biologicals using GSK Biologicals' standard grading scale based on the US Food and Drug Administration (FDA) guidelines for Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers enrolled in Preventive Vaccine Clinical Trials" [FDA, 2007].

| 0 | $:$ | $<20 \mathrm{~mm}$ diameter |
| :--- | :--- | :--- |
| 1 | $:$ | $\geq 20 \mathrm{~mm}$ to $\leq 50 \mathrm{~mm}$ diameter |
| 2 | $:$ | $>50 \mathrm{~mm}$ to $\leq 100 \mathrm{~mm}$ diameter |
| 3 | $:$ | $>100 \mathrm{~mm}$ diameter |

The investigator assessed the maximum intensity that occurred over the duration of the event for all unsolicited AEs (including SAEs) recorded during the study. The assessment was based on the investigator's clinical judgement.

The intensity was assigned to one of the following categories:

| 1 (mild) | $=\mathrm{An} \mathrm{AE}$ which was easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities. |
| :---: | :---: |
| 2 (moderate) | $=\mathrm{An} \mathrm{AE}$ which was sufficiently discomforting to interfere with normal everyday activities. |
| 3 (severe) | $=$ An AE which prevented normal, everyday activities. Such an AE would, for example have prevented attendance at work and would have necessitated the administration of medication or other medical treatment. |

An AE that was assessed as Grade 3 (severe) should not have been confused with a SAE. Grade 3 was a category used for rating the intensity of an event; and both AEs and SAEs could be assessed as Grade 3. An event was defined as 'serious' when it met one of the pre-defined outcomes as described in the protocol.

### 5.8.1.3. Assessment of causality

The investigator was obligated to assess the relationship between investigational product and the occurrence of each AE/SAE. The investigator used clinical judgement to determine the relationship. Alternative plausible causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors, and the temporal relationship of the event to the investigational product were considered and investigated. The investigator also consulted the Investigator Brochure to determine his/her assessment.

All solicited local (injection site) reactions were considered causally related to vaccination. Causality of all other AEs was assessed by the investigator using the following question:

Is there a reasonable possibility that the AE may have been caused by the investigational vaccine/product?

YES : There was a reasonable possibility that the vaccine(s) contributed to the AE.

NO : There was no reasonable possibility that the AE is causally related to the administration of the study vaccine(s). There were other, more likely causes and administration of the study vaccine(s) was not suspected to have contributed to the AE.

If an event met the criteria to be determined as 'serious', additional examinations/tests were performed by the investigator in order to determine ALL possible contributing factors for each SAE.

Possible contributing factors included:

- Medical history.
- Other medication.
- Protocol required procedure.
- Other procedure not required by the protocol.
- Lack of efficacy of the vaccine, if applicable.
- Erroneous administration.
- Other cause (specify).


### 5.8.1.4. Assessment of outcomes

The investigator assessed the outcome of all unsolicited AEs (including SAEs) recorded during the study as:

- Recovered/resolved.
- Recovering/resolving.
- Not recovered/not resolved.
- Recovered with sequelae/resolved with sequelae.
- Fatal (SAEs only).


### 5.8.1.5. Medically attended visits

For each solicited and unsolicited symptom the subject experienced, during the applicable reporting period (see Section 5.8.1), the subject was asked if he/she received medical attention defined as hospitalisation, or an otherwise unscheduled visit to or from medical personnel for any reason, including emergency room visits. This information was recorded in the eCRF.

### 5.8.1.6. Follow-up of AEs and SAEs

### 5.8.1.6.1. Follow-up during the study

After the initial $\mathrm{AE} / \mathrm{SAE}$ report, the investigator was required to proactively follow each subject and provide additional relevant information on the subject's condition to GSK Biologicals.

All SAEs, IMCs and pIMDs (serious or non-serious) at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving were reviewed at subsequent visits/contacts until the end of the study.

All AEs documented at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving were reviewed at subsequent visits/contacts until 30 days after the last vaccination.

### 5.8.1.6.2. Follow-up after the subject is discharged from the study

The investigator followed subjects:

- with SAEs, pIMDs (serious or non-serious), or subjects withdrawn from the study as a result of an AE, until the event had resolved, subsided, stabilised, disappeared, or until the event was otherwise explained, or the subject was lost to follow-up.

If the investigator received additional relevant information on a previously reported SAE, he/she provided this information to GSK Biologicals.

GSK Biologicals could request that the investigator performed or arranged the conduct of additional clinical examinations/tests and/or evaluations to elucidate as fully as possible the nature and/or causality of the AE or SAE. The investigator was obliged to assist. If a subject died during participation in the study or during a recognised follow-up period, GSK Biologicals was to be provided with any available post-mortem findings, including histopathology.

### 5.8.1.7. Treatment of adverse events

Treatment of any AE was at the sole discretion of the investigator and according to current good medical practice. Any medication administered for the treatment of an AE should be recorded in the subject's eCRF (refer to Section 5.6.1).

### 5.8.2. Serious adverse events

The standard definition for SAE is provided in the protocol.
The period for collecting and recording SAEs began at the first receipt of study vaccine/placebo and ended at Month 13 (study end), i.e., approximately 12 months following administration of the last dose of study vaccine/ placebo for each subject.

In addition to the above-mentioned reporting requirements and in order to fulfil international reporting obligations, SAEs that were related to study participation (i.e. protocol-mandated procedures, invasive tests, a change from existing therapy) or were related to a concurrent GSK medication/vaccine were collected and recorded from the time the subject consented to participate in the study until she/he was discharged from the study.

A post-study AE/SAE was defined as any event that occurred outside of the AE/SAE reporting period. Investigators were not obligated to actively seek AEs or SAEs in former study participants. However, if the investigator learned of any SAE at any time after a subject had been discharged from the study, and he/she considered the event reasonably related to the investigational vaccine/product, the investigator promptly notifed the Study Contact for Reporting SAEs.

SAEs were evaluated as described in Section 5.8.1.

### 5.8.3. Potential immune-mediated diseases

pIMDs were a subset of AEs that included autoimmune diseases and other inflammatory and/or neurologic disorders of interest which might or might not have an autoimmune aetiology. AEs that needed to be recorded and reported as pIMDs include those listed in Table 17.

However, the investigator exercised his/her medical and scientific judgement in deciding whether other diseases had an autoimmune origin (i.e., pathophysiology involving systemic or organ-specific pathogenic autoantibodies) and were also to be recorded as a pIMD.

The period for collecting and recording of pIMDs began at the first receipt of study vaccine/ placebo and ended at Month 13 (study end), i.e., approximately 12 months following administration of the last dose of study vaccine/placebo.

Table 17 List of potential immune-mediated diseases

| Neuroinflammatory disorders |  | Musculoske | orders | Skin disorders |
| :---: | :---: | :---: | :---: | :---: |
| - Cranial nerve disorders, including paralyses/paresis (e.g. Bell's palsy) <br> - Optic neuritis <br> - Multiple sclerosis <br> - Transverse myelitis <br> - Guillain-Barré syndrome, including Miller Fisher syndrome and other variants <br> - Acute disseminated encephalomyelitis, including site specific variants: e.g. noninfectious encephalitis, encephalomyelitis, myelitis, myeloradiculoneuritis <br> - Myasthenia gravis, including LambertEaton myasthenic syndrome <br> - Immune-mediated peripheral neuropathies and plexopathies, (including chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy and polyneuropathies associated with monoclonal gammopathy). <br> - Narcolepsy |  | - Systemic lupus erythematosus and associated conditions <br> - Systematic Scleroderma (Systematic sclerosis), including diffuse systemic form and CREST syndrome <br> - Idiophatic inflammatory myopathies, including Dermatomyositis, Polymyositis <br> - Antisynthetase syndrome <br> - Rheumatoid arthritis and associated conditions, including Juvenile chronic arthritis and Still's disease <br> - Polymyalgia rheumatic <br> - Spondyloarthritis, including ankylosing spondylitis, reactive arthritis (Reiter's Syndrome) and undifferentiated spondyloarthritis <br> - Psoriatic arthropathy <br> - Relapsing polychondritis <br> - Mixed connective tissue disorder |  | - Psoriasis <br> - Vitiligo <br> - Erythema nodosum <br> - Autoimmune bullous skin diseases (including pemphigus, pemphigoid and dermatitis herpetiformis) <br> - Alopecia areata <br> - Lichen planus <br> - Sweet's syndrome <br> - Localised Scleroderma (Morphoea) |
| Liver disorders |  | rointestinal disorders |  | crine disorders |
| - Autoimmune hepatitis <br> - Primary biliary cirrhosis <br> - Primary sclerosing cholangitis <br> - Autoimmune cholangitis |  | mmatory Bowel ase, including Crohn's se, ulcerative colitis, scopic colitis, ative proctitis c disease mmune pancreatitis | - Autoimm Hashimo <br> - Grave's <br> - Diabetes <br> - Addison' <br> - Polyglan syndrom <br> - Autoimm | une thyroiditis (including <br> o thyroiditis) <br> r Basedow's disease <br> mellitus type I <br> disease <br> dular autoimmune <br> une hypophysitis |
| Vasculitides |  | Blood disorders |  | Others |
| - Large vessels vasculitis including: giant cell arteritis such as Takayasu's arteritis and temporal arteritis. <br> - Medium sized and/or small vessels vasculitis including: polyarteritis nodosa, Kawasaki's disease, microscopic polyangiitis, Wegener's granulomatosis, Churg-Strauss syndrome (allergic granulomatous angiitis), Buerger's disease (thromboangiitis obliterans), necrotizing vasculitis and antineutrophil cytoplasmic antibody (ANCA) positive vasculitis (type unspecified), Henoch-Schonlein purpura, Behcet's syndrome, leukocytoclastic vasculitis. |  | mmune hemolytic <br> ia <br> mmune <br> mocytopenia <br> hospholipid syndrome <br> icious anemia <br> mmune aplastic <br> ia <br> mmune neutropenia <br> mmune pancytopenia | - Autoimm (including glomerul progress glomerul membran glomerul mesangi glomerul <br> - Ocular a (including autoimm <br> - Autoimm myocardi <br> - Sarcoido <br> - Stevens- <br> - Sjögren's <br> - Idiopathic <br> - Goodpas <br> - Raynaud' | une glomerulonephritis <br> IgA nephropathy, <br> nephritis rapidly <br> ve, membranous <br> nephritis, <br> oproliferative <br> onephritis, and <br> proliferative <br> nephritis) <br> toimmune diseases <br> autoimmune uveitis and <br> ne retinopathy <br> une <br> is/cardiomyopathy <br> is <br> Johnson syndrome <br> syndrome <br> pulmonary fibrosis <br> ture syndrome <br> s phenomenon |

When there was enough evidence to make any of the above diagnoses, the AE was to be reported as a pIMD. Symptoms, signs or conditions which might (or might not) have represented the above diagnoses, were to be recorded and reported as AEs but not as pIMDs until the final or definitive diagnosis was determined, and alternative diagnoses were eliminated or shown to be less likely.

In order to facilitate the documentation of pIMDs in the eCRF, a pIMD standard questionnaire and a list of preferred terms (PTs) and PT codes corresponding to the above diagnoses were available to investigators at study start.

### 5.8.4. Pregnancy

For female subjects of childbearing potential, a urine specimen was collected at the Prevaccination Visit, Visit 1 (Month 0 ) and Visit 2 (Month 1). In the study there were no subjects requiring a serum pregnancy test at Visit 1 or Visit 2 per local or ethics committee regulation.

Female subjects who were pregnant or lactating at the time of vaccination were not to receive additional doses of study vaccine/placebo but could continue other study procedures at the discretion of the investigator.

While pregnancy itself was not considered an AE or SAE, any adverse pregnancy outcome or complication or elective termination of a pregnancy for medical reasons was to be recorded and reported as an AE or a SAE. Refer to the protocol for information regarding adverse pregnancy outcomes always to be considered as an SAE.

Note: The pregnancy itself was always to be recorded on an electronic pregnancy report. Pregnancy which occurred prior to first vaccination did not need to be reported on an electronic pregnancy report.

Furthermore, any SAE occurring as a result of a post-study pregnancy AND considered by the investigator to be reasonably related to the investigational vaccine(s)/product(s) were to be reported to GSK Biologicals. While the investigator was not obligated to actively seek this information from former study participants, he/she might have learned of a pregnancy through spontaneous reporting.

Pregnant subjects were to be followed to determine the outcome of the pregnancy. At the end of the pregnancy, whether full-term or premature, information on the status of the mother and child were to be forwarded to GSK Biologicals. Generally, the follow-up period did not need to be longer than six to eight weeks after the estimated date of delivery.

Regardless of the reporting period for SAEs for this study, if the pregnancy outcome was a SAE, it was always to be reported as SAE.

### 5.8.5. Clinical laboratory parameters and other abnormal assessments qualifying as adverse events or serious adverse events

In absence of diagnosis, abnormal laboratory findings (e.g. clinical chemistry, haematology, urinalysis) or other abnormal assessments that were judged by the investigator to be both clinically significant and unexpected, considering the specific underlying disease and chemotherapy, were recorded as either an AE or SAE as based on whether they meet the definition of an AE or SAE. Clinically significant abnormal laboratory findings or other abnormal assessments that were present at baseline and following the start of the study, significantly worsened as judged by the investigator and were also unexpected, considering the underlying disease and chemotherapy, were also to be reported as AEs or SAEs.

The investigator exercised his or her medical and scientific judgement in deciding whether an abnormal laboratory finding or other abnormal assessment was clinically significant.

### 5.9. Statistical methods

The statistical analyses were performed using the SAS software (SAS Institute Inc, Cary, NC, US).

### 5.9.1. Primary endpoints

- Anti-gE humoral immunogenicity with respect to components of the study/investigational vaccine.
- Anti-gE Ab concentrations as determined by ELISA at Month 2.
- Occurrence of solicited local and general symptoms.
- Occurrence, intensity and duration of each solicited local symptom within 7 days (Days 0-6) after each vaccination.
- Occurrence, intensity, duration and relationship to vaccination of each solicited general symptom within 7 days (Days 0-6) after each vaccination.
- Occurrence of unsolicited AEs.
- Occurrence, intensity and relationship to vaccination of unsolicited AEs during 30 days (Days $0-29$ ) after each vaccination, according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence of SAEs.
- Occurrence and relationship to vaccination of SAEs up to 30 days post last vaccination.
- Occurrence of AEs of specific interest.
- Occurrence and relationship to vaccination of any pIMDs up to 30 days post last vaccination.


### 5.9.2. Secondary endpoints

- For immunogenicity with respect to components of the study/investigational vaccine.
- Anti-gE Ab concentrations as determined by ELISA at Month 0, Month 1, Month 2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13.
- Vaccine response for anti-gE Abs at Month 1, Month 2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13.
- Frequencies of gE-specific CD4+ T-cells, expressing at least 2 activation markers (from among IFN- $\gamma$, IL-2, TNF- $\alpha$ and CD40 $\mathrm{L}^{3}$ ), as determined by in vitro ICS, at Month 0 , Month 1 , Month 2, and Month 13.
- Vaccine response for gE-specific CD4+ T-cells expressing at least 2 activation markers (from among IFN- $\gamma$, IL-2, TNF- $\alpha$ and CD40L), as determined by in vitro ICS, at Month 1, Month 2 and Month 13.
- Occurrence of SAEs.
- Occurrence and relationship to vaccination of SAEs during the period starting after 30 days post last vaccination until study end.
- Occurrence of AEs of specific interest.
- Occurrence of any pIMDs during the period starting after 30 days post last vaccination until study end.


### 5.9.3. Determination of sample size

### 5.9.3.1. Sample size assumptions for humoral immune response endpoint

Refer to the protocol for assumptions made and details regarding the determination of the sample size required for the humoral immune response endpoints. Refer also to Section 5.3 for details regarding the provisional and actual sample size for ZOSTER-028.

Regarding the primary humoral immunogenicity endpoint, a 12.5 -fold increase over placebo and a minimum of 3-fold increase in GM as lower limit was assumed for the analyses on PreChemo subjects. The type 1 error to $2.5 \%$ one-sided was used. To obtain a power of at least $90 \%$ to see a minimum of 3 -fold increase as lower limit in anti-gE humoral immune response over placebo, assuming a 12.5 -fold increase between placebo to HZ/su, 67 evaluable subjects per treatment group were needed. A sample size of 93 subjects was targeted assuming a $27 \%$ loss rate from drop-out and non-evaluable subjects at Month 2 (see also Table 18). Assuming an $80 \%$ VRR, and 67 evaluable subjects in the $\mathrm{HZ} / \mathrm{su}$ group, there was a power of more than $92 \%$ to demonstrate that the vaccine response in the HZ/su PreChemo Group was significantly greater than $60 \%$.

[^2]For the analyses on all subjects, an 8-fold increase over placebo and a minimum of 3-fold increase in GM as lower limit of the $95 \%$ CI have been assumed. The 84 evaluable subjects per treatment group provided at least $71 \%$ power to see a minimum of 3 -fold increase in anti-gE humoral immune response over placebo. Assuming a $27 \%$ loss rate from drop-out and non-evaluable subjects at Month 2, 232 screened and eligible subjects were to be enrolled and vaccinated. The 84 evaluable subjects in the HZ/su group provided at least $44 \%$ power to demonstrate that the vaccine response in the HZ/su group (all subjects) was significantly greater than $60 \%$. Assuming a $27 \%$ loss rate from dropout and non-evaluable subjects at Month 2, 116 subjects were to be enrolled in the HZ/su group (see also Table 18).

### 5.9.3.2. Sample size assumptions for CMI

Refer to the protocol for assumptions made and details regarding the determination of the sample size required for the CMI endpoints.

At least 30 evaluable subjects per treatment group (only PreChemo groups) were needed to reach approximately $78 \%$ power to demonstrate a significant increase over placebo in frequency of gE-specific CD4+ T-cells producing at least 2 activation markers (gEspecific CD4[2+] T-cells). Assuming an $\sim 20 \%$ loss rate from drop-out and non-evaluable subjects at Month 2, the total number of subjects enrolled into the sub-cohort was to be $\sim 38$ per group (see also Table 18).

Assuming an $80 \%$ VRR, and 30 evaluable subjects, there was a power of more than $93 \%$ to demonstrate that the VRR for gE-specific CD4[2+] T-cell frequencies in the HZ/su PreChemo Group was significantly greater than $50 \%$.

Table 18 Estimated number of subjects for assessment of confirmatory objectives

| Evaluation of confirmatory <br> objectives | Study groups | Overall <br> N <br> (targeted <br> enrolment <br> subjects)* | Number of <br> evaluable subjects <br> required |
| :--- | :--- | :--- | :--- |
| Evaluation of humoral <br> immunogenicity in the PreChemo <br> group | HZ/su-PreChemo | 93 | 67 |
| Evaluation of CMI in the PreChemo <br> group | Placeb-PreChemo | HZ/su-PreChemo | 93 |
| Evaluation of humoral | Placeb-PreChemo | 38 | 30 |
| immunogenicity in all subjects | HZ/su (Pre-Chemo + OnChemo) | 116 | 84 |
|  | Placeb (Pre-Chemo + OnChemo) | 116 | 84 |

HZ/su = Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb = Placebo

* Target number of screened and eligible subjects, taking into account drop out and non-evaluable subjects at Month 2


### 5.9.4. Study cohorts /data sets analysed

### 5.9.4.1. Total Vaccinated Cohort

Note: All subjects with signed ICF and screened belonged to the Total Enrolled Cohort.
The TVC included all vaccinated subjects with respect to the vaccine actually administered.

The TVC for analysis of humoral immunogenicity included all vaccinated subjects for whom data related to humoral immunogenicity endpoints were available.

The TVC for analysis of CMI included all vaccinated subjects who where selected for the CMI sub-cohort (see Section 5.4.3.3) and for whom data related to CMI endpoints were available.

The TVC for analysis of safety included all subjects with at least one vaccine dose administered.

The TVC for analysis of reactogenicity included all subjects with at least one vaccine administration documented.

### 5.9.4.2 $\quad$ ATP cohort for analysis of safety - up to $\mathbf{3 0}$ days post last vaccination

The ATP cohort for safety - up to 30 days post last vaccination included all eligible subjects:

- who had received at least one dose of study vaccine/placebo according to their random assignment;
- for whom administration site of study vaccine/placebo was known;
- for whom administration of study vaccine/placebo was done according to protocol;
- who had not received other vaccine forbidden in the protocol up to 30 days post last vaccination;
- for whom the randomisation code had not been broken;
- who had not received study vaccine (effective treatment number) despite a temperature deviation;
- who had not received study vaccine (effective treatment number) out of the expiration date at the time of administration.


### 5.9.4.3. ATP cohort for safety - up to the study end

The ATP cohort for safety - up to the study end included all eligible subjects:

- who had received at least one dose of study vaccine/placebo according to their random assignment;
- for whom administration site of study vaccine/placebo was known;
- for whom administration of study vaccine/placebo was done according to protocol;
- who had not received other vaccine forbidden in the protocol during the entire study period;
- for whom the randomisation code had not been broken;
- who had not received study vaccine (effective treatment number) despite a temperature deviation;
- who had not received study vaccine (effective treatment number) out of the expiration date at the time of administration.


### 5.9.4.4. ATP cohort for Humoral immunogenicity

The ATP cohort for Humoral immunogenicity included all evaluable subjects from the ATP cohort for safety - up to 30 days post last vaccination:

- Who met all eligibility criteria (refer to Sections 5.3.2and 5.3.3);
- Who complied with the procedures and intervals defined below:

The immune ATP cohort analysis was based on the allowed intervals for Visit $1 \rightarrow$ Visit 2 and Visit $2 \rightarrow$ Visit 3. The allowed interval between vaccinations for inclusion in the ATP cohort was defined as 30-84 days. The allowed interval between dose 2 and blood sample at Visit 3 for inclusion in the ATP cohort was defined as 21-63 days (see Table 19).

## Table 19 Intervals between study visits for the ATP cohort for analysis of immunogenicity

| Interval between visits | Allowed interval for the ATP cohort for analysis of immunogenicity |
| :--- | :--- |
| Visit $1 \rightarrow$ Visit 2 | $30-84$ days |
| Visit $2 \rightarrow$ Visit 3 | $21-63$ days |

- who did not receive a medication leading to elimination from an ATP analysis up to Month 2 visit;
- who did not present with a medical condition leading to elimination from an ATP analysis up to Month 2 visit;
- for whom there was no concomitant infection (related or not to the vaccine) which may influence immune response up to Month 2 visit;
- for whom data concerning immunogenicity endpoint measures were available at Month 2 visit;
- for whom no obvious incoherence, abnormal serology evolution or error in data was shown;
- who completed the full vaccination course (2 doses).


### 5.9.4.5. ATP cohort for analysis of humoral persistence

The ATP cohort for analysis of humoral persistence included all evaluable subjects from the ATP cohort for safety analysis up to study end:

- Who met all eligibility criteria (refer to Sections 5.3.2 and 5.3.3).
- Who complied with the procedures and intervals defined below:

The immune ATP cohort for analysis of humoral persistence was based on the allowed intervals for Visit $1 \rightarrow$ Visit 2 and Visit $2 \rightarrow$ Visit 5 . The allowed interval between vaccinations for inclusion in the ATP cohort was defined as 30-84 days. The allowed interval between dose 2 and blood sample at Visit 5 for inclusion in the ATP cohort was defined as 335-425 days (see Table 20).

## Table 20 Intervals between study visits for the ATP cohort for analysis of humoral persistence

| Interval between visits | Allowed interval for the ATP cohort for analysis of humoral <br> persistence |
| :--- | :--- |
| Visit $1 \rightarrow$ Visit 2 | $30-84$ days |
| Visit $2 \rightarrow$ Visit 5 | $335-425$ days |

- who did not receive a medication leading to elimination from an ATP analysis up to Month 13 visit,
- who did not present with a medical condition leading to elimination from an ATP analysis up to Month 13 visit.
- for whom there was no concomitant infection (related or not to the vaccine) which could influence immune response up to Month 13 visit;
- for whom data concerning immunogenicity endpoint measures were available at Month 13 visit.
- for whom no obvious incoherence, abnormal serology evolution or error in data was shown;
- who completed the full vaccination course (2 doses).


### 5.9.4.6. ATP cohort for CMI immunogenicity

The ATP cohort for CMI immunogenicity included all evaluable subjects from the ATP cohort for Humoral immunogenicity analyses and included in the CMI sub-cohort.

### 5.9.4.7. ATP cohort for CMI persistence

The ATP cohort for CMI persistence included all evaluable subjects from the ATP cohort for Humoral persistence analyses and included in the CMI sub-cohort and for whom no obvious incoherence, abnormal serology evolution or error in data (CMI) was shown.

Note: For the immunogenicity tables where different timepoints from both study phases (i.e., active phase, persistence) were presented, the concept of 'Adapted ATP cohort for Humoral immunogenicity' and 'Adapted ATP cohort for CMI-immunogenicity' was used to denote that for each phase, the corresponding ATP cohort was used.

More specifically,

- The analyses on the active phase timepoints Months 0,1 and 2 were based on the ATP cohort for Humoral immunogenicity/ CMI-immunogenicity;
- The analyses on the persistence timepoints Months 6 (for Humoral immunogenicity only) and 13 were based on the ATP cohort for Humoral persistence/ CMI persistence.


### 5.9.5. Derived and transformed data

### 5.9.5.1. Handling of missing data

For a given subject and a given measurement, missing or non-evaluable measurements were not imputed for the primary analysis. The missing endpoint and censoring were supposed to occur independently, and the pattern of the missing value(s) being either Missing Completely At Random (MCAR) or Missing At Random (MAR) only.

For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore, the analysis of the solicited symptoms based on the TVC included only subjects/doses with documented safety data (i.e., symptom screen/sheet completed).

For the analysis of unsolicited AEs/SAEs/pIMDs/concomitant medications, all vaccinated subjects were considered and subjects who did not report an event were considered as subjects without an event.

For the analysis of immunogenicity, missing or non-evaluable measurements were not replaced. Therefore, a subject was excluded from an analysis if all measurements were missing or non-evaluable.

For a given subject and a given demographic variable, a missing measurement was not replaced except for age.

### 5.9.5.2. Demography

Age was calculated as the number of years between the date of birth and the date of first vaccination.

In case of partial dates of any of these 2 dates:

- 15 th of month, if only the day is missing
- 30th of June, if day and months are missing


### 5.9.5.3. Humoral immune response

- A seronegative subject was a subject whose Ab concentration was below the cut-off value.
- A seropositive subject was a subject whose Ab concentration was greater than or equal to the cut-off value.
- The seropositivity rate was defined as the percentage of seropositive subjects.
- The VRR for anti-gE was defined as the percentage of subjects who had at least a:
- 4-fold increase in the anti-gE antibodies concentration as compared to the prevaccination anti-gE antibodies concentration, for subjects who were seropositive at baseline, or,
- 4-fold increase in the anti-gE antibodies concentration as compared to the anti-gE antibodies cut-off value for seropositivity, for subjects who were seronegative at baseline.
- The geometric mean concentrations (GMCs) calculations were performed by taking the anti-log of the mean of the log concentration transformations. For descriptive statistics only, Ab concentrations below the cut-off of the assay $(97 \mathrm{mIU} / \mathrm{mL})$ were given an arbitrary value equal to half the cut-off for the purpose of GMC calculation.
For inferential analyses, the values below the cut-off were considered as missing.


### 5.9.5.4. Cellular-mediated immune response

- For the inferential analysis, the frequency of CD4+ T-cells producing at least 2 activation markers (IFN- $\gamma$, IL-2, TNF- $\alpha$ and/or CD40L, termed CD4 [2+]) upon in vitro stimulation with the gE-antigen (induction condition) was calculated by adding an offset of 0.5 to the number of activated CD4+ T-cells (numerator) divided by the total number of CD4+ T-cells involved (denominator). A similar calculation was made for the frequency of $\mathrm{CD} 4[2+]$ upon in vitro stimulation in medium only (background condition).

Freq $_{\text {Induction }}^{\text {CD4 }[2+]}=\frac{n_{\text {Induction }}^{2+}+0.5}{N_{\text {Induction }}^{C O 4}}$
Freq $_{\text {Background }}^{\text {CD4 }[2+]}=\frac{n_{\text {Background }}^{2+}+0.5}{N_{\text {Background }}^{\text {CD4 }}}$
$\log _{e}\left(\operatorname{Freq}_{\text {Induction }}^{C D 4}[2+]=\log _{e}\left(\frac{n_{\text {Induction }}^{2+}+0.5}{N_{\text {Induction }}^{C D 4}}\right)\right.$

$n_{\text {Induction }}^{2+}=$ number of CD4 T - cells secreting at least 2 activation markers after induction with the gE - antigen
$n_{\text {Background }}^{2+}=$ number of CD4 T -cells secreting at least 2 activation markers in the medium conditions
$N^{C D 4}=$ Total number of CD4 T-cells involved in the assay (induction of background)

- For the descriptive analyses, the frequency of CD4[2+] T-cells upon in vitro stimulation with the antigen (induction condition) was calculated by dividing the number of activated CD4[2+] T-cells (numerator) over the total number of CD4+ Tcells involved (denominator). The same calculation was performed for the frequency computation for any kinds of cells and for each individual activation marker as appropriate.

Freq ${ }_{\text {Induction }}^{C D 4[2+]}=\frac{n_{\text {Induction }}^{2+}}{N_{\text {Induction }}^{C D}}$
$n_{\text {Induction }}^{2+}=$ number of CD4 $\mathrm{T}-$ cells secreting at least 2 activation s markers after inductions with the antigen
$N^{C D 4}=$ Total number of CD4 $\mathrm{T}-$ cells involved in the assay (induction )

- The frequency of gE-specific CD4+ T-cells for each individual subject was calculated as the difference between the frequency of CD4[2+], upon in vitro stimulation with the gE-antigen (induction condition) minus the frequency of (CD4[2+] upon in vitro stimulation in medium only (background condition). For differences less or equal to one (1), the value 1 is imputed for $g E$-specific CD4[2+] T-cell per $10^{6} \mathrm{CD} 4+\mathrm{T}$-cells. The same calculation was performed for the frequency computation for any kinds of cells and for each individual activation marker as appropriate.

Freq $_{\text {Specific }}^{C D 4[2+]}=\frac{n_{\text {Induction }}^{2+}}{N_{\text {Induction }}^{C D 4}}-\frac{n_{\text {Background }}^{2+}}{N_{\text {Background }}^{\text {CD4 }}}$

$$
\text { if } \frac{n_{\text {Induction }}^{2+}}{N_{\text {Induction }}^{\text {CD4 }}}>1+\frac{n_{\text {Background }}^{2+}}{N_{\text {Background }}^{\text {CD4 }}}
$$

Freq $_{\text {Specific }}^{C D 4[2+]}=1$
$n_{\text {Induction }}^{2+}=$ number of CD4 T-cells secreting at least 2 activation markers after induction with the gE - antigen
$n_{\text {Background }}^{2+}=$ number of CD4 T - cells secreting at least 2 activation markers in the medium conditions
$N^{C D 4}=$ Total number of CD4 T-cells involved in the assay (induction of background )

- The GM frequency calculations were performed by taking the anti-log of the mean of the log frequency transformations;
- The CMI vaccine response to $g E$ were based on the gE-specific data as computed above. The cut-off of 320 positive events $/ 10^{6} \mathrm{CD} 4+$ T-cells was used as threshold for vaccine response assessment. The VRR was defined as the percentage of subjects who had at least a:
- 2-fold increase as compared to the threshold, for subjects with pre-vaccination T-cell frequencies below the threshold.
- 2-fold increase as compared to pre-vaccination T-cell frequencies, for subjects with pre-vaccination above the threshold.


### 5.9.5.5. Safety

- For a given subject and the analysis of solicited symptoms within 7 days postvaccination, missing or non-evaluable measurements were not replaced. Therefore, the analysis of the solicited symptoms based on the TVC included only vaccinated subjects for doses with documented safety data (i.e., symptom screen completed). More specifically the following rules were used:
- Subjects who documented the absence of a solicited symptom after one dose were considered not having that symptom after that dose.
- Subjects who documented the presence of a solicited symptom and fully or partially recorded daily measurement over the solicited period were included in the summaries at that dose and classified according to their maximum observed daily recording over the solicited period.
- Subjects who documented the presence of a solicited symptom after one dose without having recorded any daily measurement were assigned to the lowest intensity category at that dose (i.e., $37.5^{\circ} \mathrm{C}$ for fever or grade 1 for other symptoms).
- Doses without symptom sheets documented were excluded.
- For analysis of unsolicited adverse events, such as SAEs, pIMDs or AEs by primary MedDRA term and analysis of relapse, all vaccinated subjects were considered. Subjects who did not report the event or the concomitant medication were considered as subjects without the event or the concomitant medication respectively.
- For analysis of concomitant medications, all vaccinated subjects were considered for the analysis of concomitant medication use. Subjects who did not report the use of a concomitant medication were considered as subjects without medication. Subjects who started the use of a concomitant medication during the mentioned period and took at least one dose were considered in these analyses.

The way the percentage of subjects was derived depended on the event analysed (see the following table for details). As a result, the denominator ( N ) differed from one table to another.

| Event | N used for deriving \% | Terminology used in the tables for N |
| :--- | :--- | :--- |
| Concomitant <br> medication | All vaccinated subjects | Number of subjects with at least one <br> administered dose |
| Solicited general <br> symptom | All vaccinated subjects with at least <br> one solicited general symptom <br> documented as either present or <br> absent | For each dose and overall/subject: <br> N= number of subjects with at least one <br> documented dose <br> For overall/dose: <br> $\mathrm{N}=$ number of documented doses |
| Solicited local symptom | All vaccinated subjects with at least <br> one solicited local symptom <br> documented as either present or <br> absent | For each dose and overall/subject: <br> $\mathrm{N}=$ number of subjects with at least one <br> documented dose <br> For overall/dose: <br> N= number of documented doses |
| Unsolicited symptom <br> from day 0 to day 30 | All vaccinated subjects | Number of subjects with at least one <br> administered dose |
| SAE/pIMDs | All vaccinated subjects | Number of subjects with at least one <br> administered dose |

- All CI computed were two-sided 95\% CI.


### 5.9.5.5.1. Grading rule

For the analysis of pooled solicited symptoms, pooled general symptoms that included temperature and the analysis of temperature individually, all measurements were converted to the preferred route scale (oral) according to the following rules:

|  | Temperature (route) | rectal |
| :--- | :--- | :--- |
| Grade | Oral/axillary/tympanic | $<38.0^{\circ} \mathrm{C}$ |
| 0 | $<37.5^{\circ} \mathrm{C}$ | $\geq 38.0^{\circ} \mathrm{C}-\leq 38.5^{\circ} \mathrm{C}$ |
| 1 | $\geq 37.5^{\circ} \mathrm{C}-\leq 38.0^{\circ} \mathrm{C}$ | $>38.5^{\circ} \mathrm{C}-\leq 39.5^{\circ} \mathrm{C}$ |
| 2 | $>38.0^{\circ} \mathrm{C}-\leq 39.0^{\circ} \mathrm{C}$ | $>39.5^{\circ} \mathrm{C}$ |
| 3 | $>39.0^{\circ} \mathrm{C}$ |  |

Note that fever was defined as temperature $\geq 37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ for oral, axillary or tympanic route, or $\geq 38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$ for rectal route.

An additional analysis was performed on temperature broken down by route. The summary of temperature was broken by $0.5^{\circ}$ increase starting from $37.5^{\circ}$.

### 5.9.5.5.2. Conversion of temperature to ${ }^{\circ} \mathrm{C}$

The following conversion rule was used for the conversion of temperature to ${ }^{\circ} \mathrm{C}$
Temperature in ${ }^{\circ}$ Celsius $=\left(\left(\right.\right.$ Temperature in ${ }^{\circ}$ Fahrenheit -32 $\left.) * 5\right) / 9$
The result was rounded to 1 decimal digit.

### 5.9.6. Statistical analysis

Statistical analyses were conducted overall and by sub-groups.
The Table 21 presents the sub-group names that will be used for the statistical analyses:

Table 21 Sub-groups description

| Sub-groups | Group order <br> in tables | Group label <br> in tables | Group definition for footnote |
| :--- | :--- | :--- | :--- |
| Age strata | 1 | $18-49 y s$ | Subjects aged between 18 and 49 years |
|  | 2 | $>=50 y s$ | Subjects aged 50 years and older |
| Vaccination <br> relative to <br> chemotherapy <br> cycle | 1 | PreChemo | first vaccination 8 days ${ }^{*}$ or more prior to the <br> start of a chemotherapy cycle |
|  | 2 | OnChemo | first vaccination at the start of a <br> chemotherapy cycle $(+$ or -1 day) |

Subjects assigned to the PreChemo group at randomisation were to receive HZ/su or placebo within a maximum of 1 month to a minimum of 10 days before the administration of chemotherapy. For analyses purposes, a minimum of 8 days instead of 10 days was established in the SAP to accommodate the subjects (see Section 5.11.2). Eight days was considered the minimum allowable window post vaccination to start of chemotherapy cycle that still accommodated the needs of a few subjects able to attend the site on a specific day of the week (e.g. secondary to their available transportation) and who wanted to start chemotherapy with the shortest delay. The observation and interpretation of the immunogenicity/persistence data were not anticipated to be compromised by this minimum modification.

All analyses were performed per treatment actually administered (HZ/su or placebo).
In case a subject was randomised to the PreChemo group or OnChemo group, but the duration between the first dose and the start of the chemotherapy cycle was not consistent with his/her randomisation but was consistent with the other group, the analysis was in accordance with the other group, instead of being completely eliminated from all analyses.

### 5.9.7. Analysis of demographics and other baseline characteristics

Demographic characteristics (age at first study vaccination, gender, geographic ancestry and ethnicity*), cohort description, ECOG performance status, Tumour diagnosis and withdrawal status were summarized using descriptive statistics.

Frequency tables were generated for categorical variables such as gender.
Mean, median and standard deviation (SD) were provided for continuous data such as age.

The same tabulation was performed by age strata and by duration between the first dose and the start of chemotherapy cycle (PreChemo/ OnChemo).

* Where prohibited by local law, ethnicity and geographic ancestry information was not collected (i.e. France). These subjects appear as "Missing" in Demographic characteristics summaries.


### 5.9.8. Analysis of immunogenicity

### 5.9.8.1. Humoral response:

The primary analysis of humoral immunogenicity at Month 0,1 and 2 was based on the ATP cohort for Humoral immunogenicity, whereas the analysis at Month 6 and 13 was based on ATP cohort for Humoral persistence. If the percentage of subjects excluded from either of these ATP cohorts was greater than $5 \%$ in any treatment group, a second analysis based on the Total Vaccinated Cohort was to be performed to complement the ATP analysis.

The humoral descriptive analysis was performed by treatment group, by age strata and by by duration between the first dose and the start of chemotherapy cycle (PreChemo and OnChemo groups).

The following parameters were calculated for the humoral immune response in terms of Anti-gE Ab concentration as determined by ELISA:

### 5.9.8.1.1. Within group assessment

- GMC at Months 0, 1, 2, 6 and 13 with $95 \%$ CI.
- Seropositivity rate at Months $0,1,2,6$ and 13 with exact $95 \%$ CI.
- VRR at Months 1, 2, 6 and 13 with exact $95 \%$ CI.
- Descriptive statistics of the fold over pre-vaccination at Month 1, 2, 6 and 13 (Mean, SD , minimum [Min], first quartile [Q1], Median, third quartile [Q3], maximum [Max]).
- Mean Geometric Increase (MGI) over pre-vaccination were tabulated along with exact $95 \%$ CI at Month 1, 2 and 13 for anti-gE.
- Distribution of the fold increase from baseline at Month 1, 2, 6 and 13 was tabulated per group along with $95 \%$ CI for anti-gE.


### 5.9.8.1.2. Between group assessment

To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy, a repeated measurement model was used to assess the GM fold increase over placebo at month 2. Adjusted GM ratio of HZ/su over Placebo groups for anti-gE Ab ELISA concentrations at Month 2 was calculated and tabulated.

For the assessment of the primary confirmatory objective 'To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy (PreChemo Groups only)', the fixed-effect model included the means for all levels of the visit by treatment interaction effect.

For the assessment of the secondary confirmatory objective "To evaluate the anti-gE humoral immunogenicity response at Month 2, following a two-dose administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (all subjects)', the fixed-effect model included the means for all levels of the visit by treatment interaction effect and for the 2 levels of the first vaccination schedule (OnChemo/PreChemo).

A likelihood-based approach was used to analyse post-vaccination log-transformed antigE Ab concentrations (Month 1 to Month 2).

The pre-vaccination log-transformed Ab concentrations (Month 0 ) were included as a continuous covariate.

The goodness-of-fit Bayesian information criterion and Akaike information criteria AIC statistics were used to assess the need of a separate residual variance for placebo group or for each treatment group. GMs of Month 2 post-vaccination Ab concentrations were calculated conditionally to the means of the log-transformed concentrations at prevaccination calculated across the treatment groups. Adjusted means and difference of means between vaccines and placebo were calculated together with 2-sided CIs and backtransformed to the original units to provide GMCs and GM ratios over Placebo.

A sensitivity analysis including age strata and gender as fixed effect in the model [age strata (2-levels, $<50 \mathrm{YOA}$ and $\geq 50 \mathrm{YOA}$ ), gender (male and female)] was performed. Age strata and gender by treatment and activity interaction were tested. The P-values being higher than 0.1 , they were considered to be excluded from the model.

### 5.9.8.2. CMI response

The primary analysis of CMI immunogenicity at Month 0,1 and 2 was based on the ATP cohort for CMI immunogenicity. Whereas, the analysis at Month 13 was based on ATP cohort for CMI persistence. If the percentage of subjects excluded from either of these ATP cohorts was greater than $5 \%$ in any treatment group, a second analysis based on the Total Vaccinated Cohort for CMI was to be performed to complement the ATP analysis.

The CMI descriptive analysis was performed by treatment group and by age strata (see Section 5.11.2).

The following parameters were calculated for the CMI response in terms of gE-specific CD4+ T-cell secreting at least two activation markers (from among IFN- $\gamma$, IL-2, TNF$\alpha, \mathrm{CD} 40 \mathrm{~L}$ ) (gE-specific CD4[2+]) and for CD4+ T-cell secreting at least two activation markers following induction with $\mathrm{gE}(\mathrm{CD} 4[2+]$ following induction with gE$)$ :

### 5.9.8.2.1. Within groups assessment

- Descriptive statistics of the frequency of the gE-specific CD4[2+] T-cells and the CD4[2+] T-cells following induction with gE at Months $0,1,2$ and 13.
- Descriptive statistics of the fold over pre-vaccination in the gE-specific-CD4[2+] Tcells and the CD4[2+] T-cells following induction with gE at Month 1, 2 and 13 (Mean, SD, Min, Q1, Median, Q3, Max).
- VRR in the gE-specific CD4[2+] T-cells at Months 1, 2 and 13 with exact $95 \%$ CI.


### 5.9.8.2.2. Between groups assessment

The evaluation of the CMI responses at Month 2, following a two-dose administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only), was performed in terms of CD4[2+] T-cells following induction with gE and gE -specific CD4[2+] T-cells.

1. Evaluation of CMI immunogenicity response in term of $\mathrm{CD} 4[2+]$ T-cells following induction with gE

A likelihood-based Repeated Measurement approach with repeated measurements model was used to analyse the post-vaccination log-transformed frequencies of CD4[2+] T-cells following induction with gE.
The fixed-effect model included the means for all levels of the treatment effect by visits interaction. The continuous covariates included the pre-vaccination logtransformed CD4[2+] T-cell frequency following induction with gE (Month 0 ) and the post-vaccination log-transformed CD4[2+] T-cell frequency under the background condition.
The goodness of fit Bayesian Information Criterion and Akaike Information Criteria statistics were used to assess the need of a separate residual variance for each treatment group.

Adjusted GMs of Month 2 post-vaccination in CD4[2+] T-cell frequency following induction with gE , were calculated conditionally to the means of the pre-vaccination log-transformed CD4[2+] T-cell frequency following induction with gE and the post-vaccination log-transformed CD4[2+] T-cell frequency under background conditions. Adjusted means and difference of means between vaccines and placebo were calculated together with 2-sided CIs and back-transformed to the original units to provide frequency adjusted GMs and frequency adjusted GM ratios.
The adjusted GMs calculated as described above provided the effect of the vaccine on the sum of both antigen-specific and non-specific $\mathrm{CD} 4[2+$ ] frequencies.
2. Evaluation of CMI immunogenicity response in term of gE-specific CD4[2+] T-cells

This procedure below allowed the calculation of the GMs for the gE-specific
CD4[2+] T-cells. These estimates better represent the net effect of the vaccines over the frequency of CD4[2+] T-cells as caused by the vaccine.

The same model as described above was used to analyse the log-transformed ratio between induction frequency and background frequency of CD4[2+] T-cells. Leastsquare means and difference of least-squares means were back-transformed and used to provide estimates for the frequency difference divided by background ([induction - background] / background). The log-transformation of the ratios of these estimates between treatments was calculated. The CI for ratio of gE-specific CD4[2+] T-cell frequencies was calculated using the Delta method following the procedure below. The CIs were calculated on the $\log$ scale for $\log \left(\mathrm{W}_{\mathrm{jk}}\right)$ then back-transformed to the original units.

$$
\begin{aligned}
Y_{i j k l}-x_{i j k} & =v_{j}+\mu_{j k}+\alpha_{j} \cdot y_{i 0 k}+\beta \cdot x_{i j k}+\varepsilon_{i j k} \\
(\hat{Y}-\bar{x})_{j k} \mid \bar{y}_{0}, \bar{x} & =v_{j}+\mu_{j k}+\alpha_{j} \cdot \bar{y}_{0}+\beta \cdot \bar{x} \\
\varepsilon_{i j k} & \approx N(0, \Sigma) \quad \Sigma \text { unstructured } \\
Y_{i j k} & =\log -\text { transformed frequency following induction with antigen } \\
& \text { for subject } i, \text { visit } j \text { and treatment } k . \\
x_{i j k}= & \text { log - transformed frequency in medium condition (background) } \\
\bar{y}_{0}= & \text { mean of log - transformed induction frequency at pre - vaccination } \\
\bar{x}= & \text { mean of log - transformed background frequency post - vaccination } \\
\hat{Z}_{j k}= & \operatorname{Exp}\left(\hat{Y}_{j k}-\bar{x}\right)-1=\frac{\operatorname{Exp}\left(\hat{Y}_{j k}\right)-\operatorname{Exp}(\bar{x})}{\operatorname{Exp}(\bar{x})} \\
\log \left[\hat{W}_{j k}\right]= & \log _{e}\left(\frac{\hat{Z}_{j k_{2}}}{\hat{Z}_{j k_{1}}}\right)=\log _{e}\left(\frac{\operatorname{Exp}\left(\hat{Y}_{j k 2}-\bar{x}\right)-1}{\operatorname{Exp}\left(\hat{Y}_{j k 1}-\bar{x}\right)-1}\right)=\log _{e}\left(\frac{\operatorname{Exp}\left(\hat{Y}_{j k_{2}}\right)-\operatorname{Exp}(\bar{x})}{\left.\operatorname{Exp}\left(\hat{Y}_{j k_{1}}\right)-\operatorname{Exp}(\bar{x})\right)}\right.
\end{aligned}
$$

$\hat{Z}_{j k}=$ mean increase from background frequency to induction frequency relative to background frequency at visit k for treatment k .
$\hat{W}_{j k}=$ Vaccine effect on the antigen - specific frequency of CD4 T cells producing cytokines, following adjustment for background frequency
2.1. The derivative of $\log (\mathrm{Wjk})$ with regards to the Yjk 2 is described below.

$$
\frac{\partial}{\partial Y_{j k 2}} \log _{e}\left(\frac{\operatorname{Exp}\left(\hat{Y}_{j k 2}-\bar{x}\right)-1}{\operatorname{Exp}\left(\hat{Y}_{j k 1}-\bar{x}\right)-1}\right)=\frac{\operatorname{Exp}\left(\hat{Y}_{j k 2}-\bar{x}\right)}{\operatorname{Exp}\left(\hat{Y}_{j k 2}-\bar{x}\right)-1}=1+\frac{1}{\operatorname{Exp}\left(\hat{Y}_{j k 2}-\bar{x}\right)-1}=1+\frac{1}{\hat{Z}_{j k 2}}
$$

2.2. The derivative of $\log (\mathrm{Wjk})$ with regards to the Yjk 1 is described below.

$$
\frac{\partial}{\partial Y_{j k 1}} \log _{e}\left(\frac{\operatorname{Exp}\left(\hat{Y}_{j k 2}-\bar{x}\right)-1}{\operatorname{Exp}\left(\hat{Y}_{j k 1}-\bar{x}\right)-1}\right)=-\left(\frac{\operatorname{Exp}\left(\hat{Y}_{j k 1}-\bar{x}\right)}{\operatorname{Exp}\left(\hat{Y}_{j k 1}-\bar{x}\right)-1}\right)=-1-\frac{1}{\operatorname{Exp}\left(\hat{Y}_{j k 1}-\bar{x}\right)-1}=-1-\frac{1}{\hat{Z}_{j k 1}}
$$

2.3. The vector of partial derivative contained only the derivative for the means involved in the comparison (ie. Yjk1 and Yjk2).

$$
\operatorname{Grad}_{\hat{Y}_{\hat{y}_{k 1}, \hat{Y}_{j k 2}}}\left(\log _{e}\left(\frac{\hat{Z}_{j k_{2}}}{\hat{Z}_{j k_{1}}}\right)\right)=\binom{-1-\frac{1}{\hat{Z}_{j k 1}}}{1+\frac{1}{\hat{Z}_{j k 2}}}
$$

2.4. The covariance matrix of the means was pre-multiplied and post-multiplied by the vector of partial derivative to provide the variance of the contrast.

$$
\operatorname{Var}\left(\log _{e}\left(\frac{\hat{Z}_{j k_{2}}}{\hat{Z}_{j k_{1}}}\right)\right)=T\left(\operatorname{Grad}_{\hat{Y}_{j k 1}, \hat{Y}_{j k 2}}(\bullet)\right) \cdot \sum \cdot \operatorname{Grad}_{\hat{Y}_{\hat{y}_{k 1}, \hat{Y}_{k k_{2}}}}(\bullet)
$$

2.5. The $\log (\mathrm{Wjk}) \mathrm{CI}$ was calculated based on the T -student percentile using the degrees of freedom provided by the MIXED procedure for the difference of means under consideration (eg Yjk2 and Yjk1) and the standard error calculated above.

$$
\log _{e}\left(\operatorname{LowerCI}\left(W_{j k}\right)\right)=\log _{e}\left(\frac{\hat{Z}_{j k_{2}}}{\hat{Z}_{j k_{1}}}\right)-\operatorname{TINV}(1-\operatorname{alpha} / 2, d f) \cdot \sqrt{\operatorname{Var}\left(\log _{e}\left(\frac{\hat{Z}_{j k_{2}}}{\hat{Z}_{j k_{1}}}\right)\right)}
$$

The CIs were then back-transformed to the original units to provide the CIs for $\mathrm{W}_{\mathrm{jk}}$.

### 5.9.9. Analysis of safety

The primary analysis for safety was based on the TVC. A second analysis based on the ATP cohort was performed to complement the TVC analysis.

All safety analyses were performed by age strata and by duration between the first dose and the start of chemotherapy cycle (PreChemo/OnChemo).

### 5.9.10. Within group assessment

When appropriate, tabulations were presented overall and by time of occurrence relative to last vaccination (e.g., using windows such as Days $0-6$, Days $0-29$ and more than 30 days post-vaccination).

The results for the analysis of safety were tabulated as:

- The percentage of subjects with at least one local AE (solicited and unsolicited), with at least one general AE (solicited and unsolicited) and with any AE during the solicited 7-day follow-up period were tabulated with exact 95\% CI after each vaccine dose and overall.
- The percentage of subjects with at least one local solicited AE, with at least one general solicited AE and with any solicited AE during the solicited 7-day follow-up period were tabulated with exact $95 \%$ CI after each vaccine dose and overall.
- The percentage of subjects reporting each individual solicited local and general AE during the solicited 7 -day-follow-up period were tabulated with exact 95\% CI.
- For all solicited symptoms, the same tabulation was performed for grade 3 solicited AEs and for solicited general AEs with relationship to vaccination.
- The proportion of subjects with at least one report of unsolicited AE classified by the MedDRA Preferred Term (PT) and reported up to 30 days after each vaccination was tabulated with exact $95 \%$ CI.
- The same tabulation was performed for grade 3 unsolicited AEs and for unsolicited AEs with a relationship to vaccination. The proportion of AEs resulting in a medically attended visit was also tabulated.
- Total number/percentages of doses (per dose and overall) followed by AEs was tabulated.
- Number of subjects with pIMDs was tabulated.
- SAEs and withdrawal due to $\mathrm{AE}(\mathrm{s})$ was described in detail.

Tabulations for SAEs and pIMDs were done using a time window from first vaccination up to 30 days post last vaccination, from 30 days post last vaccination up to study end, and from first vaccination up to study end.

- Number/percentage of subjects with fatal outcomes reported up to study end was tabulated.


### 5.9.11. Interpretation of analyses

With respect to primary and secondary confirmatory objectives, a hierarchical procedure was applied to control the Type I error. The objectives were assessed sequentially in order of ascending rank as indicated in Table 22. We continued to assess the objectives until an objective was not met. At this point, we were to proceed with descriptive analyses of the remaining endpoints.

All confirmatory objectives were assessed at a 2-sided 5\% type I error rate.

## Table 22 List of ranked confirmatory objectives

| Rank | Objectives (primary/secondary: nominal $\alpha=2.5 \%$ one-sided) |
| :--- | :--- |
| 1 | To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the <br> HZ/su vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy (PreChemo <br> Groups only). (primary: nominal a $=2.5 \%$ one-sided). |
| 2 | To evaluate VRR in anti-gE humoral immunogenicity responses at Month 2, following a two-dose <br> administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (PreChemo <br> Groups only). (secondary: nominal a $=2.5 \%$ one-sided). |
| 3 | To evaluate gE-specific CD4+ T-cell immunogenicity responses at Month 2, following a two-dose <br> administration of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours receiving <br> chemotherapy (PreChemo Groups only) (in the CMI sub-cohort). (secondary: nominal a $=2.5 \%$ one-sided). |
| 4 | To evaluate VRR in gE-specific CDA+ T-cell mediated immunogenicity at Month 2, following a two-dose <br> administration of the HZ/su vaccine in subjects with solid tumours receiving chemotherapy (PreChemo <br> Groups only) (in the CMI sub-cohort). (secondary: nominal a $=2.5 \%$ one-sided). |
| 5 | To evaluate the anti--GE humoral immunogenicity response at Month 2, following a two-dose administration <br> of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (all <br> subjects). (secondary: nominal a $=2.5 \%$ one-sided). |
| 6 | To evaluate VRR in anti-gE humoral immunogenicity responses at Month 2, following a two-dose <br> administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (all subjects <br> receiving the HZ/su vaccine). (secondary: nominal a = 2.5\% one-sided). |

### 5.9.12. Sequence of analyses

Subjects were evaluated for safety on a regular basis by the iSRC using coded group names for treatment groups to prevent individual subject unblinding. Operational details for iSRC were provided in the iSRC Charter (see Section 2).

Two formal analyses were planned: a first analysis and an end of study analysis.
The first analysis of immunogenicity and reactogenicity/safety data was performed when all data up to and including Month 2 ( 30 days post dose 2 ) (active phase) were available after completion of Visit 3.

The end of study analysis was performed when all data up to and including Month 13 were available.

Assessment of the confirmatory immunogenicity objectives occurred at the first analysis.
Analyses performed at first analysis were repeated descriptively at end of study analysis using the final cleaned database.

The current report presents the study results based on the final data (see Section 5.11.2).

At end of study, CMI laboratory data were updated compared to the laboratory data provided for the first analysis due to a change in the definition of data release requirements as applicable for the study population of immune-compromised subjects (versus previously applicable for subjects $\geq 50 \mathrm{YOA}$ ).

Regarding the CMI-related confirmatory secondary objectives, both the results obtained at first analysis and and end of study analysis are presented in this report.

Regarding safety and reactogenicity analyses, the tabulations presenting the results obtained at end of study analysis are included in this report.

### 5.9.13. Interim analysis

No interim analysis was planned.

### 5.10. Data quality assurance at study level

To ensure that the study procedures conformed across all investigator sites, the protocol, eCRF and safety reporting were reviewed with the investigator(s) and his/her/their personnel responsible for the conduct of the study by the Company representative(s) prior to study start. A multi-investigator meeting was held in Barcelona, Spain on 8 February 2013, prior to the study start.

Adherence to the protocol requirements and verification of data generation accuracy were achieved through monitoring visits to each investigator site. Computer checks and blinded review of subject tabulations were performed to ensure consistency of eCRF completion. All procedures were performed according to methodologies detailed in GSK Biologicals Standard Operating Procedures (SOPs).

All protocol deviations collected during the study were reviewed by the GSK study team in order to identify important protocol deviations. Consistent with ICH E3 guidance, important deviations are defined as deviations that were likely to affect the interpretation of the results and/or led to exclusion of any subject data from an analysis. Important deviations include, but are not limited to, those related to study inclusion or exclusion criteria, adherence to the protocol, conduct of the study, subject management or subject assessment.

During the course of the study/after study completion, the following issues with regard to the conduct of the study were identified, either via site monitoring activities or were brought to GSK Vaccines' attention by other oversight mechanisms. All protocol deviations were tracked, but only information regarding important deviations was included in the CSR. These issues were investigated and where possible corrective and / preventive actions were taken.

- Refer to Section 6.3.1regarding important protocol deviations leading to elimination from specified analyses.
- Refer to Section 6.3.2 for important protocol deviations noted for individual subjects that did not meet criteria for elimination from ATP analyses.
- Between April and May 2013, two technical problems were identified in the Electronic Data Capture system (e-N@ble Web system) used in this study. The first technical issue was related to the incorrect display of the investigator's signature on the electronic screens in the system. The second technical issue was that the reason for change of the data noted in the audit trail was overwritten; the author, date and time of original entry as well as data changes were not affected. These technical issues were corrected in December 2013. This does not change the validity of the data collected nor has any impact on the data reported.
- The 8 first subjects were enrolled and inadvertently randomised, with a randomisation algorithm that did not take into account the gender as minimization factor. The SBIR application was updated to add the gender as minimisation factor and put in production on 5 April 2013. Following this, the remaining 256 subjects were properly randomised, by also taking gender into account.
CROs and central laboratories:
Information regarding CROs and laboratories that were employed to perform certain activities related to the study are described in Section 2.

The CROs 4Clinics and S-Clinica were employed to perform statistical analyses (see Section 2) according to an agreed contract. The CRO responsibilities were conducted according to GSK SOPs.

Local CROs were employed to perform monitoring activities at the country level and/or management of the country monitoring study file according to agreed contracts. The CRO responsibilities were conducted according to GSK SOPs and/or CRO SOPs.

The CRO CEVAC was employed to perform CMI testing (see Section 2) according to an agreed contract. The CRO responsibilities were conducted according to GSK SOPs.The humoral immunogenicity and CMI assay, respectively, were each performed by a single central laboratory (see Section 5.7.2).

## Independent Audit statement:

This study was subject to audit by GlaxoSmithKline's R\&D Global Quality Compliance (GQC) - Clinical Development Quality Assurance (CDQA) department.

### 5.11. Changes in the conduct of the study or planned analyses

### 5.11.1. Protocol amendments

The protocol, dated 16 August 2012, was amended two times.

## Protocol Amendment 1, dated 19 November 2012

Note that protocol amendment 1 was implemented before recruitment started.

- Subjects in the ZOSTER-028 study were randomised into two groups based on the vaccination schedule in relation to the start of chemotherapy. The OnChemo subjects receive their first HZ/su vaccination at start of chemotherapy, while the PreChemo subjects receive their first HZ/su vaccination at least 10 days before start of chemotherapy. The previous design had these two groups at an equal size.
- New unpublished data made available to the ZOSTER-028 team in 2012 from studies with other GSK candidate vaccines in cancer subjects indicated that giving the first vaccination at the start of chemotherapy can lead to a decreased/suppressed immune response, possibly due to steroids used concomitantly in high doses to prevent nausea and vomiting. The primary objective on immunogenicity in the ZOSTER-028 was confirmatory and aimed to evaluate the anti-gE humoral immunogenicity response. To increase the chance of success in obtaining a significant immune response with $\mathrm{HZ} / \mathrm{su}$, the primary objective for immunogenicity was evaluated only in the PreChemo Group. For this reason, the study groups had been changed by enlarging the proportion of PreChemo subjects to maintain a $90 \%$ power for the primary immunogenicity objective: instead of a $1: 1$ ratio ( 100 subjects in each group), the PreChemo:OnChemo ratio, was now 4:1 ( $\mathrm{N}=168 / 42$ ). The $\mathrm{HZ} / \mathrm{su}:$ Placebo ratio was maintained as $1: 1$. Thus the overall study N was increased by $5 \%$ ( 10 subjects) in order to have $90 \%$ power for the primary immunogenicity objective. A comparison of the Old and New N values for the study is indicated below.

|  | Old N | New N | Old CMI <br> Sub-cohort | New CMI <br> Sub-cohort |
| :--- | :--- | :--- | :--- | :--- |
| HZ PreChemo | 50 | 84 | 19 | 38 |
| Placebo PreChemo | 50 | 84 | 19 | 38 |
| HZ OnChemo | 50 | 21 | 19 | 0 |
| Placebo OnChemo | 50 | 21 | 19 | 0 |
| TOTAL | $\mathbf{2 0 0}$ | $\mathbf{2 1 0}$ | $\mathbf{7 6}$ | $\mathbf{7 6}$ |

The following updates were made:

- The primary objective for immunogenicity response (based on GM ratios) following the HZ/su vaccination compared to placebo was now evaluated only in the PreChemo Groups.
- The secondary objectives were now qualified to evaluate immunogenicity in either the PreChemo Groups (VRRs in anti-gE humoral immunogenicity responses and VRR and GM ratio in gE-specific CMI) or in all study subjects (VRR and GM ratio in anti-gE humoral immunogenicity responses).
- The CMI sub-cohort was now only recruited in the PreChemo Groups.
- Changes have been made since an error in the calculation (logarithm transformation) of a criteria value and one assumption was discovered in the sample size assumptions for the humoral immune response endpoint. In order to correct the error, the following calculation modifications have been performed:
- For the criteria value, the wrong value natural logarithm $(\ln (3)=1.099)$ has been replaced by decimal logarithm $\left(\log _{10}(3)=0.477\right)$.
- The assumed fold increase has been re-evaluated to 12.5 , due to the change in the population assessed (PreChemo only) for the primary immunogenicity objective, and due to new data from another HZ/su study in an IC population, showing a higher fold increase, and therefore the previous value $(\ln (5.5)=1.705)$ has been replaced by $\left(\log _{10}(12.5)=1.097\right)$.
- The overall sample size was increased by adding 10 subjects in order to maintain the power for the primary immunogenicity objective at $90 \%$.
- The updates supporting these study design changes were made in different protocol sections
- The timepoint for evaluation of the primary objective for safety/reactogenicity was reworded for clarity ('up to 30 days post last vaccination' instead of 'up to month 2').
- The word 'humoral' was removed from the first Secondary Endpoint
- The inclusion criteria for subject age now also included the requirement that the subject also needed to have reached the age of local legal consent at the time of study entry i.e., when informed consent was signed.
- It was now indicated in 3 different protocol sections that the Pre-vaccination visit was mandatory. This visit could still occur on the same day as Visit 1.
- It was clarified in footnotes what happens when the variable study Visit 4 occurs at Month 13.
- The statement 'Any condition which, in the judgment of the investigator would make IM injection unsafe' was added to the protocol sections 'Exclusion criteria for enrolment' and 'Contraindications to subsequent vaccination'.
- Notes about contraindication of vaccine administration to the non-dominant arm and to subjects with potential bleeding risk(s) were added to the end of Section 'Dosage and administration of study vaccine/ placebo'.
- The change: 'At Visit 1, all subjects will be 'informed of' instead of 'educated to recognise' the signs and symptoms of typical HZ' was made at applicable locations in the protocol.
- Edits to footnotes and changes to symbol placements were done for different tables.
- Country specific requirements from France were added.
- Typographical errors were corrected.


## Protocol Amendment 2, dated 11 August 2014

- The cut-off of the gE-specific ELISA assay was changed from 18 to $97 \mathrm{mIU} / \mathrm{mL}$. Background signal was measured with the anti-gE ELISA on samples from VZV naïve paediatric subjects. This observation of background signal on VZV naïve samples was not part of the original validation of the assay and establishment of the assay cut-off. Background signal measured with the anti-gE ELISA had no impact on Zoster project clinical conclusions as the vast majority of the samples (at all timepoints) had high titres well above the unspecific response level measured on

VZV naïve samples from Measles, Mumps, Rubella and Varicella studies and Zoster vaccine responses were very robust. However, this finding triggered re-evaluation of the assay cut-off. Based on complementary validation experiments performed in line with Clinical and Laboratory Standards Institute guidelines and taking into account internal company guidelines the technical and seropositivity cut-offs were set at 97 $\mathrm{mIU} / \mathrm{mL}$.

- Within the IC populations undergoing clinical trials with HZ/su, GSK had observed that the clinical condition of the subjects impacted their ability to meet the targeted allowed clinical intervals between study visits. For example, a subject might not be able to attend a visit within the clinically allowed interval due to being hospitalised for his/ her underlying immunocompromising disease or its treatment. Or the second vaccination visit might be delayed due to complications from the underlying IC disease or its treatment, making intramuscular injection unsafe within clinically allowed interval. Considering this, GSK had revised the allowed intervals for the ATP cohort for analysis of immunogenicity. The intervals between vaccinations (dose 1 to dose 2) and between dose 2 and blood sampling at Visit 3 (i.e. the 1 month post dose 2 visit) for inclusion in the ATP cohort for immunogenicity/persistence phase were being enlarged to respectively 30-84 days and 21-63 days. The observation and interpretation of the immunogenicity/persistence data were not anticipated to be compromised by this modification. The increased flexibility allowed meaningful analysis of the data collected in this IC population, where the underlying disease and implications of its treatment (such as cancer treatment schedule, side effects of the concomitant treatment) led to a higher number of out of window visits compared to what was observed in a healthy population.
- Secondary to the clinical course of IC populations, the projected subject loss as cancer deaths, consent withdrawals, and non-evaluable subjects at Month 2 in Zoster-028 was revised from $20 \%$ to $27 \%$. Therefore, the target enrolment was changed from 210 to 232 adults diagnosed with solid tumours receiving chemotherapy. Similarly, the targeted enrolment numbers increased for the PreChemo group from 168 (84 per treatment group) to 186 ( 93 per treatment group) and for the OnChemo group from 42 ( 21 per treatment group) to 46 ( 23 per treatment group), based on the projected $27 \%$ drop-out and non-evaluable subjects at Month 2.
- Intercurrent medical conditions were clarified with examples.
- The list of pIMDs was updated.
- Temperature measurement grading scale was removed, since all temperature measurements were recorded. The description of the temperature analyses were described in details in the Statistical Analysis Plan.
- The definition of the ATP cohort for safety was updated.
- The definition of the ATP cohort for immunogenicity was updated. Visit 4 was removed from the ATP cohort for analysis of immunogenicity as this visit did not occur for all subjects. The ATP cohort for analysis of immunogenicity was now defined by Visit $1 \rightarrow$ Visit 2, Visit $2 \rightarrow$ Visit 3 , and Visit $2 \rightarrow$ Visit 5 .
- Statistical section was updated to describe the descriptive CMI response analysis, to clarify other descriptive analysis for immunogenicity and safety.
- The requirement for reporting an abnormal laboratory finding as an AE or SAE was modified. Now, if the abnormal assessments were judged by the investigator to be clinically significant and unexpected, considering the specific underlying disease and chemotherapy, they were to be recorded as an AE or SAE. Abnormal laboratory results, which were secondary to the clinical course of malignancies and their treatment (cytotoxic or immunosuppressive chemotherapy), were to be expected and frequently occurring for the subject population in this study. The laboratory abnormalities of interest for safety reporting in this study were those judged by the investigators to be clinically significant and unexpected, as this subset could have the possibility to be related to the study vaccine.
- Minor edits in other sections were made for clarification.


### 5.11.2. Other changes

- Subjects assigned to the PreChemo sub-group at randomisation were to receive $\mathrm{HZ} / \mathrm{su}$ or placebo within a maximum of 1 month to a minimum of 10 days before the administration of chemotherapy. As was described in the statistical analysis plan (SAP), for analyses purposes, a minimum of 8 days instead of 10 days was accepted to accommodate the subjects (see Section 5.9.6).
- The following exclusion criterion was clarified in the SAP:

Previous chemotherapy course of less than 28 days (instead of one month) before first study vaccination (see Section 5.3.3).

- The first analysis of immunogenicity and reactogenicity/safety data was performed when all data up to and including Month 2/Visit 3 (30 days post dose 2 ) were available. Data from the first analysis were used for public disclosure purposes while treatment assignment at the individual subject level was kept blinded. Initially a main study report and an annex study report were planned to be written as described in Protocol Amendment 2, Section 9.11.1. Based upon feedback from regulatory authorities and ICH E6 guidelines for the reporting of clinical studies, a decision was made to issue only one clinical study report at the end of the study, presenting the totality of data from the study.After the first analysis the study remained blinded for the subjects and study staff. The end of study analysis was performed when all data up to and including Month 13 were available. Analyses performed at first analysis were repeated descriptively at end of study analysis using the final cleaned database (see also Section 5.9.12).
- The assessment of the confirmatory objectives was conducted on active phase data from first vaccination through 30 days post last vaccination and referred to as a "first analysis" in this CSR. The immunogenicity tables and figures were generated on active phase data at first analysis and end of study analysis using the respective clinical database. The active phase results on humoral immunogenicity generated at first analysis and at end of study analysis were the same. The tabulations and figures generated at end of study analysis are presented in this report (see also Sections 5.9.12 and 7.1).
- The active phase results on CMI generated at first analysis and at end of study were not the same, as a result of changes in the laboratory CMI data release definitions allowing for more CMI data to be released. Despite this, there was no impact on study conclusions. Regarding the CMI-related confirmatory secondary objectives, the results obtained at first analysis and end of study analysis) are both presented in this report (see also Sections 5.9.12 and 7.1).
- Regarding safety and reactogenicity, the tabulations presenting the results obtained at end of study analysis are included in this report (see also Sections 5.9.12 and 8.1).
- To address a request from FDA for ZOSTER studies, additional tables were provided presenting data on duration of solicited symptoms ongoing beyond the 7-day (Days $0-6$ ) post-vaccination period for the TVC (post-hoc analysis): overall (Section 8.2.2, Table 8.265 and Table 8.266), and by age strata (Sections 8.4.2 and 8.4.3; Table 8.260, Table 8.261, Table 8.263, Table 8.264, Table 8.267 and Table 8.268).
- Additional post-hoc analyses for local and general solicited symptoms (Section 8.4.2, Table 8.259, Section 8.4.3, Table 8.262) were requested in order to have a complementary overview of the reactogenicity data by age strata.
- A tabulation was provided (post-hoc analysis) listing the subjects withdrawn from vaccinations and the reasons for withdrawal (Section 6.2.1, Table 6.45) to have a harmonised approach for the IC program.


## 6. STUDY POPULATION RESULTS

### 6.1. Study dates

The first subject was enrolled in the study on 6 March 2013 (pre-vaccination visit). The last subject completed the active phase (Visit 3, Month 2) on 18 June 2015. The last subject completed the study on 20 May 2016.

### 6.2. Subject disposition

### 6.2.1. Subjects disposition: overall analysis in subjects with solid tumours receiving chemotherapy

From the 266 subjects enrolled, 232 subjects were vaccinated (TVC), 117 subjects in the $\mathrm{HZ} /$ su group and 115 in the Placebo group (Table 6.12); 209 of the subjects included in the TVC completed Visit 3, and 23 subjects were withdrawn from the study ( 15 subjects in the HZ/su group and 8 subjects in the Placebo group) (Table 6.4). Up to Visit 3, the most common reason for discontinuation from study was consent withdrawal (11 subjects in the HZ/su group and 5 subjects in the Placebo group). Three subjects in the HZ/su group and 2 subjects in the Placebo group were withdrawn from the study due to an SAE.

Visit 5 was completed by 180 of the subjects included in the TVC, and 52 subjects were withdrawn from the study ( 27 subjects in the HZ/su group, 25 subjects in the Placebo group) (Table 23). Up to study end, the most common reason for discontinuation was an SAE; 13 subjects in the HZ/su group and 12 subjects in the Placebo group were withdrawn due to an SAE.

The number of subjects by center overall for the TVC is shown in Table 6.1.
The number of subjects at each visit and the list of subjects withdrawn from the study, overall for the TVC are shown in Table 6.9.

Table 23 Number of subjects vaccinated, completed up to study end and withdrawn with reason for withdrawal (Total Vaccinated Cohort)

|  | HZ/su | Placebo | Total |
| :--- | :--- | :--- | :--- |
| Number of subjects vaccinated | 117 | 115 | 232 |
| Number of subjects completed | 90 | 90 | 180 |
| Number of subjects withdrawn | 27 | 25 | 52 |
| Reasons for withdrawal: |  |  |  |
| Serious Adverse Event | 13 | 12 | 25 |
| Non-Serious Adverse Event | 0 | 0 | 0 |
| Protocol violation | 0 | 0 | 0 |
| Consent withdrawal (not due to an adverse event) | 12 | 9 | 21 |
| Migrated/moved from study area | 1 | 1 | 2 |
| Lost to follow-up (subjects with incomplete vaccination course) | 0 | 0 | 0 |
| Lost to follow-up (subjects with complete vaccination course) | 1 | 1 | 2 |
| Suspected HZ Episode | 0 | 0 | 0 |
| Sponsor study termination | 0 | 0 | 0 |
| Others | 0 | 2 | 2 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed last study visit
Withdrawn = number of subjects who did not come back for the last visit

## Withdrawal from vaccination

A total of 22 ( $9.5 \%$ ) subjects out of 232 included in the TVC did not receive the second vaccination; i.e $17(14.5 \%)$ out of 117 subjects in the HZ/su group and $5(4.3 \%)$ out of 115 subjects in the Placebo group (see also Section 8.2, Table 8.1; Section 6.3.1.1, Table 6.13):

- Fourteen subjects ( 10 subjects and 4 subjects in the HZ/su and Placebo group respectively) withdrew consent and discontinued from the study prior to Visit 2 and therefore did not receive the second vaccination (Table 6.45, refer also to Section 5.11.2; Table 6.9).
- One subject in the HZ/su group came to Visit 2 but at the visit withdrew the consent, was not vaccinated and discontinued from the study (Table 6.45, Table 6.9).
- Three subjects ( 2 subjects and 1 subject in the HZ/su and Placebo group, respectively) were withdrawn from the study prior to Visit 2 due to a fatal SAE not considered related to vaccination as per investigator assessment (Table 6.45, Table 6.9, Table 8.269).
- Four subjects, who did not receive the second vaccination, were retained in the study for safety evaluations. One of these subjects came to Visit 2 but did not receive the second vaccination per his/her decision. Two of the 4 subjects returned for Visit 2 but did not receive the second vaccination at investigator's discretion secondary to AEs. One additional subject could not attend Visit 2 and did not receive the second vaccination secondary to an SAE (Table 6.45, refer also to Section 8.2.6).

Regarding the PreChemo group, the percentage of subjects having received only one dose was $14(15.6 \%)$ out of 90 subjects and $4(4.4 \%)$ out of 91 subjects in the HZ/su and Placebo groups, respectively; regarding the OnChemo group, 3 (11.1\%) out of 27 subjects and $1(4.2 \%)$ out of 24 subjects in the HZ/su and Placebo groups, respectively (see also Section 8.3, Table 8.91; Section 6.3.1.3, Table 6.16).

### 6.2.2. Subject disposition: analyses in the PreChemo/On Chemo groups

Regarding the PreChemo group, for the active phase, out of the 90 subjects from the TVC included in the HZ/su group, 77 subjects completed Visit 3, and 13 subjects were withdrawn; and out of the 91 subjects from the TVC included in the Placebo group, 84 subjects completed Visit 3, and 7 subjects were withdrawn from the study. The most common reason for discontinuation from study was consent withdrawal ( 9 subjects in the HZ/su group and 4 subjects in the Placebo group); 3 subjects in the HZ/su group and 2 subjects in the Placebo group were withdrawn from the study due to an SAE (Table 6.5). Up to study end, out of the 90 subjects from the TVC included in the HZ/su group, 68 subjects completed Visit 5, and 22 subjects were withdrawn from the study; and out of the 91 subjects from the TVC included in the Placebo group, 72 subjects completed Visit 5 , and 19 subjects were withdrawn from the study. The most common reasons for discontinuation from the study up to study end were an SAE and consent withdrawal; 10 subjects in the HZ/su group and 11 subjects in the Placebo group were withdrawn from the study due to an SAE; 10 subjects in the HZ/su group and 5 subjects in the Placebo group were withdrawn from the study due to consent withdrawal (not due to an AE) (Table 6.7).

Regarding the OnChemo group, for the active phase, out of the 27 subjects from the TVC included in the HZ/su group, 25 subjects completed Visit 3, and 2 subjects were withdrawn from the study; and out of the 24 subjects from the TVC included in the Placebo group, 23 subjects completed Visit 3, and 1 subject was withdrawn from the study. Consent withdrawal was the only reason for discontinuation from the study (Table 6.5). Up to study end, out of the 27 subjects from the TVC included in the HZ/su group, 22 subjects completed Visit 5, and 5 subjects were withdrawn from the study; and out of the 24 subjects from the TVC included in the Placebo group, 18 subjects completed Visit 5 , and 6 subjects were withdrawn from the study. Up to study end, 3 subjects in the $\mathrm{HZ} /$ su group and 1 subject in the Placebo group were withdrawn from the study due to an SAE; 2 subjects in the HZ/su group and 4 subjects in the Placebo group were withdrawn from the study due to consent withdrawal (not due to an AE), 1 subject in the Placebo group was withdrawn for another reason (Table 6.7).

The number of subjects by center in the PreChemo and OnChemo groups for the TVC is shown in Table 6.2.

The number of subjects at each visit and the list of withdrawn subjects in the PreChemo and OnChemo groups for the TVC are shown in Table 6.10.

### 6.2.3. Subject disposition: analyses by age strata (18-49 YOA and $\geq 50$ YOA)

Regarding the 18-49 YOA stratum, for the active phase, out of the 31 subjects from the TVC included in the HZ/su group, and out of the 30 subjects from the TVC included in the Placebo group, all subjects completed Visit 3 (Table 6.6). Up to study end, out of the 31 subjects from the TVC included in the HZ/su group, 30 subjects completed Visit 5, and 1 subject was withdrawn from the study; and out of the 30 subjects from the TVC included in the Placebo group, 26 subjects completed Visit 5, and 4 subjects were withdrawn from the study. Up to study end, 1 subject in the HZ/su group and 2 subjects in the Placebo group were withdrawn from the study due to an SAE; and 1 subject in the Placebo group was withdrawn from the study due to consent withdrawal (Table 6.8).

Regarding the $\geq \mathbf{5 0}$ YOA stratum, for the active phase, out of the 86 subjects from the TVC included in the HZ/su group, 71 subjects completed Visit 3, and 15 subjects were withdrawn; and out of the 85 subjects from the TVC included in the Placebo group, 77 subjects completed Visit 3, and 8 subjects were withdrawn from the study. Reasons for discontinuation from the study were consent withdrawal and SAEs (see also Section 6.2.1) (Table 6.6). Up to study end, out of the 86 subjects from the TVC included in the HZ/su group, 60 subjects completed Visit 5, and 26 subjects were withdrawn from the study; and out of the 85 subjects from the TVC included in the Placebo group, 64 subjects completed Visit 5, and 21 subjects were withdrawn from the study. Up to study end, 12 subjects in the HZ/su group and 10 subjects in the Placebo group were withdrawn from the study due to an SAE; 12 subjects in the HZ/su group and 8 subjects in the Placebo group were withdrawn from the study due to consent withdrawal, 2 subjects in the Placebo group were withdrawn from the study for another reason (Table 6.8).

The number of subjects by center by age strata for the TVC is shown in Table 6.3.
The number of subjects at each visit and the list of withdrawn subjects by age strata for the TVC is shown in Table 6.11.

### 6.3. Important Protocol deviations at subject level

### 6.3.1. Protocol Deviations leading to elimination from ATP analyses

### 6.3.1.1. Overall analysis in subjects with solid tumours receiving chemotherapy

The number of subjects enrolled into the study as well as the number excluded from the ATP cohort for Safety up to 30 days post last vaccination with reasons for exclusion is shown in Table 6.12. Out of the 117 and 115 subjects included in the TVC in the HZ/su group and Placebo group, respectively, 113 and 112 subjects were included in the ATP cohort for Safety up to 30 days post last vaccination in the $\mathrm{HZ} / \mathrm{su}$ and Placebo group respectively.

The following protocol deviations leading to elimination from the ATP cohort for Safety up to 30 days post last vaccination were applicable.

One subject in the Placebo group received a vaccine forbidden up to Month 2, i.e. a tetanus vaccine given 6 days after Dose 2 after hospitalisation for rash and risk of infection. The randomisation code was also broken by the investigator for this subject following the development of a widespread severe macular rash. This subject was excluded from the ATP cohort for Safety up to 30 days post last vaccination (Table 6.12).

Six subjects (4 in HZ/su group and 2 in Placebo group) were excluded from the ATP cohort for Safety up to 30 days post last vaccination due to a protocol violation linked to inclusion or exclusion criteria (Table 6.12).

Compared to the criteria applied to exclude subject from the ATP safety up to 30 days post last vaccination, additional criteria were applied to exclude subjects from the ATP cohort for Humoral immunogenicity. The number of subjects enrolled into the study as well as the number excluded from the ATP cohort for Humoral immunogenicity with reasons for exclusion is shown in Table 6.13. Out of the 117 and 115 subjects included in the TVC in the HZ/su group and Placebo group respectively, 87 and 98 subjects were included in the ATP cohort for Humoral immunogenicity in the $\mathrm{HZ} / \mathrm{su}$ and Placebo group respectively.

The following criteria were considered to exclude subjects from the ATP cohort for Humoral immunogenicity:

- Up to Month 2 / up to 30 days post last dose, one subject in the Placebo group received a vaccine forbidden in the protocol; for this subject the randomisation code was broken at the investigator site.
- For 4 subjects in the HZ/su group and 2 in the Placebo group, a protocol violation linked to the inclusion/exclusion criteria including age was applicable.

Note that the criteria described here above also led to elimination from the ATP cohort of safety up to 30 days post last vaccination. Additional criteria applicable for exclusion from the ATP cohort for Humoral immunogenicity are described here below. Note that more than 1 criterion could be applicable for a subject.

- One subject in each group received medication forbidden per protocol.
- For 1 subject in the HZ/su group randomised to PreChemo arm was diagnosed at Visit 2 (Month 1) with a suspected HZ episode.
- For 3 subjects in each group, the blood sample taken was not compliant with the per protocol blood sampling schedule.
- For 18 subjects in the HZ/su group and 11 subjects in the Placebo group, immunogenicity data at Month 2 ( 1 month post last vaccination) were absent.
- 17 subjects in the HZ/su group and 5 subjects in the Placebo group did not receive the second dose (see also Section 6.2.1 for more details).

The number of subjects enrolled into the study as well as the number excluded from the ATP cohort for Safety up to study end with reasons for exclusion is shown in Table 6.20 .

Compared to the ATP cohort for Safety up to 30 days post last vaccination (Table 6.12), no additional subjects were eliminated from the ATP cohort for Safety up to study end.

The number of subjects enrolled into the study as well as the number excluded from the ATP cohort for Humoral persistence with reasons for exclusion is shown in Table 6.21. Out of the 117 and 115 subjects included in the TVC in the HZ/su group and Placebo group respectively, 68 and 70 subjects were included in the ATP cohort for Humoral persistence in the $\mathrm{HZ} / \mathrm{su}$ and Placebo group respectively.

The following criteria were considered to exclude subjects from the ATP cohort for Humoral persistence:

- Up to study end, one subject in the Placebo group received a vaccine forbidden in the protocol; for this subject the randomisation code was broken at the investigator site;
- A protocol violation linked to the inclusion/exclusion criteria including age was applicable for 4 subjects in the HZ/su group and 2 in the Placebo group.

Note that criteria described here above also led to elimination from the ATP cohort of safety up to 30 days post last vaccination. Additional criteria considered for exclusion from the ATP cohort for Humoral persistence are described here below. Note that more than 1 criterion could be applicable for a subject.

- Up to Visit 5 (Month 13), a total of 2 subjects in each group received medication forbidden per protocol.
- For 1 subject in the HZ/su group at Visit 2 (Month 1) and 2 subjects in the Placebo group at Visit 4 (Month 6) and at Visit 5 (Month 13) respectively, a suspected HZ episode was reported. The 3 subjects were randomised in the PreChemo group (see Table 6.23). Note that the HZ episode at Visit 2 was also a reason for exclusion from the ATP cohort for Humoral immunogenicity.
- For 6 subjects in the HZ/su group and 5 subjects in the Placebo group, the blood sample taken at Visit 5 (Month 13) was not compliant with the per protocol blood sampling schedule.
- For 35 subjects in the HZ/su group and 33 subjects in the Placebo group, immunogenicity data at Visit 5 (Month 13) were absent.
- 17 subjects in the HZ/su group and 5 subjects in the Placebo group did not receive the second dose. Note that these deviations were also considered for exclusion from the ATP cohort for Humoral immunogenicity.
Information regarding deviations from specifications for age and intervals between study visits is shown in Table 6.26.


### 6.3.1.2. Analysis in the PreChemo groups

Only subjects from the PreChemo group were included in the CMI sub-cohort. The TVC for the CMI immunogenicity included 39 and 37 subjects in the $\mathrm{HZ} /$ su group and Placebo group respectively (Table 6.14). The ATP cohort for CMI immunogenicity included 27 and 31 subjects in the HZ/su and Placebo group respectively (Table 6.15).

For subjects included in the TVC for CMI, exclusion from the ATP cohort for CMI immunogenicity due to the following criteria is detailed (see Table 6.15). Note that more than 1 criterion could be applicable for a subject.

- For 2 subjects in each group, a protocol violation linked to inclusion or exclusion criteria was applicable.
- For 1 subject in the HZ/su group, a suspected HZ episode was reported at Visit 2 (Month 1) (see also Section 6.3.1.1).
- For 1 subject in each group, the blood sampling was not compliant with the per protocol blood sampling schedule.
- For 7 subjects in the HZ/su group and 3 subjects in the Placebo group, immunogenicity data at Month 2 were absent.
- 8 subjects in the HZ/su group, did not receive the second dose.

Twenty subjects in the HZ/su group and 20 subjects in the Placebo group were included in the ATP cohort for CMI persistence (Table 6.22).

For subjects included in the TVC for CMI, the following criteria were considered to exclude subjects from the ATP cohort for Humoral persistence.

Note that more than 1 criterion could be applicable for a subject.

- A protocol violation linked to inclusion or exclusion criteria for 2 subjects in each group.
- Up to Visit 5 (Month 13), one subject in each group received medication forbidden per protocol.
- For 1 subject in each group, a suspected HZ episode was reported (see also Section 6.3.1.1).
- For 1 subject in the HZ/su group and 2 subjects in the Placebo group, the blood sample taken at Visit 5 (Month 13) was not compliant with the per protocol blood sampling schedule.
- For 14 subjects in the HZ/su group and 11 subjects in the Placebo group, immunogenicity data at Month 13 were absent.
- 8 subjects in the HZ/su group did not receive the second dose.
- For 1 subject in the HZ/su group, the CMI sample was not processed per protocol.


### 6.3.1.3. Analysis in PreChemo and OnChemo groups

The number of subjects enrolled into the study as well as the number excluded from ATP analyses for Humoral immunogenicity with reasons for exclusion in the PreChemo and OnChemo groups is shown in Table 6.16.

The number of subjects enrolled into the study as well as the number excluded from ATP analyses for Humoral persistence with reasons for exclusion in the PreChemo and OnChemo groups is shown in Table 6.23.

Information regarding deviations from specifications for age and intervals between study visits in the PreChemo and OnChemo groups is presented for the TVC in Table 6.27.

### 6.3.1.4. Analysis by age strata ( $18-49 \mathrm{YOA}$ and $\geq 50 \mathrm{YOA}$ )

The number of subjects enrolled into the study as well as the number excluded from ATP analyses for Humoral immunogenicity with reasons for exclusion by age strata is shown in Table 6.17. The number of subjects enrolled into the study as well as the number excluded from ATP analyses for Humoral persistence with reasons for exclusion by age strata is shown in Table 6.24.

The number of subjects enrolled into the study as well as the number included in the TVC for CMI by age strata is shown in Table 6.18. The number of subjects vaccinated in the CMI sub-cohort as well as the number excluded from ATP analyses for CMI immunogenicity with reasons for exclusion by age strata is shown in Table 6.19. The number of subjects vaccinated in the CMI sub-cohort as well as the number excluded from ATP analyses for CMI persistence with reasons for exclusion by age strata is shown in Table 6.25.

Information regarding deviations from specifications for age and intervals between study visits by age strata is presented for the TVC in Table 6.28.

### 6.3.2. Protocol Deviations not leading to elimination from ATP analyses

The following deviations noted for individual subjects that did not meet criteria for elimination from ATP analyses and actions taken are described below:

- In the study, 33 instances (involving 27 subjects) of late reporting of safety events (SAEs or pIMDs) have been identified via active monitoring and managed through the protocol deviations tracking process. These safety events were reported late either to GSK (i.e. not within 24 hours) or to local ECs or both. Each issue was investigated for reason of late report and the site staff was re-trained when necessary. All IECs/IRBs were informed wherever it was required by local regulation. There was no impact on subjects' safety.
- Six minor deviations were noted with regard to the correct completion of the informed consent form (ICF). Each issue was documented and proper ICF corrections were made in a transparent manner with each subject. These protocol deviations did not affect subjects' safety or rights nor the subject's post consenting intention to participate in the study.
- In 3 instances a pregnancy test was not performed at Visit 1 but a negative pregnancy test was obtained at Visit 2. Site Staff were retrained regarding the protocol-specified pregnancy testing to be performed at the Pre-vaccination visit, Visit 1 and Visit 2. According to local regulations, the IEC and/or IRB and Competent Authorities were informed by the investigators. It is noted that no pregnancies were reported during the study (see Section 8.8).
- There were 3 incidents at a single site where it was noted that the treatments injected underwent a temperature excursion of up to $32.6^{\circ} \mathrm{C}$ for up to 15 minutes (max temperature allowed $30^{\circ} \mathrm{C}$ ). The protocol deviations were documented and reported to the EC. The unblinded nurse was re-trained by the monitor. The issues were escalated for review in regards to vaccine viability and possible elimination of subjects. GSK Quality Assurance product stability experts declared they were confident that incubation at $32.6^{\circ} \mathrm{C}$ for 15 minutes has no impact on the quality of the vaccine.
- On one occasion, one subject had Visit 1 performed by a resident (not listed as subinvestigator, but under the responsibility of the principal investigator) who reviewed the assessments at Visit 1, the subject's eligibility, and signed off. There was no impact on subject's safety.


### 6.4. Demographic characteristics and other baseline characteristics

### 6.4.1. Overall analysis in subjects with solid tumours receiving chemotherapy

The summary of demographic characteristics (age in years at first vaccination, gender, ethnicity, geographic ancestry, solid tumor diagnosis, performance Status [ECOG]) for the TVC is shown in Table 24. As age, gender, ethnicity and geographic ancestry were considered in minimisation (see Section 5.4.3.2.2), these parameters are generally well balanced between the HZ/su and Placebo groups.

Note: Where prohibited by local law (i.e. France), ethnicity and geographic ancestry information was not collected. These subjects appear as "Missing" in Demographic characteristics summaries.

Regarding the TVC, the mean age was 57.1 and 58.5 years for the HZ/su and Placebo group respectively.

More female than male subjects were included in the TVC ( $59.8 \%$ and $60.0 \%$ female in the $\mathrm{HZ} / \mathrm{su}$ and Placebo group, respectively).

Table 24 Summary of demographic characteristics (Total Vaccinated Cohort)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=117 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=115 \end{aligned}$ |  | Total$\mathrm{N}=232$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Characteristics <br> Age[years] at vaccination dose:1 | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% |
|  | Mean | 57.1 | - | 58.5 | - | 57.8 | - |
|  | SD | 10.8 | - | 11.7 | - | 11.3 | - |
|  | Median | 57.0 | - | 59.0 | - | 58.0 | - |
|  | Minimum | 35.0 | - | 31.0 | - | 31.0 | - |
|  | Maximum | 85.0 | - | 87.0 | - | 87.0 | - |
|  | Missing | 0 | - | 0 | - | 0 | - |
| Gender | Male | 47 | 40.2 | 46 | 40.0 | 93 | 40.1 |
|  | Female | 70 | 59.8 | 69 | 60.0 | 139 | 59.9 |
| Ethnicity | American Hispanic or Latino | 5 | 4.6 | 6 | 5.6 | 11 | 5.1 |
|  | Not American Hispanic or Latino | 103 | 95.4 | 101 | 94.4 | 204 | 94.9 |
|  | Missing | 9 | - | 8 | - | 17 | - |
| Geographic Ancestry | African Heritage / African American | 2 | 1.9 | 2 | 1.9 | 4 | 1.9 |
|  | American Indian or Alaskan Native | 2 | 1.9 | 0 | 0.0 | 2 | 0.9 |
|  | Asian - East Asian Heritage | 11 | 10.2 | 14 | 13.1 | 25 | 11.6 |
|  | Asian - South East Asian Heritage | 0 | 0.0 | 2 | 1.9 | 2 | 0.9 |
|  | White - Arabic / North African Heritage | 1 | 0.9 | 0 | 0.0 | 1 | 0.5 |
|  | White - Caucasian / European Heritage | 92 | 85.2 | 88 | 82.2 | 180 | 83.7 |
|  | Other | 0 | 0.0 | 1 | 0.9 | 1 | 0.5 |
|  | Missing | 9 | - | 8 | - | 17 | - |
| Solid Tumor diagnosis | Bladder | 1 | 0.9 | 4 | 3.5 | 5 | 2.2 |
|  | Breast | 53 | 45.3 | 52 | 45.2 | 105 | 45.3 |
|  | Colorectal | 25 | 21.4 | 22 | 19.1 | 47 | 20.3 |
|  | Lung | 8 | 6.8 | 13 | 11.3 | 21 | 9.1 |
|  | Melanoma | 1 | 0.9 | 0 | 0.0 | 1 | 0.4 |
|  | Pancreas | 1 | 0.9 | 1 | 0.9 | 2 | 0.9 |
|  | Prostate | 5 | 4.3 | 4 | 3.5 | 9 | 3.9 |
|  | Other^ | 23 | 19.7 | 19 | 16.5 | 42 | 18.1 |
| Performance Status (ECOG) | Fully active* | 95 | 83.3 | 86 | 74.8 | 181 | 79.0 |
|  | Restricted in physically strenuous activity** | 18 | 15.8 | 28 | 24.3 | 46 | 20.1 |
|  | Ambulatory and capable of all selfcare*** | 1 | 0.9 | 1 | 0.9 | 2 | 0.9 |
|  | Missing | 3 | - | 0 | - | 3 | - |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** $=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
*** $=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

The summary of demographic characteristics for the ATP cohort for safety up to 30 days post last vaccination is shown in Table 6.29.

The summary of demographic characteristics for the ATP cohort for safety up to study end is shown in Table 6.32.

The summary of demographic characteristics for the ATP cohort for Humoral immunogenicity is shown in Table 6.30.

The summary of demographic characteristics for the ATP cohort for Humoral persistence is shown in Table 6.33.

### 6.4.2. Analysis in the Pre-Chemo groups only

The summary of demographic characteristics for the TVC for CMI is shown in Table 6.31. Age, gender, ethnicity and geographic ancestry were generally well balanced between HZ/su and Placebo groups in the TVC for CMI.

The summary of demographic characteristics for the ATP cohort for CMI immunogenicity (PreChemo groups only) is shown in Table 25.

The summary of demographic characteristics for the ATP cohort for CMI persistence is shown in Table 6.34.

Table 25 Summary of demographic characteristics in PreChemo Groups only (ATP cohort for CMI immunogenicity)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=31 \end{aligned}$ |  | Total$\mathrm{N}=58$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Characteristics <br> Age[years] at vaccination dose:1 | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% |
|  | Mean | 57.0 | - | 57.3 | - | 57.2 | - |
|  | SD | 12.1 | - | 11.5 | - | 11.7 | - |
|  | Median | 56.0 | - | 56.0 | - | 56.0 | - |
|  | Minimum | 41.0 | - | 36.0 | - | 36.0 | - |
|  | Maximum | 85.0 | - | 78.0 | - | 85.0 | - |
|  | Missing | 0 | - | 0 | - | 0 | - |
| Gender | Male | 12 | 44.4 | 14 | 45.2 | 26 | 44.8 |
|  | Female | 15 | 55.6 | 17 | 54.8 | 32 | 55.2 |
| Ethnicity | American Hispanic or Latino | 1 | 4.5 | 1 | 3.6 | 2 | 4.0 |
|  | Not American Hispanic or Latino | 21 | 95.5 | 27 | 96.4 | 48 | 96.0 |
|  | Missing | 5 | - | 3 | - | 8 | - |
| Geographic Ancestry | African Heritage / African American | 1 | 4.5 | 1 | 3.6 | 2 | 4.0 |
|  | American Indian or Alaskan Native | 1 | 4.5 | 0 | 0.0 | 1 | 2.0 |
|  | White - Caucasian / European Heritage | 20 | 90.9 | 27 | 96.4 | 47 | 94.0 |
|  | Missing | 5 | - | 3 | - | 8 | - |
| Solid Tumor diagnosis | Breast | 10 | 37.0 | 15 | 48.4 | 25 | 43.1 |
|  | Colorectal | 4 | 14.8 | 5 | 16.1 | 9 | 15.5 |
|  | Lung | 2 | 7.4 | 4 | 12.9 | 6 | 10.3 |
|  | Melanoma | 1 | 3.7 | 0 | 0.0 | 1 | 1.7 |
|  | Prostate | 2 | 7.4 | 1 | 3.2 | 3 | 5.2 |
|  | Other^ | 8 | 29.6 | 6 | 19.4 | 14 | 24.1 |
| Performance Status (ECOG) | Fully active* | 21 | 77.8 | 22 | 71.0 | 43 | 74.1 |
|  | Restricted in physically strenuous activity** | 6 | 22.2 | 8 | 25.8 | 14 | 24.1 |
|  | Ambulatory and capable of all selfcare*** | 0 | 0.0 | 1 | 3.2 | 1 | 1.7 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** $=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
*** $=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.


### 6.4.3. Analysis in PreChemo and OnChemo groups

The summary of demographic characteristics in the PreChemo and OnChemo groups for the TVC is shown in Table 6.35. In both the PreChemo and OnChemo groups, age, gender, ethnicity and geographic ancestry were generally well balanced between HZ/su and Placebo groups, and similar to the characteristics as observed for the TVC overall.

The summary of demographic characteristics in the PreChemo and OnChemo groups for the ATP cohort for Humoral immunogenicity is shown in Table 26.

The summary of demographic characteristics in the PreChemo and OnChemo groups for the ATP cohort for Humoral persistence is shown in Table 6.36.

Table 26 Summary of demographic characteristics by PreChemo/OnChemo groups (ATP cohort for Humoral immunogenicity)

|  |  | PreChemo |  |  |  | OnChemo |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=65 \end{aligned}$ |  | Placebo$\mathrm{N}=78$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=22 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=20 \end{aligned}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=87 \end{aligned}$ |  | Placebo$N=98$ |  |
| Characteristics | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ |  | Value or $n$ | \% |
| Age[years] at vaccination dose:1 | Mean | 55.5 | - | 56.9 | - | 55.6 | - | 57.2 | - | 55.5 | - | 57.0 | - |
|  | SD | 11.3 | - | 11.0 | - | 10.5 | - | 11.9 | - | 11.0 | - | 11.1 | - |
|  | Median | 55.0 | - | 57.0 | - | 57.5 | - | 56.0 |  | 56.0 | - | 57.0 | - |
|  | Minimum | 36.0 | - | 36.0 | - | 35.0 | - | 31.0 | - | 35.0 | - | 31.0 | - |
|  | Maximum | 85.0 | - | 78.0 | - | 77.0 | - | 77.0 | - | 85.0 | - | 78.0 | - |
|  | Missing | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - |
| Gender | Male | 23 | 35.4 | 31 | 39.7 | 7 | 31.8 | 7 | 35.0 | 30 | 34.5 | 38 | 38.8 |
|  | Female | 42 | 64.6 | 47 | 60.3 | 15 | 68.2 | 13 | 65.0 | 57 | 65.5 | 60 | 61.2 |
| Ethnicity | American Hispanic or Latino | 4 | 6.8 | 4 | 5.5 | 0 | 0.0 | 2 | 11.1 | 4 | 5.1 | 6 | 6.6 |
|  | Not American Hispanic or Latino | 55 | 93.2 | 69 | 94.5 | 20 | 100 | 16 | 88.9 | 75 | 94.9 | 85 | 93.4 |
|  | Missing | 6 | - | 5 | - | 2 | - | 2 | - | 8 | - | 7 | - |
| Geographic Ancestry | African Heritage / African American | 2 | 3.4 | 2 | 2.7 | 0 | 0.0 | 0 | 0.0 | 2 | 2.5 | 2 | 2.2 |
|  | American Indian or Alaskan Native | 2 | 3.4 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 2 | 2.5 | 0 | 0.0 |
|  | Asian - East Asian Heritage | 6 | 10.2 | 11 | 15.1 | 2 | 10.0 | 2 | 11.1 | 8 | 10.1 | 13 | 14.3 |
|  | Asian - South East Asian Heritage | 0 | 0.0 | 1 | 1.4 | 0 | 0.0 | 1 | 5.6 | 0 | 0.0 | 2 | 2.2 |
|  | White - Arabic / North African Heritage | 1 | 1.7 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 1.3 | 0 | 0.0 |
|  | White - Caucasian / European Heritage | 48 | 81.4 | 59 | 80.8 | 18 | 90.0 | 14 | 77.8 | 66 | 83.5 | 73 | 80.2 |
|  | Other | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 5.6 | 0 | 0.0 | 1 | 1.1 |
|  | Missing | 6 | - | 5 | - | 2 | - | 2 | - | 8 | - | 7 | - |
| Solid Tumor diagnosis | Bladder | 1 | 1.5 | 1 | 1.3 | 0 | 0.0 | 0 | 0.0 | 1 | 1.1 | 1 | 1.0 |
|  | Breast | 34 | 52.3 | 39 | 50.0 | 13 | 59.1 | 9 | 45.0 | 47 | 54.0 | 48 | 49.0 |
|  | Colorectal | 12 | 18.5 | 20 | 25.6 | 5 | 22.7 | 2 | 10.0 | 17 | 19.5 | 22 | 22.4 |
|  | Lung | 4 | 6.2 | 7 | 9.0 | 0 | 0.0 | 3 | 15.0 | 4 | 4.6 | 10 | 10.2 |
|  | Melanoma | 1 | 1.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 1.1 | 0 | 0.0 |
|  | Pancreas | 1 | 1.5 | 0 | 0.0 | 0 | 0.0 | 1 | 5.0 | 1 | 1.1 | 1 | 1.0 |
|  | Prostate | 2 | 3.1 | 1 | 1.3 | 0 | 0.0 | 1 | 5.0 |  | 2.3 | 2 | 2.0 |
|  | Other ${ }^{\wedge}$ | 10 | 15.4 | 10 | 12.8 | 4 | 18.2 | 4 | 20.0 | 14 | 16.1 | 14 | 14.3 |
| Performance Status (ECOG) | Fully active* | 55 | 87.3 | 62 | 79.5 | 19 | 90.5 | 15 | 75.0 | 74 | 88.1 | 77 | 78.6 |
|  | Restricted in physically strenuous activity** | 8 | 12.7 | 15 | 19.2 | 2 | 9.5 | 5 | 25.0 | 10 | 11.9 | 20 | 20.4 |
|  | Ambulatory and capable of all selfcare*** | 0 | 0.0 | 1 | 1.3 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 1.0 |
|  | Missing | 2 | - | 0 | - | 1 | - | 0 | - | 3 | - | 0 | - |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** $=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
${ }^{* * *}=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.


### 6.4.4. Analysis by age strata (18-49 YOA and $\geq 50 \mathrm{YOA})$

The summary of demographic characteristics by age strata for the TVC is shown in Table 6.37.

The summary of demographic characteristics by age strata for the ATP cohort for Humoral immunogenicity is shown in Table 6.38

The summary of demographic characteristics by age strata for the ATP cohort for Humoral persistence is shown in Table 6.40.

The summary of demographic characteristics by age strata for the ATP cohort for CMI immunogenicity is shown in Table 6.39.

The summary of demographic characteristics by age strata for the ATP cohort for CMI persistence is shown in Table 6.41.

The summary of demographic characteristics by age strata for the TVC in the PreChemo groups only is shown in Table 6.42.

The summary of demographic characteristics by age strata for the ATP cohort for Humoral immunogenicity in the PreChemo Group only is shown in Table 6.43.

The summary of demographic characteristics by age strata for the ATP cohort for Humoral persistence in the PreChemo Group only is shown in Table 6.44.

## 7. IMMUNOGENICITY RESULTS

### 7.1. Datasets analysed

Anti-gE humoral immunogenicity data obtained for all subjects at Month $0,1,2$ (active phase time points) and at Month 6 and Month 13 (persistence time points) are presented in this report.

The gE-specific CMI data obtained for subjects included in the CMI sub-cohort, at Month $0,1,2$ (active phase time points) and Month 13 (persistence time point) are also presented in this report.

The confirmatory objectives were assessed sequentially in order of ascending rank (see Section 5.9.11). The objectives were assessed until an objective was not met.

At this point, a descriptive analysis of the remaining endpoints was conducted. The assessment of the confirmatory objectives was conducted on active phase data from first vaccination through 30 days post last vaccination and referred to as a "first analysis" in this CSR.

The immunogenicity tables and figures were generated on active phase data at first analysis and end of study analysis using the respective clinical database. The active phase results on humoral immunogenicity generated at first analysis and at end of study analysis were the same, the tabulations and figures generated at end of study analysis are presented in this report. The active phase results on CMI generated at first analysis and at end of study were not the same, secondary to changes in the lab CMI data release definitions allowing more CMI data release, even so there was no impact on study conclusions.

Regarding the CMI-related confirmatory secondary objectives, the results obtained at first analysis (i.e. Table 31 and Table 33) and end of study analysis (i.e. Table 32 and Table 34) are both presented in this report.. In these cases, the tabulations from the first analysis have 'first analysis' added in the table title. For other descriptive CMI results, tabulations and figures generated at end of study analysis are presented in this report.

Analyses of humoral immunogenicity were conducted in the PreChemo group(Section 7.2.1.1), in all subjects (Section 7.2.1.2), by PreChemo and OnChemo groups (Section 7.2.1.3), in all subjects by age strata ( $18-49 \mathrm{YOA}$ and $\geq 50 \mathrm{YOA}$ ) (Section 7.2.1.4), and in the PreChemo groups by age strata (Section 7.2.1.5). Analyses of CMI objectives were conducted for subjects in the PreChemo group, overall (Section 7.2.2.1) and by age strata (18-49 YOA and $\geq 50 \mathrm{YOA}$ ) (Section 7.2.2.2).

The analysis of humoral immunogenicity was performed on the ATP cohort for Humoral immunogenicity for Months 0,1 and 2 and on the ATP cohort for Humoral persistence for Month 6 and Month 13. The analysis of CMI immunogenicity was performed on ATP cohort for CMI immunogenicity for Month 0,1 and 2 and on the ATP cohort for CMI persistence for Month 13.

For the immunogenicity tables where timepoints from active phase and persistence phase were presented, the concept of 'Adapted ATP cohort for Humoral immunogenicity' and 'Adapted ATP cohort for CMI-immunogenicity' was used to denote that for each phase, the corresponding ATP cohort was used (see Section 5.9.4.7).

The percentage of subjects excluded from the ATP cohort for Humoral immunogenicity/Humoral persistence, and from the ATP cohort for CMI immunogenicity/CMI persistence, respectively, was greater than $5 \%$ in any treatment group; therefore, per protocol, a second analysis based on the TVC, and on the humoral and CMI TVCs was performed to complement the ATP analysis (Sections 7.3.1 and 7.3.2).

### 7.2. According-to-protocol analysis

### 7.2.1. ATP analysis: humoral immunogenicity

### 7.2.1.1. ATP analysis: humoral immunogenicity in the PreChemo groups

Results of confirmatory objectives assessed in the PreChemo groups on the ATP cohort for Humoral immunogenicity are presented.

The confirmatory primary objective of the study was met as the lower limit of the $95 \%$ CI of the GM ratio (HZ/su PreChemo Group over Placebo PreChemo group) in anti-gE Ab concentrations at Month 2 (post second vaccination) was 17.9. Therefore, the success criterion (greater than 3) was demonstrated. The adjusted GM ratio was 23.2 ( $95 \% \mathrm{CI}$ : 17.9 - 30.0; $\mathrm{P}<0.0001$ ) (Table 27).

The first confirmatory secondary objective of the study was met as the lower limit of the $95 \%$ CI of the VRR for anti-gE Ab concentrations in the HZ/su PreChemo group at Month 2 (post second vaccination) was $85.0 \%$. Therefore, the success criterion (at least $60 \%$ ) was demonstrated. The VRR was $93.8 \%$ ( $95 \%$ CI: $85.0-98.3$ ) (Table 28).

Table 27 Adjusted geometric means and ratio of HZ/su over placebo for antigE antibody ELISA concentrations at Month 2 in PreChemo Groups only (ATP cohort for Humoral immunogenicity)

|  |  | Adjusted geometric mean |  |  |  | Adjusted geometric mean ratio |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  |  |  | $\mathbf{9 5 \%} \mathbf{~ C l}$ |  |  |  |  |  |  |
| Timing | Group | N | Value | LL | UL | Value | LL | UL | P-value for the ratio |
| PII(M2) | HZ/su | 65 | 24501.57 | 19051.99 | 31509.94 | 23.2 | 17.9 | 30.0 | $<.0001$ |
|  | Placebo | 76 | 1056.77 | 990.37 | 1127.62 |  | . | . | . |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval Confidence Interval (CI) were back transformed to original units The $p$-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$ PII(M2) = Post-vaccination Dose II (Month 2)

Table 28 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 2 in PreChemo Groups only (ATP cohort for Humoral immunogenicity)

|  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% |  |
| Test description | Group | N | n | \% | LL | UL |
| VZV.gE Ab.lgG | HZ/su | 65 | 61 | 93.8 | 85.0 | 98.3 |
|  | Placebo | 76 | 0 | 0.0 | 0.0 | 4.7 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as:
For initially seronegative subjects, antibody concentration at Month $2 \geq 4$ fold the cut-off for Anti-gE ( $4 \times 97 \mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at Month $2 \geq 4$ fold the pre-vaccination antibody concentration
$\mathrm{N}=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
$95 \% \mathrm{Cl}=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

### 7.2.1.2. ATP analysis: humoral immunogenicity in all subjects

Results of confirmatory objectives assessed in all subjects on the ATP cohort for Humoral immunogenicity are presented.

According to to the hierarchical procedure applied, the confirmatory objectives were assessed sequentially in order of ascending rank until an objective was not met, and remaining objectives were to be analysed descriptively (see Section 5.9.11).

As the third secondary confirmatory objective was not met (see Section 7.2.2.1), the following objectives were analysed descriptively:

- Regarding the anti-gE humoral immune response at Month 2 (post second vaccination) in the HZ/su group compared to the Placebo group (all subjects), the observed adjusted GM ratio was 14.4 ( $95 \%$ CI: 10.7 - 19.5) (Table 29).
- The VRR in anti-gE humoral immune response at Month 2 (post second vaccination) in the HZ/su group (all subjects) was $86.2 \%$ ( $95 \%$ CI: 77.1-92.7) (Table 30).

Table 29 Adjusted geometric means and ratio of HZ/su over placebo for antigE antibody ELISA concentrations at Month 2 in all subjects (ATP cohort for Humoral immunogenicity)

|  |  | Adjusted geometric mean |  |  |  | Adjusted geometric mean ratio |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  |  |  | $95 \% \mathrm{Cl}$ |  |  |  |  |  |  |
| Timing | Group | N | Value | LL | UL | Value | LL | UL | P-value for the ratio |
|  | HZ/su | 87 | 14781.59 | 11028.12 | 19812.56 | 14.4 | 10.7 | 19.5 | <.0001 |
|  | Placebo | 94 | 1025.71 | 954.82 | 1101.87 | . | . | . | . |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval Confidence Interval (Cl) were back transformed to original units The p -value is relative to the null hypothesis Ho : Vaccine $/$ Placebo $=1$ PII(M2) = Post-vaccination Dose II (Month 2)

Table 30 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 2 in all subjects (ATP cohort for Humoral immunogenicity)

|  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% |  |
| Test description | Group | N | n | \% | LL | UL |
| VZV.gE Ab.lgG | HZ/su | 87 | 75 | 86.2 | 77.1 | 92.7 |
|  | Placebo | 94 | 0 | 0.0 | 0.0 | 3.8 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as:
For initially seronegative subjects, antibody concentration at Month $2 \geq 4$ fold the cut-off for Anti-gE ( $4 \times 97 \mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at Month $2 \geq 4$ fold the pre-vaccination antibody concentration
$\mathrm{N}=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
$95 \% \mathrm{Cl}=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
Results from descriptive analyses in all subjects performed on the ATP cohort for Humoral immunogenicity and the ATP cohort for Humoral persistence (or Adapted ATP cohort Humoral immunogenicity, as applicable) are presented.

The majority of subjects in the HZ/su and Placebo groups were seropositive for anti-gE Abs at pre-vaccination and the subsequent time points. In both the HZ/su and Placebo groups the baseline seropositivity rate was $98.9 \%$. In the HZ/su group seropositivity increased to $100 \%$ at Month 1 and remained so thereafter (Table 7.1).

Pre-vaccination anti-gE Ab GMCs were 1049.8 ( $95 \%$ CI: 865.8 - 1273.0) and 1116.7 ( $95 \%$ CI: $918.4-1358.0$ ) mIU/mL respectively for HZ/su and Placebo groups. Postvaccination, anti-gE Ab GMCs at Month 1 (post first vaccination) and Month 2 (post second vaccination) were 24793.1 ( $95 \%$ CI: 18747.8 - 32787.6 ) and 18291.7 ( $95 \% \mathrm{CI}$ : 14432.1 - 23183.5 ) $\mathrm{mIU} / \mathrm{mL}$ respectively for the HZ/su group. Anti-gE Ab GMCs at Month 6 and Month 13 were 7730.4 ( $95 \%$ CI: 5358.4 - 11152.2) and 4477.3 ( $95 \% \mathrm{CI}$ : $3482.4-5756.3$ ) $\mathrm{mIU} / \mathrm{mL}$ respectively for the HZ/su group. The post-vaccination anti-gE Ab GMCs in the Placebo group remained near pre-vaccination level (Table 7.1).

VRRs in the HZ/su group at Months 1 (post first vaccination) and Month 2 (post second vaccination) were $85.9 \%$ ( $95 \%$ CI: $76.6-92.5$ ) and $86.2 \%$ ( $95 \% \mathrm{CI}: 77.1-92.7$ ) respectively, and at Months 6 and Month 13, $73.8 \%$ ( $95 \%$ CI: $58.0-86.1$ ) and 51.5\% ( $95 \%$ CI: $39.0-63.8$ ) respectively In the Placebo group, there were no subjects meeting the definition of responder at Months 1, 2 and 13. However at Month 6 in the Placebo group, there was 1 subject meeting the definition of responder; VRR was $2.4 \%(95 \% \mathrm{CI}$ : $0.1-12.6$ ) (Table 7.2); there is no record of HZ occurring in this subject during the study period.

The MGIs from pre-vaccination baseline in the HZ/su group at Month 1 and Month 2 were 24.1 ( $95 \%$ CI: $17.7-33.0$ ) and 17.4 ( $95 \%$ CI: $13.2-23.0$ ) respectively, and at Month 6 and Month 13, 8.7 ( $95 \%$ CI: $5.8-12.8$ ) and 4.3 ( $95 \% \mathrm{CI}: 3.4-5.6$ ) respectively. In the Placebo group, the MGI was not higher than 1.0 at any time point (Table 7.3).

Descriptive statistics of the fold increase for anti-gE Ab concentrations at Months 1, 2, 6 and 13 are shown in Table 7.4. The distribution of the fold increase from baseline for anti-gE Ab concentrations at Months $1,2,6$ and 13 is shown in Table 7.5.

The reverse cumulative curve for anti-gE Ab concentrations at Months $0,1,2,6$ and 13 is shown in Figure 7.1, Figure 7.2, Figure 7.3, Figure 7.4 and Figure 7.5, respectively.

### 7.2.1.3. ATP analysis: humoral immunogenicity in PreChemo and OnChemo groups

Results from descriptive analyses in the PreChemo and On Chemo groups performed on the ATP cohort for Humoral immunogenicity, the ATP cohort for Humoral persistence (or Adapted ATP cohort Humoral immunogenicity, as applicable) are presented.

In the $\mathrm{HZ} / \mathrm{su}$ and Placebo PreChemo groups the baseline (at pre-vaccination) seropositivity rates for anti-gE Abs were $98.5 \%$ and $98.7 \%$ respectively. In the HZ/su group seropositivity increased to $100 \%$ at Month 1 and remained so thereafter. In the Placebo group, the seropositivity was 98.7 at Month 2 and $100 \%$ at Month 6 and Month 13 (Table 7.6).

In the $\mathrm{HZ} / \mathrm{su}$ and Placebo OnChemo groups, all subjects were seropositive at all time points (Months 0, 1, 2, 6 and 13) (Table 7.6).

In the PreChemo groups, pre-vaccination anti-gE Ab GMCs were 1032.3 ( $95 \% \mathrm{CI}: 821.0$ - 1298.0) and 1185.4 ( $95 \% \mathrm{CI}$ : 959.3 - 1464.7) $\mathrm{mIU} / \mathrm{mL}$ respectively for $\mathrm{HZ} / \mathrm{su}$ and Placebo groups. Post-vaccination, anti-gE Ab GMCs at Months 1 (post first vaccination) and 2 (post second vaccination) were 34729.8 ( $95 \%$ CI: 27485.9 - 43882.8) and 22974.3 ( $95 \%$ CI: $19080.0-27663.5$ ) mIU $/ \mathrm{mL}$ respectively, and at Month 6 and 13, 8528.2 ( $95 \%$ CI: $6150.1-11825.9$ ) and $4563.0(95 \% \mathrm{CI}: 3532.8-5893.7) \mathrm{mIU} / \mathrm{mL}$ respectively for the HZ/su PreChemo group (Table 7.6).

In the OnChemo groups, pre-vaccination anti-gE Ab GMCs were 1103.4 (95\% CI: 753.4 $-1616.0)$ and 868.2 ( $95 \% \mathrm{CI}: 512.9-1469.7$ ) mIU/mL respectively for $\mathrm{HZ} / \mathrm{su}$ and Placebo groups. Post-vaccination, anti-gE Ab GMCs at Month 1 (post first vaccination), and Month 2 (post second vaccination) were 8876.6 ( $95 \%$ CI: 4134.3 - 19058.6) and 9328.0 ( $95 \%$ CI: $4492.5-19368.2$ ) mIU $/ \mathrm{mL}$ respectively, and at Month 6 and Month 13, 5645.4 ( $95 \%$ CI: 1531.9 - 20805.3) and 4229.5 ( $95 \%$ CI: 2073.8 - 8626.0) $\mathrm{mIU} / \mathrm{mL}$ respectively for the HZ/su OnChemo group (Table 7.6).

The post-vaccination anti-gE Ab GMCs in the Placebo PreChemo and OnChemo groups remained at pre-vaccination level (Table 7.6). To note that the anti-gE Ab GMC was 1185.4 ( $95 \%$ CI: 959.3 - 1464.7) mIU/mL at pre-vaccination and 1325.9 ( $95 \% \mathrm{CI}$ : 989.6-1776.5) $\mathrm{mIU} / \mathrm{mL}$ at Month 6 in the Placebo PreChemo group and 868.2 ( $95 \% \mathrm{CI}$ : 512.9 - 1469.7) $\mathrm{mIU} / \mathrm{mL}$ at pre-vaccination and 1768.2 ( $95 \% \mathrm{CI}$ : 1016.7-3075.1) $\mathrm{mIU} / \mathrm{mL}$ at Month 6 in the Placebo OnChemo group (Table 7.6).

VRRs in the HZ/su PreChemo group at Month 1 (post first vaccination) and Month 2 (post second vaccination) were $93.8 \%$ ( $95 \%$ CI: 84.8 - 98.3 ) and $93.8 \%$ ( $95 \% \mathrm{CI}: 85.0$ 98.3) respectively and at Months 6 and Month 13, $75.0 \%$ ( $95 \%$ CI: 56.6 - 88.5) and $52.9 \%$ ( $95 \%$ CI: $38.5-67.1$ ) respectively. VRRs in the HZ/su OnChemo group at Month 1 (post first vaccination) and Month 2 (post second vaccination) were $61.9 \%$ ( $95 \% \mathrm{CI}$ : $38.4-81.9$ ) and $63.6 \%$ ( $95 \%$ CI: $40.7-82.8$ ) respectively, and at Months 6 and Month $13,70.0 \%(95 \%$ CI: $34.8-93.3)$ and $47.1 \%$ ( $95 \%$ CI: $23.0-72.2$ ) respectively. In the Placebo PreChemo group, there was no subject meeting the definition of responder at any time point. In the Placebo OnChemo group, there was 1 subject meeting the definition of responder but only at Month 6 (Table 7.7).

The MGIs (from pre-vaccination baseline) in the HZ/su PreChemo group at Month 1 and Month 2 were 34.4 ( $95 \%$ CI: $25.3-46.6$ ) and 22.3 ( $95 \%$ CI: $17.1-29.0$ ) respectively and at Month 6 and Month 13, 9.2 ( $95 \%$ CI: $6.2-13.8$ ) and 4.6 ( $95 \%$ CI: $3.5-6.1$ ) respectively. The MGIs (from pre-vaccination baseline) in the HZ/su OnChemo group at Month 1 and Month 2 were 8.2 ( $95 \%$ CI: $4.0-16.7$ ) and 8.5 ( $95 \%$ CI: $4.1-17.5$ ) respectively and at Months 6 and 13, 7.0 ( $95 \%$ CI: $2.1-23.7$ ) and 3.6 ( $95 \%$ CI: $2.0-6.4$ ) respectively. In the Placebo PreChemo and OnChemo groups, the MGI was not higher than 1.1 and 1.2 respectively, at any time point (Table 7.8).

Descriptive statistics of the fold increase for anti-gE Ab concentrations at Month 1, 2, 6 and 13 in the PreChemo and On Chemo groups are shown in Table 7.9.

The distribution of the fold increase from baseline for anti-gE Ab concentrations at Month 1, 2, 6 and 13 in the PreChemo and On Chemo groups is shown in Table 7.10.

The reverse cumulative curve for anti-gE Ab concentrations at Month $0,1,2,6$ and 13 in the PreChemo and On Chemo groups is shown in Figure 7.6, Figure 7.7, Figure 7.8, Figure 7.9 and Figure 7.10, respectively.

### 7.2.1.4. ATP analysis: humoral immunogenicity by age strata in all subjects

Results from descriptive analyses by age strata (18-49 YOA and $\geq 50 \mathrm{YOA}$ ) in all subjects performed on the ATP cohort for Humoral immunogenicity and the ATP cohort for Humoral persistence (or Adapted ATP cohort Humoral immunogenicity, as applicable) are presented:

- Seropositivity rates and anti-gE Ab GMCs at Months $0,1,2,6$ and 13 (Table 7.11).
- VRRs for anti-gE Ab concentrations at Months 1, 2, 6 and 13 (Table 7.12).
- MGIs of anti-gE Ab concentrations at Months 1, 2, 6 and 13 (Table 7.13).
- Descriptive statistics of the fold increase for anti-gE Ab concentrations at Month 1, 2, 6 and 13 (Table 7.14).
- Distribution of the fold increase from baseline for anti-gE Ab concentrations at Month 1, 2, 6 and 13 (Table 7.15).
- Reverse cumulative curve for anti-gE Ab concentrations at Months $0,1,2,6$ and 13 respectively (Figure 7.11, Figure 7.12, Figure 7.13, Figure 7.14 and Figure 7.15).

The following results are detailed:
Regarding the 18-49 YOA stratum, in the HZ/su and Placebo groups the seropositivity rates for anti-gE Abs were $100 \%$ at all timepoints (Table 7.11).

Regarding the $\geq 50$ YOA stratum, in the HZ/su group and Placebo group, the baseline (at pre-vaccination) seropositivity rates for anti-gE Abs was $98.3 \%$ and $98.5 \%$ respectively. In the $\mathrm{HZ} /$ su group seropositivity increased to $100 \%$ at Month 1 and remained so thereafter. In the Placebo group, the seropositivity was $98.6 \%$ at Month 1 and Month 2, and $100 \%$ at Month 6 and Month 13) (Table 7.11).

Regarding the 18-49 YOA stratum, pre-vaccination anti-gE Ab GMCs were 992.1 (95\% CI: 722.8 - 1361.7) and 1067.1 ( $95 \%$ CI: $801.4-1420.7$ ) $\mathrm{mIU} / \mathrm{mL}$ respectively for $\mathrm{HZ} / \mathrm{su}$ and Placebo groups. Post-vaccination, anti-gE Ab GMCs at Month 1 (post first vaccination) and Month 2 (post second vaccination) were 24450.8 ( $95 \% \mathrm{CI}$ : 13910.242978.6) and 15710.4 ( $95 \%$ CI: $10327.8-23898.5$ ) $\mathrm{mIU} / \mathrm{mL}$ respectively, and at Month 6 and $13,5591.3$ ( $95 \%$ CI: $3408.1-9173.0$ ) and 3328.5 ( $95 \%$ CI: $2149.4-5154.5$ ) $\mathrm{mIU} / \mathrm{mL}$ respectively for the HZ/su group (Table 7.11).

Regarding the $\geq 50$ YOA stratum, pre-vaccination anti-gE Ab GMCs were 1076.9 (95\% CI: $842.0-1377.3$ ) and 1138.5 ( $95 \%$ CI: 882.2 - 1469.4) mIU/mL respectively for HZ/su and Placebo groups. Post-vaccination, anti-gE Ab GMCs at Month 1 (post first vaccination), and Month 2 (post second vaccination) were 24954.0 ( $95 \%$ CI: 17993.7 34606.7 ) and 19587.7 ( $95 \%$ CI: 14604.7 - 26271.1) $\mathrm{mIU} / \mathrm{mL}$ respectively, and at Month 6 and Month 13, 9435.8 ( $95 \%$ CI: 5623.5 - 15832.5) and 5159.3 ( $95 \%$ CI: 3785.6 7031.7 ) $\mathrm{mIU} / \mathrm{mL}$ respectively for the $\mathrm{HZ} /$ su group (Table 7.11).

For both age strata, the post-vaccination anti-gE Ab GMCs in the Placebo group remained near the pre-vaccination level. To note that the anti-gE Ab GMC was 1138.5 ( $95 \%$ CI: $882.2-1469.4$ ) mIU $/ \mathrm{mL}$ at pre-vaccination and 1597.5 ( $95 \% \mathrm{CI}: 1150.7-$ 2217.9) $\mathrm{mIU} / \mathrm{mL}$ at Month 6 in the $\geq 50$ YOA stratum (Table 7.11).

Regarding the 18-49 YOA stratum, VRRs in the HZ/su group both at Month 1 (post first vaccination) and Month 2 (post second vaccination) were $85.2 \%$ ( $95 \%$ CI: 66.3 - 95.8 ) and at Month 6 and Month 13, 68.8\% (95\% CI: 41.3 - 89.0) and 45.5\% (95\% CI: 24.4 67.8) respectively. Regarding the $\geq 50$ YOA stratum, VRRs in the HZ/su group at Month 1 (post first vaccination) and Month 2 (post second vaccination) were $86.2 \%$ ( $95 \% \mathrm{CI}$ : $74.6-93.9$ ) and $86.7 \%$ ( $95 \%$ CI: $75.4-94.1$ ) respectively, and at Month 6 and Month $13,76.9 \%(95 \%$ CI: $56.4-91.0)$ and $54.3 \%$ ( $95 \%$ CI: $39.0-69.1$ ) respectively. In the Placebo group for both age strata, there were no subjects meeting the definition of responder, except for 1 subject at Month 6 in the 18-49 YOA stratum (Table 7.12).

Regarding the 18-49 YOA stratum, the MGIs (from pre-vaccination baseline) in the HZ/su group at Month 1 and Month 2 were 24.6 ( $95 \%$ CI: $13.9-43.5$ ) and 15.8 ( $95 \% \mathrm{CI}$ : $10.0-25.1)$ respectively and at Month 6 and Month 13, $6.3(95 \%$ CI: $4.0-10.0)$ and 3.6 ( $95 \%$ CI: $2.4-5.2$ ) respectively. Regarding the $\geq 50$ YOA stratum, the MGIs (from prevaccination baseline) in the HZ/su group at Month 1 and Month 2 were 23.9 ( $95 \% \mathrm{CI}$ : $16.3-35.1)$ and 18.2 ( $95 \%$ CI: $12.8-25.9$ ) respectively and at Month 6 and Month 13, 10.5 ( $95 \%$ CI: $5.9-18.8$ ) and $4.7(95 \%$ CI: $3.4-6.6)$ respectively. In the Placebo group in both age strata, the MGI was not higher than 1.0, at any time point (Table 7.13).

### 7.2.1.5. ATP analysis: Humoral immunogenicity by age strata in the PreChemo groups only

Results from descriptive analyses by age strata in the PreChemo groups only performed on the Adapted ATP cohort Humoral immunogenicity are presented:

- Seropositivity rates and anti-gE Ab GMCs at Month $0,1,2,6$ and 13 (Table 7.16).
- VRRs for anti-gE Ab concentrations at Month 1, 2, 6 and 13 (Table 7.17).
- MGIs of anti-gE Ab concentrations at Month 1, 2, 6 and 13 (Table 7.18).
- Descriptive statistics of the fold increase for anti-gE Ab concentrations at Month 1, 2, 6 and 13 (Table 7.19).
- Distribution of the fold increase from baseline for anti-gE Ab concentrations at Month 1, 2, 6 and 13 (Table 7.20).

The following results are detailed:
Regarding the 18-49 YOA stratum, in the HZ/su and Placebo groups the seropositivity rates for anti-gE Abs were $100 \%$ at all timepoints (Table 7.16).

Regarding the $\geq 50$ YOA stratum, in the HZ/su group and Placebo group, the baseline (at pre-vaccination) seropositivity rates for anti-gE Abs was $97.8 \%$ and $98.1 \%$ respectively. In the HZ/su group seropositivity increased to $100 \%$ at Month 1 and remained so thereafter. In the Placebo group, the seropositivity was $98.2 \%$ at Month 1 and Month 2, and $100 \%$ at Month 6 and Month 13 (Table 7.16).

Regarding the 18-49 YOA stratum, pre-vaccination anti-gE Ab GMCs were 930.2 (95\% CI: 618.9-1398.1) and 1088.7 ( $95 \%$ CI: $833.6-1421.8$ ) mIU/mL respectively for $\mathrm{HZ} / \mathrm{su}$ and Placebo groups. Post-vaccination, anti-gE Ab GMCs at Month 1 (post first vaccination) and Month 2 (post second vaccination) were 41519.9 ( $95 \% \mathrm{CI}$ : $27568.8-$ $62531.1) \mathrm{mIU} / \mathrm{mL}$ and 20955.9 ( $95 \%$ CI: $15025.6-29226.7$ ) $\mathrm{mIU} / \mathrm{mL}$ respectively, and at Month 6 and Month 13, 5893.1 ( $95 \%$ CI: 4121.8 - 8425.4) and 3785.9 ( $95 \% \mathrm{CI}: 2468.1$ -5807.3 ) $\mathrm{mIU} / \mathrm{mL}$ respectively for the HZ/su group (Table 7.16).

Regarding the $\geq 50$ YOA stratum, pre-vaccination anti-gE Ab GMCs were 1077.7 (95\% CI: 810.2-1433.4) and 1227.2 ( $95 \%$ CI: 925.8 - 1626.6) $\mathrm{mIU} / \mathrm{mL}$ respectively for $\mathrm{HZ} / \mathrm{su}$ and Placebo groups. Post-vaccination, anti-gE Ab GMCs at Month 1 (post first vaccination), and Month 2 (post second vaccination) were 32207.5 ( $95 \%$ CI: $24065.8-$ 43103.6 ) and 23863.7 ( $95 \%$ CI: 18947.3 - 30055.8 ) mIU/mL respectively, and at Month 6 and Month 13, 10645.5 ( $95 \%$ CI: $6635.5-17079.0$ ) and 4969.6 ( $95 \%$ CI: $3581.6-$ $6895.5) \mathrm{mIU} / \mathrm{mL}$ respectively for the $\mathrm{HZ} /$ su group (Table 7.16).

For both age strata, the post-vaccination anti-gE Ab GMCs in the Placebo group remained near pre-vaccination level. To note that the anti-gE Ab GMC was 1227.2 (95\% CI: $925.8-1626.6$ ) $\mathrm{mIU} / \mathrm{mL}$ at pre-vaccination and 1535.5 ( $95 \% \mathrm{CI}: 1073.2-2197.0$ ) $\mathrm{mIU} / \mathrm{mL}$ at Month 6 in the $\geq 50$ YOA stratum (Table 7.16).

Regarding the 18-49 YOA stratum, VRRs in the HZ/su group both at Month 1 (post first vaccination) and Month 2 (post second vaccination) were $100.0 \%$ ( $95 \% \mathrm{CI}: 82.4-100$ ) and $94.7 \%$ ( $95 \%$ CI: 74.0 - 99.9) and at Months 6 and Month 13, $75.0 \%$ ( $95 \%$ CI: 42.8 94.5 ) and $50.0 \%$ ( $95 \% \mathrm{CI}$ : $24.7-75.3$ ) respectively. Regarding the $\geq 50$ YOA stratum, VRRs in the HZ/su group at Month 1 (post first vaccination) and Month 2 (post second vaccination) were $91.1 \%$ ( $95 \%$ CI: 78.8 - 97.5 ) and $93.5 \%$ ( $95 \%$ CI: $82.1-98.6$ ) respectively, and at Month 6 and Month 13, $75.0 \%$ ( $95 \%$ CI: 50.9 - 91.3 ) and $54.3 \%$ ( $95 \%$ CI: $36.6-71.2$ ) respectively. In the Placebo group for both age strata, there were no subjects meeting the definition of responder (Table 7.17).

Regarding the 18-49 YOA stratum, the MGIs (from pre-vaccination baseline) in the HZ/su group at Month 1 and Month 2 were 44.6 ( $95 \%$ CI: $27.9-71.5$ ) and 22.5 ( $95 \% \mathrm{CI}$ : 14.3 - 35.5) respectively and at Month 6 and Month 13, 7.6 ( $95 \%$ CI: $4.8-12.0$ ) and 4.4 ( $95 \%$ CI: $2.9-6.7$ ) respectively. Regarding the $\geq 50$ YOA stratum, the MGIs (from prevaccination baseline) in the HZ/su group at Months 1 and Month 2 were 30.8 ( $95 \% \mathrm{CI}$ : $20.8-45.5)$ and 22.1 ( $95 \%$ CI: $15.8-31.0$ ) respectively and at Month 6 and Month 13, 10.4 ( $95 \% \mathrm{CI}: 5.7-19.2$ ) and 4.7 ( $95 \% \mathrm{CI}: 3.2-6.8$ ) respectively. In the Placebo group in both age strata, the MGI was not higher than 1.0, at any time point (Table 7.18).

### 7.2.2. ATP analysis: cell-mediated immunogenicity

### 7.2.2.1. ATP analysis: cell-mediated immunogenicity, overall

Results of confirmatory objectives assessed in the CMI sub-cohort on the ATP cohort for CMI are presented.

The second confirmatory secondary objective of the study was met as the lower limit of the $95 \%$ CI of the GM ratio (HZ/su PreChemo group over Placebo PreChemo group) in gE-specific CD4[2+] T-cell frequencies at Month 2 (post second vaccination) was 3.79. Therefore the success criterion (greater than 1) was demonstrated. The observed GM ratio was 13.67 ( $95 \% \mathrm{CI}: 3.79-49.38 ; \mathrm{P}=0.0002$ ) (Table 31).

Descriptive results obtained with the end of study analysis are presented in Table 32; the observed GM ratio at Month 2 was 9.94 ( $95 \%$ CI: 3.63 - 27.19).

The third confirmatory secondary objective of the study was not met as the lower limit of the $95 \%$ CI of the VRR for gE-specific CD4[2+] T-cell frequencies in the HZ/su PreChemo group at Month 2 (post second vaccination) was $33.5 \%$. Therefore, the success criterion (at least 50\%) was not demonstrated. The observed VRR was $57.9 \% ~(95 \% \mathrm{CI}$ : 33.5 - 79.7) (Table 33).

Descriptive results obtained with the end of study analysis are presented in Table 34; the observed VRR at Month 2 was 50.0\% (95\% CI: 28.2 -71.8).

Table 31 Adjusted geometric means and ratio of $\mathrm{HZ} / \mathrm{su}$ over placebo for gEspecific CD4[2+] T-cells frequencies at Month 2 in PreChemo Groups only (ATP cohort for CMI immunogenicity) (first analysis)

|  |  |  | Adjusted geometric mean |  |  | Adjusted geometric mean ratio |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Timing | Group | N | Value | LL | UL | Value | LL | UL | P-value for the ratio |
| Pll(M2) | HZ/su | 19 | 923.7 | 616.4 | 1346.8 | 13.67 | 3.79 | 49.38 | 0.0002 |
|  | Placebo | 20 | 67.6 | -3.4 | 164.2 |  | . |  | . |

HZ/su = Herpes Zoster sub-unit vaccine
Placebo = Placebo group
$N=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval
Confidence Interval (CI) were back transformed to original units
The $p$-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)
Table 32 Adjusted geometric means and ratio of HZ/su over placebo for gEspecific CD4[2+] T-cells frequencies at Month 2 in PreChemo Groups only (ATP cohort for CMI immunogenicity)

|  |  | Adjusted geometric mean |  |  |  | Adjusted geometric mean ratio |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  |  |  | $95 \% \mathrm{Cl}$ |  |  | $95 \% \mathrm{CI}$ |  |  |  |
| Timing | Group | N | Value | LL | UL | Value | LL | UL | P-value for the ratio |
| PII(M2) | HZ/su | 22 | 781.8 | 535.2 | 1110.4 | 9.94 | 3.63 | 27.19 | $<.0001$ |
|  | Placebo | 27 | 78.7 | 13.7 | 162.9 | . | . | . | . |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval
Confidence Interval (CI) were back transformed to original units The $p$-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)
Table 33 Vaccine response rates for gE-specific CD4[2+] T-cells frequencies at Month 2 in PreChemo Groups only (ATP cohort for CMI immunogenicity) (first analysis)

|  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |
| Test description | Group | N | n | \% | LL | UL |
| CD4[2+] | HZ/su | 19 | 11 | 57.9 | 33.5 | 79.7 |
|  | Placebo | 20 | 0 | 0.0 | 0.0 | 16.8 |

## HZ/su = Herpes Zoster sub-unit vaccine

Placebo = Placebo group
Vaccine response defined as:
For initially subjects with pre-vaccination T cell frequencies below the threshold, at least a 2 -fold increase as compared to the threshold ( $2 \times 320$ Events/10E6 CD4+ T cellls)
For initially subjects with pre-vaccination $T$ cell frequencies above the threshold, at least a 2-fold increase as compared to pre-vaccination $T$ cell frequencies
$\mathrm{N}=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 34 Vaccine response rates for gE-specific CD4[2+] T-cells frequencies at Month 2 in PreChemo Groups only (ATP cohort for CMI immunogenicity)

|  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% |  |
| Test description | Group | N | n | \% | LL | UL |
| CD4[2+] | HZ/su | 22 | 11 | 50.0 | 28.2 | 71.8 |
|  | Placebo | 27 | 0 | 0.0 | 0.0 | 12.8 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as:
For initially subjects with pre-vaccination T cell frequencies below the threshold, at least a 2-fold increase as compared to the threshold ( $2 x<320>$ Events/10E6 CD4+ T cells)
For initially subjects with pre-vaccination $T$ cell frequencies above the threshold, at least a 2 -fold increase as compared to pre-vaccination $T$ cell frequencies
$N=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit
Results from descriptive analyses in the PreChemo Groups performed on the ATP cohort for the Adapted ATP cohort for CMI are presented.

Results of descriptive statistics of the frequency of gE-specific CD4[2+] T-cells for Month 1, Month 2 and Month 13 are presented in Table 7.45.

In the HZ/su group, the observed median (min - max) frequency of gE-specific CD4[2+] T-cells (per $10^{6}$ total CD4+ T-cells) was 127.3 (1.0-662.4), 391.9 (1.0-3276.6) and 778.8 (1.0-4835.8) at Month 0 (pre-vaccination), Month 1 (post first vaccination) and Month 2 (post second vaccination) respectively, and 332.9 (1.0-2416.0) at Month 13. In the Placebo group, the observed median frequency of gE-specific CD4[2+] T-cells (point estimate) was $104.8,50.0$ and 61.8 at Month 0,1 and 2 respectively, and 51.2 at Month 13 (Table 7.45).

In the HZ/su group, the observed median (min - max) fold increase over pre-vaccination in the frequency of gE-specific CD4[2+] T-cells was $2.5(0.0-426.5)$ and $4.9(0.5-$ 880.8) at Month 1and Month 2 respectively, and $2.0(0.0-94.4)$ at Month 13. In the Placebo group, the observed median fold increase over pre-vaccination in the frequency of gE-specific CD4[2+] T-cells (point estimate) was 0.8 and 0.9 at Months 1 and 2, respectively, and 0.7 at Month 13 (Table 7.46).

Results regarding VRRs for gE-specific CD4[2+] T-cells at Month 1, Month 2 and Month 13 are presented in Table 7.47.

In the HZ/su group, the VRR in the frequency of gE-specific CD4[2+] T-cells was 20.0\% ( $95 \%$ CI: $6.8-40.7$ ) and $50.0 \%$ ( $95 \%$ CI: $28.2-71.8$ ) at Month 1, 2 and $17.6 \%(95 \% \mathrm{CI}$ : $3.8-43.4$ ) at Month 13. In the Placebo group, there were no subjects meeting the definition of responder at any timepoint (Table 7.47).

Results from additional descriptive analyses in the PreChemo Groups performed on the Adapted ATP cohort for CMI are presented:

- Descriptive statistics of the frequency in CD4[2+] T-cells following induction with gE (Table 7.48).
- Descriptive statistics of the fold increase of frequency in CD4[2+] T-cells at Month 1,2 and 13 from pre-vaccination following induction with gE (Table 7.49).
- Adjusted geometric means and ratio of $\mathrm{HZ} /$ su over placebo in frequency at Month 2 of CD4[2+] T-cells following induction with gE (Table 7.50).


### 7.2.2.2. ATP analysis: cell-mediated immunogenicity by age strata

Results from descriptive analyses by age strata in the PreChemo groups performed on the Adapted ATP cohort for CMI, are presented:

- Descriptive statistics of the frequency of gE-specific CD4[2+] T-cells (Table 7.51).
- Descriptive statistics of the fold increase of the frequency of gE-specific CD4[2+] Tcells at Months 1, 2 and 13 from pre-vaccination (Table 7.52).
- VRRs in the frequency of gE-specific CD4[2+] T-cells at Months 1, 2 and 13 (Table 7.53).
- Adjusted GMs and ratio of HZ/su over placebo in the frequency of gE-specific CD4[2+] T-cells at Month 2 (Table 7.54).
- Descriptive statistics of the frequency in CD4[2+] T-cells following induction with gE (Table 7.55).
- Descriptive statistics of the fold increase of the frequency of CD4[2+] T-cells at Month 1, 2 and 13 from pre-vaccination following induction with gE (Table 7.56).
- Adjusted GMs and ratio of HZ/su over placebo in the frequency of CD4[2+] T-cells following induction with gE at Month 2 (Table 7.57).
Following results are detailed:
Regarding the 18-49 YOA stratum, in the HZ/su group, the observed median (min - max) frequency of gE-specific CD4[2+] T-cells (per $10^{6}$ total CD4 T-cells) was 141.7 (1.0 573.8), $437.6(1.0-3276.6)$ and $652.6(1.0-4835.8)$ at Month 0 (pre-vaccination), Month 1 (post first vaccination) and Month 2 (post second vaccination) respectively and 322.7 (1.0-2416.0) at Month 13. In the Placebo group, the observed median frequency of gE-specific CD4[2+] T-cells (point estimate) was 126.5, 126.6 and 139.5 at Month 0,1 and 2 respectively, and 288.6 at Month 13 (Table 7.51).

Regarding the $\geq 50 \mathrm{YOA}$ stratum, in the HZ/su group, the observed median (min - max) frequency of gE-specific CD4[2+] T-cells (per $10^{6}$ total CD4 T-cells) was 127.3 (1.0 662.4), $364.0(38.2-1273.4)$ and 783.4 (187.4-3752.4) at Month 0 (pre-vaccination), Month 1 (post first vaccination) and Month 2 (post second vaccination) respectively, and 345.3 (1.1-1038.2) at Month 13. In the Placebo group, the observed median frequency of gE-specific CD4[2+] T-cells (point estimate) was $85.4,39.5$ and 58.4 at Month 0,1 and 2 respectively and 28.6 at Month 13 (Table 7.51).

Regarding the 18-49 YOA stratum, in the HZ/su group, the observed median (min - max) fold increase over pre-vaccination in the frequency of gE-specific CD4[2+] T-cells was $4.6(0.0-55.7)$ and $4.6(0.5-97.3)$ at Month 1 and Month 2 respectively, and $1.9(0.9-$ 48.6) at Month 13. In the Placebo group, the observed median fold increase over prevaccination in the frequency of gE-specific CD4[2+] T-cells (point estimate) was 1.0 and 1.1 at Month 1 and Month 2, respectively, and 4.7 at Month 13 (Table 7.52).

Regarding the $\geq 50 \mathrm{YOA}$ stratum, in the HZ/su group, the observed median (min - max) fold increase over pre-vaccination in the frequency of gE-specific CD4[2+] T-cells was $2.1(0.3-426.5)$ and $6.4(1.2-880.8)$ at Month land Month 2 respectively, and $3.0(0.0$ - 94.4) at Month 13. In the Placebo group, the observed median fold increase over prevaccination in the frequency of gE-specific CD4[2+] T-cells (point estimate) was 0.8 at Month 1 and Month 2, respectively and 0.4 at Month 13 (Table 7.52).

Regarding the 18-49 YOA stratum, in the HZ/su group, the VRR in the frequency of gEspecific CD4[2+] T-cells was $33.3 \%$ ( $95 \%$ CI: 7.5 - 70.1) and 55.6\% (95\% CI: 21.2 86.3) at Month 1 and Month 2, and $33.3 \%$ ( $95 \%$ CI: $4.3-77.7$ ) at Month 13. In the Placebo group, there were no subjects meeting the definition of responder at any timepoint (Table 7.53).

Regarding the $\geq 50$ YOA stratum, in the $\mathrm{HZ} /$ su group, the VRR in the frequency of gEspecific CD4[2+] T-cells was $12.5 \%$ ( $95 \%$ CI: 1.6 - 38.3 ) and $46.2 \%$ ( $95 \%$ CI: 19.2 74.9) at Month 1 and Month 2 and $9.1 \%$ ( $95 \%$ CI: $0.2-41.3$ ) at Month 13. In the Placebo group, there were no subjects meeting the definition of responder at any timepoint (Table 7.53).

### 7.3. Total vaccinated cohort analysis

### 7.3.1. TVC analysis: humoral immununogenicity

The percentage of vaccinated subjects excluded from the ATP cohort for Humoral immunogenicity and ATP cohort for Humoral persistence, respectively was more than $5 \%$ in any treatment group (Table 6.13 and Table 6.21). Therefore, an analysis based on the TVC was performed to complement the ATP analysis as per protocol.

The results for the PreChemo group only at Month 2 are presented in Table 7.21 and Table 7.22.

The results for all subjects are presented in Table 7.23 to Table 7.29, and Figure 7.16 to Figure 7.20.

The results for the PreChemo group and OnChemo group are presented in Table 7.30 to Table 7.34 and Figure 7.21 to Figure 7.25.

The results by age strata in all subjects are presented in Table 7.35 to Table 7.39 and in Figure 7.26 to 7.30 .

The results by age strata in the the PreChemo group only are presented in Table 7.40 to Table 7.44.

Results of the analyses performed on the TVC cohort were consistent with results of the analyses performed on the ATP cohort for Humoral immunogenicity and the ATP cohort for Humoral persistence (adapted ATP cohort for Humoral immunogenicity, as applicable).

### 7.3.2. TVC analysis: cell-mediated immunogenicity

The percentage of vaccinated subjects excluded from the ATP cohort for CMI immunogenicity and ATP cohort for CMI persistence, respectively was more than $5 \%$ in any treatment group (Table 6.15 and Table 6.22). Therefore, an analysis based on the TVC for CMI immunogenicity was performed to complement the ATP analysis as per protocol.

The results for the PreChemo group are presented in Table 7.58 to Table 7.64 and in Table 7.71.

The results by age strata in the the PreChemo group are presented in Table 7.65 to Table 7.70 and in Table 7.72.

Results of the analyses performed on the TVC cohort for were consistent with results of the analyses performed on the ATP cohort for Humoral immunogenicity and the ATP cohort for Humoral persistence (adapted ATP cohort for CMI immunogenicity, as applicable).

### 7.4. Immunogenicity summary

## Assessment of confirmatory objectives

Results of confirmatory humoral immunogenicity objectives assessed on the ATP cohort for Humoral immunogenicity, and confirmatory CMI objectives assessed on the ATP cohort for CMI, are presented.

The confirmatory objectives were assessed sequentially in order of ascending rank. The objectives were assessed until an objective was not met. At this point, a descriptive analysis of the remaining endpoints was conducted. The assessment of the confirmatory objectives was conducted on active phase data and referred to as a "first analysis" in this CSR. The immunogenicity tables and figures were generated on active phase data at first analysis and end of study analysis using the respective clinical database. The active phase results on humoral immunogenicity generated at first analysis and at end of study analysis were the same, the tabulations and figures generated at end of study analysis are presented in this report.

The active phase results on CMI generated at first analysis and at end of study were not the same, as a result of changes in the laboratory CMI data release definitions allowing for more CMI data to be released, even so, there was no impact on study conclusions. Regarding the CMI-related confirmatory secondary objectives, the results obtained at first analysis and end of study analysis are both presented in this report.

- The confirmatory primary objective of the study was met as the lower limit of the 95\% CI of the GM ratio (HZ/su PreChemo Group over Placebo PreChemo group) in anti-gE Ab concentrations at Month 2 (post second vaccination) was 17.9. Therefore, the success criterion (greater than 3) was demonstrated. The adjusted GM ratio was 23.2 ( $95 \% \mathrm{CI}: 17.9-30.0 ; \mathrm{P}<0.0001$ ).
- The first confirmatory secondary objective of the study was met as the lower limit of the $95 \%$ CI of the VRR for anti-gE Ab concentrations in the HZ/su PreChemo group at Month 2 (post second vaccination) was $85.0 \%$. Therefore, the success criterion (at least $60 \%$ ) was demonstrated. The VRR was $93.8 \%$ ( $95 \%$ CI: $85.0-98.3$ ).
- The second confirmatory secondary objective of the study was met as the lower limit of the $95 \%$ CI of the GM ratio (HZ/su PreChemo group over Placebo PreChemo group) in gE-specific CD4[2+] T-cell frequencies at Month 2 (post second vaccination) was 3.79 (greater than 1), therefore, the success criterion was demonstrated. The observed GM ratio was 13.67 ( $95 \% \mathrm{CI}: 3.79-49.38 ; \mathrm{P}=0.0002$ ).
Descriptive results obtained with the end of study analysis: the observed GM ratio at Month 2 was 9.94 ( $95 \%$ CI: 3.63 - 27.19).
- The third confirmatory secondary objective of the study was not met as the lower limit of the $95 \%$ CI of the VRR for gE -specific CD4[2+] T-cell frequencies in the $\mathrm{HZ} / \mathrm{su}$ PreChemo group at Month 2 (post second vaccination) was $33.5 \%$. Therefore, the success criterion (at least $50 \%$ ) was not demonstrated. The observed VRR was 57.9\% (95\% CI: 33.5 - 79.7).

Descriptive results obtained with the end of study analysis: the observed VRR at Month 2 was 50.0\% (95\% CI: 28.2 - 71.8).
According to the hierarchical procedure applied, the confirmatory objectives were assessed sequentially in order of ascending rank until an objective was not met. Therefore, the following objectives were analysed descriptively.

- Regarding the anti-gE humoral immune response at Month 2 (post second vaccination) in the $\mathrm{HZ} /$ su group compared to the Placebo group (all subjects), the observed adjusted GM ratio was 14.4 ( $95 \%$ CI: 10.7 - 19.5).
- The VRR in anti-gE humoral immune response at Month 2 (post second vaccination) in the HZ/su group (all subjects) was $86.2 \%$ ( $95 \% \mathrm{CI}$ : 77.1-92.7).


## Results of descriptive analyses

## Humoral immunogenicity overall

Results obtained for all subjects are presented for the ATP cohort for Humoral immunogenicity/Humoral persistence

- Anti-gE humoral immune responses relative to the pre-vaccination level were observed in the $\mathrm{HZ} /$ su group at 1 month following the first and second dose and persisted up to 1 year post-dose 2 , relative to pre-vaccination levels.
- Pre-vaccination anti-gE Ab GMCs were 1049.8 (95\% CI: 865.8 - 1273.0) and 1116.7 ( $95 \%$ CI: 918.4 - 1358.0) $\mathrm{mIU} / \mathrm{mL}$ respectively for $\mathrm{HZ} / \mathrm{su}$ and Placebo groups. Post-vaccination, anti-gE Ab GMCs at Months 1 (post first vaccination) and Month 2 (post second vaccination) were 24793.1 ( $95 \%$ CI: 18747.8 32787.6 ) and 18291.7 ( $95 \%$ CI: $14432.1-23183.5$ ) $\mathrm{mIU} / \mathrm{mL}$ respectively for the HZ/su group. Anti-gE Ab GMC at Month 13 was 4477.3 ( $95 \%$ CI: $3482.4-$ $5756.3) \mathrm{mIU} / \mathrm{mL}$ for the HZ/su group. The post-vaccination anti-gE Ab GMCs in the Placebo group remained near pre-vaccination level.
- VRRs in the HZ/su group at Month 1 (post first vaccination) and Month 2 (post second vaccination) were $85.9 \%$ ( $95 \%$ CI: $76.6-92.5$ ) and $86.2 \%$ ( $95 \%$ CI: 77.1 -92.7 ) respectively, and at Month $13,51.5 \%$ ( $95 \%$ CI: $39.0-63.8$ ). In the Placebo group, there were no subjects meeting the definition of responder at Months 1, 2 and 13.

Results obtained for the PreChemo and OnChemo groups are presented for the ATP cohort for Humoral immunogenicity/Humoral persistence.

- Anti-gE humoral immune responses were observed in the HZ/su PreChemo and HZ/su OnChemo groups 1 month post first vaccination and 1 month post second vaccination. Persistence of humoral immunogenicity at 1 year post second vaccination was also observed in HZ/su subjects and appeared to be similar for PreChemo and OnChemo groups despite the different administration schedules of each group. Secondary to the small number of subjects included in the OnChemo group (per stratification factor at randomisation), results obtained for the OnChemo group need to be interpreted with caution.
- In the PreChemo group, pre-vaccination anti-gE Ab GMCs were 1032.3 (95\% CI: $821.0-1298.0$ ) and 1185.4 ( $95 \% \mathrm{CI}$ : $959.3-1464.7$ ) mIU/mL respectively for $\mathrm{HZ} / \mathrm{su}$ and Placebo groups. Post-vaccination, anti-gE Ab GMCs at Month 1 (post first vaccination) and Month 2 (post second vaccination) were 34729.8 ( $95 \%$ CI: 27485.9 - 43882.8) and 22974.3 (95\% CI: 19080.0 - 27663.5 ) $\mathrm{mIU} / \mathrm{mL}$ respectively, and at Month 13, 4563.0 ( $95 \%$ CI: 3532.8 - 5893.7) $\mathrm{mIU} / \mathrm{mL}$ for the $\mathrm{HZ} / \mathrm{su}$ PreChemo group. The post-vaccination anti-gE Ab GMCs in the Placebo PreChemo group remained near pre-vaccination level.
- In the OnChemo group, pre-vaccination anti-gE Ab GMCs were 1103.4 (95\% CI: 753.4 - 1616.0) and 868.2 ( $95 \%$ CI: 512.9 - 1469.7) mIU/mL respectively for HZ/su and Placebogroups. Post-vaccination, anti-gE Ab GMCs at Months 1 (post first vaccination), and Month 2 (post second vaccination) were 8876.6 ( $95 \% \mathrm{CI}$ : 4134.3 - 19058.6) and 9328.0 ( $95 \%$ CI: $4492.5-19368.2$ ) mIU/mL respectively, and at Month 13, 4229.5 ( $95 \% \mathrm{CI}$ : 2073.8 - 8626.0) $\mathrm{mIU} / \mathrm{mL}$ for the $\mathrm{HZ} / \mathrm{su}$ OnChemo group. The post-vaccination anti-gE Ab GMCs in the Placebo OnChemo group remained near pre-vaccination level.
- In the PreChemo group, VRRs in the HZ/su group at Month 1 (post first vaccination) and Month 2 (post second vaccination) were $93.8 \%$ ( $95 \%$ CI: 84.8 98.3) and $93.8 \%$ ( $95 \%$ CI: $85.0-98.3$ ) respectively, and at Month 13, $52.9 \%$ ( $95 \%$ CI: $38.5-67.1$ ). In the Placebo group, there were no subjects meeting the definition of responder at any time point.
- In the OnChemo group, VRRs in the HZ/su group at Month 1 (post first vaccination) and Month 2 (post second vaccination) were $61.9 \%$ ( $95 \%$ CI: 38.4 81.9) and $63.6 \%$ ( $95 \%$ CI: 40.7 - 82.8) respectively, and at Month 13, 47.1\% ( $95 \%$ CI: $23.0-72.2$ ). In the Placebo group, there were no subjects meeting the definition of responder at Month 1, 2 and 13.


## CMI

Results obtained for the CMI sub-cohort are presented for the ATP cohort for CMI immunogenicity/ CMI persistence.

- gE-specific CMI responses to HZ/su in the PreChemo group were above prevaccination levels 1 month after the first vaccination; stronger immune responses were observed 1 month after the second dose. Additionally, the persistence of gEspecific CMI at 1 year post-dose 2 in PreChemo HZ/su subjects was observed. However secondary to the small number of subjects with evaluable CMI results, these results need to be interpreted with caution.
- In the HZ/su group, the observed median (min - max) frequency of gE-specific CD4[2+] T-cells (per 106 total CD4+ T-cells) was 127.3 (1.0-662.4), 391.9 ( 1.0-3276.6) and 778.8 (1.0-4835.8) at Months 0 (pre-vaccination), 1 (post first vaccination) and 2 (post second vaccination) respectively, and 332.9 (1.02416.0) at Month 13. In the Placebo group, the observed median frequency of gE-specific CD4[2+] T-cells (point estimate) was 104.8, 50.0 and 61.8 at Month 0,1 and 2 respectively, and 51.2 at Month 13.
- In the HZ/su group, the VRR in the frequency of gE-specific CD4[2+] T-cells was $20.0 \%$ ( $95 \% \mathrm{CI}: 6.8-40.7$ ) and $50.0 \%$ ( $95 \% \mathrm{CI}: 28.2-71.8$ ) at Month 1 and Month 2 and $17.6 \%(95 \% \mathrm{CI}: 3.8-43.4)$ at Month 13. In the Placebo group, there were no subjects meeting the definition of responder at any timepoint.


## Analysis by age strata (18-49 YOA and $\geq 50$ YOA) in the PreChemo group (anti-gE humoral immunogenicity and gE-specific CMI); and in all subjects (anti-gE humoral immunogenicity).

Comparable immune responses for both age strata were observed 1 month post first and 1 month post second vaccination up to 1 year post dose 2 .

Secondary to the small number of subjects included in the 18-49 YOA stratum (miminisation procedure applied at randomisation), results obtained for the 18-49 YOA stratum need to be interpreted with caution.

## 8. SAFETY RESULTS

### 8.1. Datasets analysed

The analysis (i.e., descriptive analysis) of safety was performed on the TVC (primary cohort for analysis), i.e., for analysis of solicited AEs, unsolicited AEs, SAEs, AEs leading to withdrawal, other AEs of interest (pIMDs) and concomitant medications/vaccinations. The tabulations and figures presenting the final data generated at end of study analysis are presented in this report (see Section 5.11.2).

Results are described in Section 8.2 (in all subjects), Section 8.3 (in PreChemo and OnChemo groups) and Section 8.4 (by age strata, $18-49$ YOA and $\geq 50 \mathrm{YOA}$ ).

To complement the analysis of safety on the TVC, an analysis of safety was also performed on the ATP cohort for Safety up to 30 days post last vaccination (active phase results) and the ATP cohort for Safety up to study end. Data are presented in Section 8.5 (in all subjects), Section 8.6 (by duration between the first dose and the start of a chemotherapy cycle, in PreChemo and OnChemo groups) and in Section 8.7 (by age strata, $18-49 \mathrm{YOA}$ and $\geq 50 \mathrm{YOA}$ ).

### 8.2. TVC: Safety analysis, overall

The vaccination compliance in the TVC and compliance in returning symptom sheets in the TVC is provided in Table 8.1 and Table 8.2, respectively. A total of $9.5 \%$ of subjects in the TVC did not receive the second dose; i.e $14.5 \%$ in the HZ/su group and $4.3 \%$ in the Placebo group. Refer also to Section 6.2.1 for details.

The compliance in returning local and general symptom information, observed for the $\mathrm{HZ} / \mathrm{su}$ and Placebo groups, ranged from $95.1 \%$ to $96.8 \%$ for doses overall (dose 1 and 2).

### 8.2.1. TVC: Overall incidence of adverse events

Data for subjects included in the TVC are presented.
The incidence and nature of symptoms (solicited and unsolicited) reported during the 7day (Days 0-6) post-vaccination period following each dose and overall is presented in Table 8.3.

Overall per subject (dose 1 and dose 2 considered), at least one solicited or unsolicited AE (local or general) (any grade) was reported for $93.2 \%$ and $80.0 \%$ of subjects during the 7 -day (Days $0-6$ ) post-vaccination period in the $\mathrm{HZ} / \mathrm{su}$ and Placebo group, respectively (Table 8.3).

Overall per subject, at least one local AE (solicited or unsolicited) was reported for $80.3 \%$ and $7.8 \%$ of subjects in the HZ/su and Placebo group, respectively. Overall per subject, at least one general AE (solicited or unsolicited) was reported for $84.6 \%$ and $80.0 \%$ of subjects in the HZ/su and Placebo group, respectively (Table 8.3).

Overall per dose, at least one solicited or unsolicited AE (local or general) (any grade) was reported after $86.6 \%$ and $63.1 \%$ of doses during the 7 -day (Days $0-6$ ) postvaccination period in the HZ/su and Placebo group, respectively (Table 8.3).

Overall per dose, at least one local AE (solicited or unsolicited) was reported after 66.4\% and $4.4 \%$ of doses in the $\mathrm{HZ} / \mathrm{su}$ and Placebo group, respectively. Overall per dose, at least one general AE (solicited or unsolicited) was reported after $73.7 \%$ and $62.7 \%$ of doses in the HZ/su and Placebo group, respectively (Table 8.3).

In the Placebo group, after the second dose an increase was observed in the number of subjects for whom at least one AE (solicited or unsolicited) was reported ( $50.4 \%$ after dose 1 and $76.4 \%$ after dose 2). In this group, the percentage of subjects for whom at least one general AE (solicited or unsolicited) was reported was $49.6 \%$ and $76.4 \%$ after dose 1 and 2 respectively; the percentage subjects with at least one local AE (solicited or unsolicited) was reported was $3.5 \%$ and $5.5 \%$ after dose 1 and 2 respectively (Table 8.3).

In the $\mathrm{HZ} / \mathrm{su}$ group, the number of subjects for whom at least one AE (solicited or unsolicited) was reported was $90.6 \%$ after dose 1 and $82.0 \%$ after dose 2 . In this group, the percentage of subjects for whom at least one general AE (solicited or unsolicited) was reported was $71.8 \%$ and $76.0 \%$ after dose 1 and 2 respectively; the percentage subjects with at least one local AE (solicited or unsolicited) was reported was $75.2 \%$ and $56.0 \%$ after dose 1 and 2 respectively (Table 8.3).

The incidence and nature of grade 3 symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall is presented in Table 8.4.

The incidence and nature of symptoms (solicited only) reported during the 7-day (Days $0-6$ ) post-vaccination period following each dose and overall is presented in Table 35.

Th incidence and nature of grade 3 symptoms (solicited only) reported during the 7 -day (Days 0-6) post-vaccination period following each dose and overall is presented in Table 36.

Table 35 Incidence and nature of symptoms (solicited only) reported during the 7 -day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated Cohort)

|  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  | N | n | \% | 95\% CI |  |
|  | Group | N | n | \% | LL | UL | N | n | \% | LL | UL |  |  |  | LL | UL |
| Dose 1 | HZ/su | 112 | 104 | 92.9 | 86.4 | 96.9 | 112 | 80 | 71.4 | 62.1 | 79.6 | 112 | 88 | 78.6 | 69.8 | 85.8 |
|  | Placebo | 110 | 53 | 48.2 | 38.6 | 57.9 | 110 | 52 | 47.3 | 37.7 | 57.0 | 110 | 3 | 2.7 | 0.6 | 7.8 |
| Dose 2 | HZ/su | 98 | 75 | 76.5 | 66.9 | 84.5 | 97 | 67 | 69.1 | 58.9 | 78.1 | 98 | 56 | 57.1 | 46.7 | 67.1 |
|  | Placebo | 105 | 60 | 57.1 | 47.1 | 66.8 | 104 | 60 | 57.7 | 47.6 | 67.3 | 105 | 5 | 4.8 | 1.6 | 10.8 |
| Overall/dose | HZ/su | 210 | 179 | 85.2 | 79.7 | 89.7 | 209 | 147 | 70.3 | 63.6 | 76.4 | 210 | 144 | 68.6 | 61.8 | 74.8 |
|  | Placebo | 215 | 113 | 52.6 | 45.7 | 59.4 | 214 | 112 | 52.3 | 45.4 | 59.2 | 215 | 8 | 3.7 | 1.6 | 7.2 |
| Overall/subject | HZ/su | 112 | 107 | 95.5 | 89.9 | 98.5 | 112 | 91 | 81.3 | 72.8 | 88.0 | 112 | 94 | 83.9 | 75.8 | 90.2 |
|  | Placebo | 110 | 73 | 66.4 | 56.7 | 75.1 | 110 | 73 | 66.4 | 56.7 | 75.1 | 110 | 7 | 6.4 | 2.6 | 12.7 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine
administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 36 Incidence and nature of grade 3 symptoms (solicited only) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated Cohort)

|  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | HZ/su | 112 | 20 | 17.9 | 11.3 | 26.2 | 112 | 15 | 13.4 | 7.7 | 21.1 | 112 | 10 | 8.9 | 4.4 | 15.8 |
|  | Placebo | 110 | 11 | 10.0 | 5.1 | 17.2 | 110 | 11 | 10.0 | 5.1 | 17.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Dose 2 | HZ/su | 98 | 17 | 17.3 | 10.4 | 26.3 | 97 | 16 | 16.5 | 9.7 | 25.4 | 98 | 4 | 4.1 | 1.1 | 10.1 |
|  | Placebo | 105 | 10 | 9.5 | 4.7 | 16.8 | 104 | 10 | 9.6 | 4.7 | 17.0 | 105 | 0 | 0.0 | 0.0 | 3.5 |
| Overall/dose | HZ/su | 210 | 37 | 17.6 | 12.7 | 23.5 | 209 | 31 | 14.8 | 10.3 | 20.4 | 210 | 14 | 6.7 | 3.7 | 10.9 |
|  | Placebo | 215 | 21 | 9.8 | 6.1 | 14.5 | 214 | 21 | 9.8 | 6.2 | 14.6 | 215 | 0 | 0.0 | 0.0 | 1.7 |
| Overall/subject | HZ/su | 112 | 28 | 25.0 | 17.3 | 34.1 | 112 | 25 | 22.3 | 15.0 | 31.2 | 112 | 13 | 11.6 | 6.3 | 19.0 |
|  | Placebo | 110 | 17 | 15.5 | 9.3 | 23.6 | 110 | 17 | 15.5 | 9.3 | 23.6 | 110 | 0 | 0.0 | 0.0 | 3.3 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine
administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

### 8.2.2 TVC: Solicited local adverse events

Data for subjects included in the TVC are presented.
Overall per subject, at least one solicited local symptom was reported for $83.9 \%$ and $6.4 \%$ of subjects in the HZ/su and Placebo group, respectively (Section 8.2.1, Table 35).

Overall per dose, at least one solicited local symptom was reported after $68.6 \%$ and $3.7 \%$ of doses in the HZ/su and Placebo group, respectively (Section 8.2.1, Table 35).

After dose 1 and dose 2, respectively, at least one solicited local symptom was reported for $78.6 \%$ and $57.1 \%$ of subjects in the $\mathrm{HZ} /$ su group, and for $2.7 \%$ and $4.8 \%$ of subjects in the Placebo group (Section 8.2.1, Table 35).

Overall per subject, at least one grade 3 solicited local symptom was reported for $11.6 \%$ and $0.0 \%$ of subjects in the HZ/su and Placebo group, respectively (Section 8.2.1, Table 36).

Overall per dose, at least one grade 3 solicited local symptom was reported after 6.7\% and $0.0 \%$ of doses in the $\mathrm{HZ} / \mathrm{su}$ and Placebo group, respectively (Section 8.2.1, Table 36).

After dose 1 and dose 2, respectively, at least one grade 3 solicited local symptom was reported for $8.9 \%$ and $4.1 \%$ of subjects in the $\mathrm{HZ} / \mathrm{su}$ group, and for none of the subjects in the Placebo group (Section 8.2.1, Table 36).

The incidence of solicited local symptoms reported during the 7-day (Days 0-6) postvaccination period following each dose and overall is presented in Table 37.

The most frequently reported solicited local symptom in the HZ/zu group was pain (any grade, overall per subject: $80.4 \%$ in the HZ/su group versus $6.4 \%$ in the Placebo group). Pain (any grade) was reported after dose 1 for $74.1 \%$ and $1.8 \%$ of subjects, and after dose 2 for $53.1 \%$ and $4.8 \%$ in the $\mathrm{HZ} /$ su group and Placebo group, respectively (Table 37).

Overall per subject, grade 3 pain was reported for $9.8 \%$ and $0.0 \%$ of subjects in the $\mathrm{HZ} /$ su group and Placebo group, respectively. Grade 3 pain after dose 1 was reported for $7.1 \%$ and $0.0 \%$ of subjects, and after dose 2 for $4.1 \%$ and $0.0 \%$ of subjects in the $\mathrm{HZ} / \mathrm{su}$ group and Placebo group, respectively (Table 37).

Table 37 Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated Cohort)

|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 112 | 83 | 74.1 | 65.0 | 81.9 | 110 | 2 | 1.8 | 0.2 | 6.4 |
|  | Grade 2 or 3 | 112 | 27 | 24.1 | 16.5 | 33.1 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Grade 3 | 112 | 8 | 7.1 | 3.1 | 13.6 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 1 | 0.9 | 0.0 | 4.9 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Redness (mm) | All | 112 | 33 | 29.5 | 21.2 | 38.8 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | $>50$ | 112 | 18 | 16.1 | 9.8 | 24.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >100 | 112 | 2 | 1.8 | 0.2 | 6.3 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Swelling (mm) | All | 112 | 15 | 13.4 | 7.7 | 21.1 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | $>50$ | 112 | 8 | 7.1 | 3.1 | 13.6 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >100 | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 98 | 52 | 53.1 | 42.7 | 63.2 | 105 | 5 | 4.8 | 1.6 | 10.8 |
|  | Grade 2 or 3 | 98 | 19 | 19.4 | 12.1 | 28.6 | 105 | 1 | 1.0 | 0.0 | 5.2 |
|  | Grade 3 | 98 | 4 | 4.1 | 1.1 | 10.1 | 105 | 0 | 0.0 | 0.0 | 3.5 |
|  | Medical advice | 98 | 0 | 0.0 | 0.0 | 3.7 | 105 | 0 | 0.0 | 0.0 | 3.5 |
| Redness (mm) | All | 98 | 20 | 20.4 | 12.9 | 29.7 | 105 | 0 | 0.0 | 0.0 | 3.5 |
|  | $>50$ | 98 | 8 | 8.2 | 3.6 | 15.5 | 105 | 0 | 0.0 | 0.0 | 3.5 |
|  | $>100$ | 98 | 0 | 0.0 | 0.0 | 3.7 | 105 | 0 | 0.0 | 0.0 | 3.5 |
|  | Medical advice | 98 | 0 | 0.0 | 0.0 | 3.7 | 105 | 0 | 0.0 | 0.0 | 3.5 |
| Swelling (mm) | All | 98 | 8 | 8.2 | 3.6 | 15.5 | 105 | 0 | 0.0 | 0.0 | 3.5 |
|  | $>50$ | 98 | 4 | 4.1 | 1.1 | 10.1 | 105 | 0 | 0.0 | 0.0 | 3.5 |
|  | >100 | 98 | 0 | 0.0 | 0.0 | 3.7 | 105 | 0 | 0.0 | 0.0 | 3.5 |
|  | Medical advice | 98 | 0 | 0.0 | 0.0 | 3.7 | 105 | 0 | 0.0 | 0.0 | 3.5 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 210 | 135 | 64.3 | 57.4 | 70.8 | 215 | 7 | 3.3 | 1.3 | 6.6 |
|  | Grade 2 or 3 | 210 | 46 | 21.9 | 16.5 | 28.1 | 215 | 1 | 0.5 | 0.0 | 2.6 |
|  | Grade 3 | 210 | 12 | 5.7 | 3.0 | 9.8 | 215 | 0 | 0.0 | 0.0 | 1.7 |
|  | Medical advice | 210 | 1 | 0.5 | 0.0 | 2.6 | 215 | 0 | 0.0 | 0.0 | 1.7 |
| Redness (mm) | All | 210 | 53 | 25.2 | 19.5 | 31.7 | 215 | 0 | 0.0 | 0.0 | 1.7 |
|  | $>50$ | 210 | 26 | 12.4 | 8.2 | 17.6 | 215 | 0 | 0.0 | 0.0 | 1.7 |
|  | >100 | 210 | 2 | 1.0 | 0.1 | 3.4 | 215 | 0 | 0.0 | 0.0 | 1.7 |
|  | Medical advice | 210 | 0 | 0.0 | 0.0 | 1.7 | 215 | 0 | 0.0 | 0.0 | 1.7 |
| Swelling (mm) | All | 210 | 23 | 11.0 | 7.1 | 16.0 | 215 | 1 | 0.5 | 0.0 | 2.6 |
|  | $>50$ | 210 | 12 | 5.7 | 3.0 | 9.8 | 215 | 0 | 0.0 | 0.0 | 1.7 |
|  | >100 | 210 | 0 | 0.0 | 0.0 | 1.7 | 215 | 0 | 0.0 | 0.0 | 1.7 |
|  | Medical advice | 210 | 0 | 0.0 | 0.0 | 1.7 | 215 | 0 | 0.0 | 0.0 | 1.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 112 | 90 | 80.4 | 71.8 | 87.3 | 110 | 7 | 6.4 | 2.6 | 12.7 |
|  | Grade 2 or 3 | 112 | 35 | 31.3 | 22.8 | 40.7 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | Grade 3 | 112 | 11 | 9.8 | 5.0 | 16.9 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 1 | 0.9 | 0.0 | 4.9 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Redness (mm) | All | 112 | 40 | 35.7 | 26.9 | 45.3 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | $>50$ | 112 | 19 | 17.0 | 10.5 | 25.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >100 | 112 | 2 | 1.8 | 0.2 | 6.3 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |

Report Final

|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Swelling (mm) | All | 112 | 18 | 16.1 | 9.8 | 24.2 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | >50 | 112 | 10 | 8.9 | 4.4 | 15.8 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >100 | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; $\mathrm{LL}=$ lower limit, UL = upper limit
The number of days with local symptoms during the solicited post-vaccination period is presented in Table 8.10.

The number of days with grade 3 local symptoms during the solicited post-vaccination period is presented in Table 8.11.

The duration of solicited local symptoms (in days), not limited to the 7-day postvaccination period, following each dose and overall per dose, is presented in Table 8.12. This table includes all solicited local events through resolution.

Overall per dose, regarding the local symptoms, the median duration was 2.0 to 4.0 days in the $\mathrm{HZ} / \mathrm{su}$ group and 1.0 to 7.0 days in the Placebo group. The median duration of local symptoms in the HZ/su and Placebo group was within the 7-day observation period. Individual subjects from both $\mathrm{HZ} / \mathrm{su}$ and Placebo group had symptoms lasting beyond the 7-day period however the majority were not of prolonged duration. Regarding the specified local symptoms reported, the maximum duration was 15.0 days in the $\mathrm{HZ} / \mathrm{su}$ group and 17.0 days in the Placebo group (Table 8.12).

Information regarding the incidence and nature of local symptoms (solicited only) reported during the 7 -day (Days $0-6$ ) post-vaccination period and lasting beyond this period following each dose and overall is presented in Table 8.265.

Information regarding the incidence and nature of grade 3 local symptoms (solicited only) reported during the 7 -day (Days $0-6$ ) post-vaccination period and lasting beyond this period following each dose and overall is presented in Table 8.266.

Information regarding the different solicited local symptoms ongoing beyond the 7-day (Days 0-6) post-vaccination period is presented in Table 8.13.

Refer to Section 5.11.2 regarding Table 8.265 and Table 8.266 (post-hoc analysis).

### 8.2.3. TVC: Solicited general adverse events

Data for subjects included in the TVC are presented.
Overall per subject, at least one solicited general symptom was reported for $81.3 \%$ and $66.4 \%$ of subjects in the HZ/su and Placebo group, respectively (Section 8.2.1, Table 35).

Overall per dose, at least one solicited general symptom was reported after $70.3 \%$ and $52.3 \%$ of doses in the $\mathrm{HZ} / \mathrm{su}$ and Placebo group, respectively (Section 8.2.1, Table 35).

After dose 1 and dose 2, respectively, at least one solicited general symptom was reported for $71.4 \%$ and $69.1 \%$ of subjects in the HZ/su group, and for $47.3 \%$ and $57.7 \%$ of subjects in the Placebo group (Section 8.2.1, Table 35)

Overall per subject, at least one grade 3 solicited general symptom was reported for $22.3 \%$ and $15.5 \%$ of subjects in the HZ/su and Placebo group, respectively (Section 8.2.1, Table 36).

Overall per dose, at least one grade 3 solicited general symptom was reported after 14.8\% and $9.8 \%$ of doses in the HZ/su and Placebo group, respectively (Section 8.2.1, Table 36).

After dose 1 and dose 2, respectively, at least one grade 3 solicited general symptom was reported for $13.4 \%$ and $16.5 \%$ of subjects in the HZ/su group, and for $10.0 \%$ and $9.6 \%$ of subjects in the Placebo group (Section 8.2.1, Table 36).

The incidence of solicited general symptoms reported during the 7-day (Days 0-6) postvaccination period following each dose and overall for the TVC is presented in Table 38.

For the 7-day (Days 0-6) post-vaccination period following each dose, the most frequently reported solicited general symptom in the $\mathrm{HZ} /$ su group was fatigue (any grade, overall/subject: $69.6 \%$ in HZ/su group versus $61.8 \%$ in Placebo group) and myalgia (any grade, overall/subject: $53.6 \%$ in HZ/su group versus $28.2 \%$ in Placebo group) (Table 38).

Fatigue (any grade) was after dose 1 reported for $50.0 \%$ and $40.0 \%$ of subjects, and after dose 2 for $58.8 \%$ and $54.8 \%$ in the HZ/su group and Placebo group, respectively. Myalgia (any grade) was after dose 1 reported for $44.6 \%$ and $15.5 \%$ of subjects, and after dose 2 for $33.0 \%$ and $22.1 \%$ in the $\mathrm{HZ} /$ su group and the Placebo group, respectively (Table 38).

Overall per subject, grade 3 fatigue was reported for $14.3 \%$ and $7.3 \%$ of subjects in the $\mathrm{HZ} /$ su group and Placebo group, respectively. Grade 3 fatigue was after dose 1 reported for $8.9 \%$ and $2.7 \%$ of subjects, and after dose 2 for $9.3 \%$ and $5.8 \%$ in the $\mathrm{HZ} /$ su group and Placebo group, respectively (Table 38).

Overall per subject, grade 3 myalgia was reported for $10.7 \%$ and $3.6 \%$ of subjects in the $\mathrm{HZ} /$ su group and the Placebo group, respectively. Grade 3 myalgia was reported after dose 1 for $7.1 \%$ and $2.7 \%$ of subjects, and after dose 2 for $4.1 \%$ and $1.0 \%$ in the HZ/su group and the Placebo group, respectively (Table 38).

Overall per subject, fatigue assessed by the investigator as related to vaccination, was reported for $17.0 \%$ and $12.7 \%$ of subjects in the HZ/su group and Placebo group, respectively. Overall per subject, myalgia assessed as related to vaccination was reported for $26.8 \%$ and $4.5 \%$ of subjects in the HZ/su group and the Placebo group, respectively (Table 38).

Overall per subject, grade 3 fatigue assessed by the investigator as related to vaccination, was reported for $2.7 \%$ and $0.9 \%$ of subjects in the HZ/su group and Placebo group, respectively. Overall per subject, grade 3 myalgia assessed by the investigator as related to vaccination was reported for $6.3 \%$ and $0.0 \%$ of subjects in the HZ/su group and the Placebo group, respectively. It is noted that grade 3 shivering assessed by the investigator as related to vaccination was reported (overall per subject) for $3.6 \%$ and $0.0 \%$ in the HZ/su and Placebo group, respectively (Table 38).

Table 38 Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated Cohort)

|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 112 | 56 | 50.0 | 40.4 | 59.6 | 110 | 44 | 40.0 | 30.8 | 49.8 |
|  | Grade 2 or 3 | 112 | 30 | 26.8 | 18.9 | 36.0 | 110 | 15 | 13.6 | 7.8 | 21.5 |
|  | Grade 3 | 112 | 10 | 8.9 | 4.4 | 15.8 | 110 | 3 | 2.7 | 0.6 | 7.8 |
|  | Related | 112 | 15 | 13.4 | 7.7 | 21.1 | 110 | 10 | 9.1 | 4.4 | 16.1 |
|  | Grade 2 or 3 Related | 112 | 9 | 8.0 | 3.7 | 14.7 | 110 | 4 | 3.6 | 1.0 | 9.0 |
|  | Grade 3 Related | 112 | 3 | 2.7 | 0.6 | 7.6 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Gastrointestinal symptoms | All | 112 | 32 | 28.6 | 20.4 | 37.9 | 110 | 21 | 19.1 | 12.2 | 27.7 |
|  | Grade 2 or 3 | 112 | 14 | 12.5 | 7.0 | 20.1 | 110 | 11 | 10.0 | 5.1 | 17.2 |
|  | Grade 3 | 112 | 2 | 1.8 | 0.2 | 6.3 | 110 | 5 | 4.5 | 1.5 | 10.3 |
|  | Related | 112 | 9 | 8.0 | 3.7 | 14.7 | 110 | 2 | 1.8 | 0.2 | 6.4 |
|  | Grade 2 or 3 Related | 112 | 2 | 1.8 | 0.2 | 6.3 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | Grade 3 Related | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | Medical advice | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 2 | 1.8 | 0.2 | 6.4 |
| Headache | All | 112 | 28 | 25.0 | 17.3 | 34.1 | 110 | 24 | 21.8 | 14.5 | 30.7 |
|  | Grade 2 or 3 | 112 | 14 | 12.5 | 7.0 | 20.1 | 110 | 8 | 7.3 | 3.2 | 13.8 |
|  | Grade 3 | 112 | 3 | 2.7 | 0.6 | 7.6 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | Related | 112 | 10 | 8.9 | 4.4 | 15.8 | 110 | 4 | 3.6 | 1.0 | 9.0 |
|  | Grade 2 or 3 Related | 112 | 6 | 5.4 | 2.0 | 11.3 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | Grade 3 Related | 112 | 2 | 1.8 | 0.2 | 6.3 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Myalgia | All | 112 | 50 | 44.6 | 35.2 | 54.3 | 110 | 17 | 15.5 | 9.3 | 23.6 |
|  | Grade 2 or 3 | 112 | 21 | 18.8 | 12.0 | 27.2 | 110 | 9 | 8.2 | 3.8 | 15.0 |
|  | Grade 3 | 112 | 8 | 7.1 | 3.1 | 13.6 | 110 | 3 | 2.7 | 0.6 | 7.8 |
|  | Related | 112 | 25 | 22.3 | 15.0 | 31.2 | 110 | 3 | 2.7 | 0.6 | 7.8 |
|  | Grade 2 or 3 Related | 112 | 14 | 12.5 | 7.0 | 20.1 | 110 | 2 | 1.8 | 0.2 | 6.4 |
|  | Grade 3 Related | 112 | 7 | 6.3 | 2.5 | 12.5 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Shivering | All | 112 | 27 | 24.1 | 16.5 | 33.1 | 110 | 13 | 11.8 | 6.4 | 19.4 |
|  | Grade 2 or 3 | 112 | 9 | 8.0 | 3.7 | 14.7 | 110 | 6 | 5.5 | 2.0 | 11.5 |
|  | Grade 3 | 112 | 5 | 4.5 | 1.5 | 10.1 | 110 | 2 | 1.8 | 0.2 | 6.4 |
|  | Related | 112 | 12 | 10.7 | 5.7 | 18.0 | 110 | 4 | 3.6 | 1.0 | 9.0 |


|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 2 or 3 Related | 112 | 7 | 6.3 | 2.5 | 12.5 | 110 | 2 | 1.8 | 0.2 | 6.4 |
|  | Grade 3 Related | 112 | 4 | 3.6 | 1.0 | 8.9 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Temperature/(*) $\left({ }^{\circ} \mathrm{C}\right)$ | All | 112 | 13 | 11.6 | 6.3 | 19.0 | 110 | 4 | 3.6 | 1.0 | 9.0 |
|  | $\geq 37.5$ | 112 | 13 | 11.6 | 6.3 | 19.0 | 110 | 4 | 3.6 | 1.0 | 9.0 |
|  | $>38.0$ | 112 | 2 | 1.8 | 0.2 | 6.3 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | $>38.5$ | 112 | 1 | 0.9 | 0.0 | 4.9 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | $>39.0$ | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | $>39.5$ | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >40.0 | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Related | 112 | 11 | 9.8 | 5.0 | 16.9 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | >38.0 Related | 112 | 2 | 1.8 | 0.2 | 6.3 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >39.0 Related | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  |  | se 2 |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 97 | 57 | 58.8 | 48.3 | 68.7 | 104 | 57 | 54.8 | 44.7 | 64.6 |
|  | Grade 2 or 3 | 97 | 28 | 28.9 | 20.1 | 39.0 | 104 | 30 | 28.8 | 20.4 | 38.6 |
|  | Grade 3 | 97 | 9 | 9.3 | 4.3 | 16.9 | 104 | 6 | 5.8 | 2.1 | 12.1 |
|  | Related | 97 | 6 | 6.2 | 2.3 | 13.0 | 104 | 8 | 7.7 | 3.4 | 14.6 |
|  | Grade 2 or 3 Related | 97 | 2 | 2.1 | 0.3 | 7.3 | 104 | 4 | 3.8 | 1.1 | 9.6 |
|  | Grade 3 Related | 97 | 0 | 0.0 | 0.0 | 3.7 | 104 | 1 | 1.0 | 0.0 | 5.2 |
|  | Medical advice | 97 | 1 | 1.0 | 0.0 | 5.6 | 104 | 1 | 1.0 | 0.0 | 5.2 |
| Gastrointestinal symptoms | All | 97 | 41 | 42.3 | 32.3 | 52.7 | 104 | 39 | 37.5 | 28.2 | 47.5 |
|  | Grade 2 or 3 | 97 | 21 | 21.6 | 13.9 | 31.2 | 104 | 15 | 14.4 | 8.3 | 22.7 |
|  | Grade 3 | 97 | 5 | 5.2 | 1.7 | 11.6 | 104 | 3 | 2.9 | 0.6 | 8.2 |
|  | Related | 97 | 6 | 6.2 | 2.3 | 13.0 | 104 | 2 | 1.9 | 0.2 | 6.8 |
|  | Grade 2 or 3 Related | 97 | 2 | 2.1 | 0.3 | 7.3 | 104 | 2 | 1.9 | 0.2 | 6.8 |
|  | Grade 3 Related | 97 | 1 | 1.0 | 0.0 | 5.6 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | Medical advice | 97 | 1 | 1.0 | 0.0 | 5.6 | 104 | 0 | 0.0 | 0.0 | 3.5 |
| Headache | All | 97 | 29 | 29.9 | 21.0 | 40.0 | 104 | 25 | 24.0 | 16.2 | 33.4 |
|  | Grade 2 or 3 | 97 | 14 | 14.4 | 8.1 | 23.0 | 104 | 7 | 6.7 | 2.7 | 13.4 |
|  | Grade 3 | 97 | 3 | 3.1 | 0.6 | 8.8 | 104 | 2 | 1.9 | 0.2 | 6.8 |
|  | Related | 97 | 7 | 7.2 | 3.0 | 14.3 | 104 | 2 | 1.9 | 0.2 | 6.8 |
|  | Grade 2 or 3 Related | 97 | 4 | 4.1 | 1.1 | 10.2 | 104 | 1 | 1.0 | 0.0 | 5.2 |
|  | Grade 3 Related | 97 | 0 | 0.0 | 0.0 | 3.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | Medical advice | 97 | 1 | 1.0 | 0.0 | 5.6 | 104 | 0 | 0.0 | 0.0 | 3.5 |
| Myalgia | All | 97 | 32 | 33.0 | 23.8 | 43.3 | 104 | 23 | 22.1 | 14.6 | 31.3 |
|  | Grade 2 or 3 | 97 | 15 | 15.5 | 8.9 | 24.2 | 104 | 13 | 12.5 | 6.8 | 20.4 |
|  | Grade 3 | 97 | 4 | 4.1 | 1.1 | 10.2 | 104 | 1 | 1.0 | 0.0 | 5.2 |
|  | Related | 97 | 13 | 13.4 | 7.3 | 21.8 | 104 | 4 | 3.8 | 1.1 | 9.6 |
|  | Grade 2 or 3 Related | 97 | 6 | 6.2 | 2.3 | 13.0 | 104 | 2 | 1.9 | 0.2 | 6.8 |
|  | Grade 3 Related | 97 | 0 | 0.0 | 0.0 | 3.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | Medical advice | 97 | 0 | 0.0 | 0.0 | 3.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |
| Shivering | All | 97 | 20 | 20.6 | 13.1 | 30.0 | 104 | 17 | 16.3 | 9.8 | 24.9 |
|  | Grade 2 or 3 | 97 | 10 | 10.3 | 5.1 | 18.1 | 104 | 1 | 1.0 | 0.0 | 5.2 |
|  | Grade 3 | 97 | 3 | 3.1 | 0.6 | 8.8 | 104 | 1 | 1.0 | 0.0 | 5.2 |
|  | Related | 97 | 6 | 6.2 | 2.3 | 13.0 | 104 | 4 | 3.8 | 1.1 | 9.6 |
|  | Grade 2 or 3 Related | 97 | 3 | 3.1 | 0.6 | 8.8 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | Grade 3 Related | 97 | 1 | 1.0 | 0.0 | 5.6 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | Medical advice | 97 | 0 | 0.0 | 0.0 | 3.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |


|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Temperature/(*) ( ${ }^{( } \mathrm{C}$ ) | All | 97 | 8 | 8.2 | 3.6 | 15.6 | 104 | 1 | 1.0 | 0.0 | 5.2 |
|  | $\geq 37.5$ | 97 | 8 | 8.2 | 3.6 | 15.6 | 104 | 1 | 1.0 | 0.0 | 5.2 |
|  | >38.0 | 97 | 1 | 1.0 | 0.0 | 5.6 | 104 | 1 | 1.0 | 0.0 | 5.2 |
|  | $>38.5$ | 97 | 0 | 0.0 | 0.0 | 3.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | >39.0 | 97 | 0 | 0.0 | 0.0 | 3.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | $>39.5$ | 97 | 0 | 0.0 | 0.0 | 3.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | >40.0 | 97 | 0 | 0.0 | 0.0 | 3.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | Related | 97 | 4 | 4.1 | 1.1 | 10.2 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | >38.0 Related | 97 | 1 | 1.0 | 0.0 | 5.6 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | >39.0 Related | 97 | 0 | 0.0 | 0.0 | 3.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | Medical advice | 97 | 0 | 0.0 | 0.0 | 3.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 209 | 113 | 54.1 | 47.1 | 61.0 | 214 | 101 | 47.2 | 40.4 | 54.1 |
|  | Grade 2 or 3 | 209 | 58 | 27.8 | 21.8 | 34.3 | 214 | 45 | 21.0 | 15.8 | 27.1 |
|  | Grade 3 | 209 | 19 | 9.1 | 5.6 | 13.8 | 214 | 9 | 4.2 | 1.9 | 7.8 |
|  | Related | 209 | 21 | 10.0 | 6.3 | 14.9 | 214 | 18 | 8.4 | 5.1 | 13.0 |
|  | Grade 2 or 3 Related | 209 | 11 | 5.3 | 2.7 | 9.2 | 214 | 8 | 3.7 | 1.6 | 7.2 |
|  | Grade 3 Related | 209 | 3 | 1.4 | 0.3 | 4.1 | 214 | 1 | 0.5 | 0.0 | 2.6 |
|  | Medical advice | 209 | 1 | 0.5 | 0.0 | 2.6 | 214 | 1 | 0.5 | 0.0 | 2.6 |
| Gastrointestinal symptoms | All | 209 | 73 | 34.9 | 28.5 | 41.8 | 214 | 60 | 28.0 | 22.1 | 34.6 |
|  | Grade 2 or 3 | 209 | 35 | 16.7 | 12.0 | 22.5 | 214 | 26 | 12.1 | 8.1 | 17.3 |
|  | Grade 3 | 209 | 7 | 3.3 | 1.4 | 6.8 | 214 | 8 | 3.7 | 1.6 | 7.2 |
|  | Related | 209 | 15 | 7.2 | 4.1 | 11.6 | 214 | 4 | 1.9 | 0.5 | 4.7 |
|  | Grade 2 or 3 Related | 209 | 4 | 1.9 | 0.5 | 4.8 | 214 | 3 | 1.4 | 0.3 | 4.0 |
|  | Grade 3 Related | 209 | 1 | 0.5 | 0.0 | 2.6 | 214 | 1 | 0.5 | 0.0 | 2.6 |
|  | Medical advice | 209 | 1 | 0.5 | 0.0 | 2.6 | 214 | 2 | 0.9 | 0.1 | 3.3 |
| Headache | All | 209 | 57 | 27.3 | 21.4 | 33.8 | 214 | 49 | 22.9 | 17.4 | 29.1 |
|  | Grade 2 or 3 | 209 | 28 | 13.4 | 9.1 | 18.8 | 214 | 15 | 7.0 | 4.0 | 11.3 |
|  | Grade 3 | 209 | 6 | 2.9 | 1.1 | 6.1 | 214 | 3 | 1.4 | 0.3 | 4.0 |
|  | Related | 209 | 17 | 8.1 | 4.8 | 12.7 | 214 | 6 | 2.8 | 1.0 | 6.0 |
|  | Grade 2 or 3 Related | 209 | 10 | 4.8 | 2.3 | 8.6 | 214 | 2 | 0.9 | 0.1 | 3.3 |
|  | Grade 3 Related | 209 | 2 | 1.0 | 0.1 | 3.4 | 214 | 0 | 0.0 | 0.0 | 1.7 |
|  | Medical advice | 209 | 1 | 0.5 | 0.0 | 2.6 | 214 | 0 | 0.0 | 0.0 | 1.7 |
| Myalgia | All | 209 | 82 | 39.2 | 32.6 | 46.2 | 214 | 40 | 18.7 | 13.7 | 24.6 |
|  | Grade 2 or 3 | 209 | 36 | 17.2 | 12.4 | 23.0 | 214 | 22 | 10.3 | 6.6 | 15.2 |
|  | Grade 3 | 209 | 12 | 5.7 | 3.0 | 9.8 | 214 | 4 | 1.9 | 0.5 | 4.7 |
|  | Related | 209 | 38 | 18.2 | 13.2 | 24.1 | 214 | 7 | 3.3 | 1.3 | 6.6 |
|  | Grade 2 or 3 Related | 209 | 20 | 9.6 | 5.9 | 14.4 | 214 | 4 | 1.9 | 0.5 | 4.7 |
|  | Grade 3 Related | 209 | 7 | 3.3 | 1.4 | 6.8 | 214 | 0 | 0.0 | 0.0 | 1.7 |
|  | Medical advice | 209 | 0 | 0.0 | 0.0 | 1.7 | 214 | 0 | 0.0 | 0.0 | 1.7 |
| Shivering | All | 209 | 47 | 22.5 | 17.0 | 28.8 | 214 | 30 | 14.0 | 9.7 | 19.4 |
|  | Grade 2 or 3 | 209 | 19 | 9.1 | 5.6 | 13.8 | 214 | 7 | 3.3 | 1.3 | 6.6 |
|  | Grade 3 | 209 | 8 | 3.8 | 1.7 | 7.4 | 214 | 3 | 1.4 | 0.3 | 4.0 |
|  | Related | 209 | 18 | 8.6 | 5.2 | 13.3 | 214 | 8 | 3.7 | 1.6 | 7.2 |
|  | Grade 2 or 3 Related | 209 | 10 | 4.8 | 2.3 | 8.6 | 214 | 2 | 0.9 | 0.1 | 3.3 |
|  | Grade 3 Related | 209 | 5 | 2.4 | 0.8 | 5.5 | 214 | 0 | 0.0 | 0.0 | 1.7 |
|  | Medical advice | 209 | 0 | 0.0 | 0.0 | 1.7 | 214 | 0 | 0.0 | 0.0 | 1.7 |
| Temperature/(*) ( ${ }^{( } \mathrm{C}$ ) | All | 209 | 21 | 10.0 | 6.3 | 14.9 | 214 | 5 | 2.3 | 0.8 | 5.4 |
|  | $\geq 37.5$ | 209 | 21 | 10.0 | 6.3 | 14.9 | 214 | 5 | 2.3 | 0.8 | 5.4 |
|  | $>38.0$ | 209 | 3 | 1.4 | 0.3 | 4.1 | 214 | 1 | 0.5 | 0.0 | 2.6 |
|  | >38.5 | 209 | 1 | 0.5 | 0.0 | 2.6 | 214 | 0 | 0.0 | 0.0 | 1.7 |
|  | $>39.0$ | 209 | 0 | 0.0 | 0.0 | 1.7 | 214 | 0 | 0.0 | 0.0 | 1.7 |
|  | >39.5 | 209 | 0 | 0.0 | 0.0 | 1.7 | 214 | 0 | 0.0 | 0.0 | 1.7 |


|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | >40.0 | 209 | 0 | 0.0 | 0.0 | 1.7 | 214 | 0 | 0.0 | 0.0 | 1.7 |
|  | Related | 209 | 15 | 7.2 | 4.1 | 11.6 | 214 | 1 | 0.5 | 0.0 | 2.6 |
|  | >38.0 Related | 209 | 3 | 1.4 | 0.3 | 4.1 | 214 | 0 | 0.0 | 0.0 | 1.7 |
|  | >39.0 Related | 209 | 0 | 0.0 | 0.0 | 1.7 | 214 | 0 | 0.0 | 0.0 | 1.7 |
|  | Medical advice | 209 | 0 | 0.0 | 0.0 | 1.7 | 214 | 1 | 0.5 | 0.0 | 2.6 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 112 | 78 | 69.6 | 60.2 | 78.0 | 110 | 68 | 61.8 | 52.1 | 70.9 |
|  | Grade 2 or 3 | 112 | 45 | 40.2 | 31.0 | 49.9 | 110 | 37 | 33.6 | 24.9 | 43.3 |
|  | Grade 3 | 112 | 16 | 14.3 | 8.4 | 22.2 | 110 | 8 | 7.3 | 3.2 | 13.8 |
|  | Related | 112 | 19 | 17.0 | 10.5 | 25.2 | 110 | 14 | 12.7 | 7.1 | 20.4 |
|  | Grade 2 or 3 Related | 112 | 11 | 9.8 | 5.0 | 16.9 | 110 | 8 | 7.3 | 3.2 | 13.8 |
|  | Grade 3 Related | 112 | 3 | 2.7 | 0.6 | 7.6 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | Medical advice | 112 | 1 | 0.9 | 0.0 | 4.9 | 110 | 1 | 0.9 | 0.0 | 5.0 |
| Gastrointestinal symptoms | All | 112 | 51 | 45.5 | 36.1 | 55.2 | 110 | 49 | 44.5 | 35.1 | 54.3 |
|  | Grade 2 or 3 | 112 | 26 | 23.2 | 15.8 | 32.1 | 110 | 21 | 19.1 | 12.2 | 27.7 |
|  | Grade 3 | 112 | 6 | 5.4 | 2.0 | 11.3 | 110 | 7 | 6.4 | 2.6 | 12.7 |
|  | Related | 112 | 11 | 9.8 | 5.0 | 16.9 | 110 | 3 | 2.7 | 0.6 | 7.8 |
|  | Grade 2 or 3 Related | 112 | 3 | 2.7 | 0.6 | 7.6 | 110 | 3 | 2.7 | 0.6 | 7.8 |
|  | Grade 3 Related | 112 | 1 | 0.9 | 0.0 | 4.9 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | Medical advice | 112 | 1 | 0.9 | 0.0 | 4.9 | 110 | 2 | 1.8 | 0.2 | 6.4 |
| Headache | All | 112 | 43 | 38.4 | 29.4 | 48.1 | 110 | 40 | 36.4 | 27.4 | 46.1 |
|  | Grade 2 or 3 | 112 | 22 | 19.6 | 12.7 | 28.2 | 110 | 14 | 12.7 | 7.1 | 20.4 |
|  | Grade 3 | 112 | 6 | 5.4 | 2.0 | 11.3 | 110 | 3 | 2.7 | 0.6 | 7.8 |
|  | Related | 112 | 16 | 14.3 | 8.4 | 22.2 | 110 | 6 | 5.5 | 2.0 | 11.5 |
|  | Grade 2 or 3 Related | 112 | 9 | 8.0 | 3.7 | 14.7 | 110 | 2 | 1.8 | 0.2 | 6.4 |
|  | Grade 3 Related | 112 | 2 | 1.8 | 0.2 | 6.3 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 1 | 0.9 | 0.0 | 4.9 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Myalgia | All | 112 | 60 | 53.6 | 43.9 | 63.0 | 110 | 31 | 28.2 | 20.0 | 37.6 |
|  | Grade 2 or 3 | 112 | 31 | 27.7 | 19.6 | 36.9 | 110 | 19 | 17.3 | 10.7 | 25.7 |
|  | Grade 3 | 112 | 12 | 10.7 | 5.7 | 18.0 | 110 | 4 | 3.6 | 1.0 | 9.0 |
|  | Related | 112 | 30 | 26.8 | 18.9 | 36.0 | 110 | 5 | 4.5 | 1.5 | 10.3 |
|  | Grade 2 or 3 Related | 112 | 17 | 15.2 | 9.1 | 23.2 | 110 | 4 | 3.6 | 1.0 | 9.0 |
|  | Grade 3 Related | 112 | 7 | 6.3 | 2.5 | 12.5 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Shivering | All | 112 | 39 | 34.8 | 26.1 | 44.4 | 110 | 25 | 22.7 | 15.3 | 31.7 |
|  | Grade 2 or 3 | 112 | 15 | 13.4 | 7.7 | 21.1 | 110 | 7 | 6.4 | 2.6 | 12.7 |
|  | Grade 3 | 112 | 6 | 5.4 | 2.0 | 11.3 | 110 | 3 | 2.7 | 0.6 | 7.8 |
|  | Related | 112 | 16 | 14.3 | 8.4 | 22.2 | 110 | 5 | 4.5 | 1.5 | 10.3 |
|  | Grade 2 or 3 Related | 112 | 8 | 7.1 | 3.1 | 13.6 | 110 | 2 | 1.8 | 0.2 | 6.4 |
|  | Grade 3 Related | 112 | 4 | 3.6 | 1.0 | 8.9 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Temperature/(*) ( ${ }^{( } \mathrm{C}$ ) | All | 112 | 20 | 17.9 | 11.3 | 26.2 | 110 | 5 | 4.5 | 1.5 | 10.3 |
|  | $\geq 37.5$ | 112 | 20 | 17.9 | 11.3 | 26.2 | 110 | 5 | 4.5 | 1.5 | 10.3 |
|  | $>38.0$ | 112 | 3 | 2.7 | 0.6 | 7.6 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | $>38.5$ | 112 | 1 | 0.9 | 0.0 | 4.9 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | $>39.0$ | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | $>39.5$ | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | $>40.0$ | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Related | 112 | 14 | 12.5 | 7.0 | 20.1 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | >38.0 Related | 112 | 3 | 2.7 | 0.6 | 7.6 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >39.0 Related | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | Medical advice | 112 | 0 | 0.0 | 0.0 | 3.2 | 110 | 1 | 0.9 | 0.0 | 5.0 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit
$\left(^{*}\right)=$ Temperature is measured by oral, axillary or tympanic routes
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for oral, axillary or tympanic route
The number and percentage of subjects who reported temperature by half degree measured during the 7-day (Days 0-6) post-vaccination period following each dose (no conversion) is presented in Table 8.5.

The number and percentage of subjects who reported temperature by half degree measured via oral, axillary, tympanic and rectal route during the 7 -day (Days 0-6) postvaccination period following each dose (no conversion) is presented in Table 8.6, Table 8.7, Table 8.8 and Table 8.9 respectively.

The number of days with general symptoms during the solicited post-vaccination period is presented in Table 8.14.

The number of days with grade 3 general symptoms during the solicited post-vaccination period is presented in Table 8.15.

The duration of solicited general symptoms (in days), not limited to the 7 -day postvaccination period, following each dose and overall per dose, is presented in Table 8.16. This table includes all solicited general events through resolution.

Overall per dose, regarding the general symptoms, the median duration was 1.0 to 4.0 days in the $\mathrm{HZ} /$ su group and 1.0 to 5.0 days in the Placebo group. The median duration of general symptoms in the $\mathrm{HZ} /$ su and Placebo group was within the 7 -day observation period. Individual subjects from both HZ/su and Placebo group had symptoms lasting beyond the 7-day period however the majority was not of prolonged duration. The maximum duration for the reported specified general symptoms was 161.0 days in the HZ/su group and 139.0 days in the Placebo group (Table 8.16).

Information regarding the incidence and nature of general symptoms (solicited only) reported during the 7 -day (Days 0-6) post-vaccination period and lasting beyond this period following each dose and overall is presented in Table 8.265.

Information regarding the incidence and nature of grade 3 general symptoms (solicited only) reported during the 7 -day (Days $0-6$ ) post-vaccination period and lasting beyond this period following each dose and overall is presented in Table 8.266.

Information regarding the different solicited general symptoms ongoing beyond the 7-day (Days $0-6$ ) post-vaccination period is presented in Table 8.17.

### 8.2.4. TVC: Unsolicited adverse events

Data for subjects included in the TVC are presented.
Results for the incidence of unsolicited AEs in the 30-day post-vaccination period are presented in this section. Solicited local or general symptoms, collected from subjects, including those that may be ongoing after the 7-day post-vaccination period, are not included in the reporting of unsolicited AEs during the 30-day post-vaccination period.

In Table 8.18, Table 8.19 and Table 39 respectively, the following results for the TVC are presented:

- the percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary SOC and PT within the 30-day (Days 0-29) postvaccination period (Table 8.18);
- the percentage of doses with unsolicited symptoms classified by MedDRA Primary SOC and PT within the 30-day (Days 0-29) post-vaccination period (Table 8.19);
- the global summary of unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period (Table 39).

Overall, 100 ( $85.5 \%$ ) subjects in the HZ/su group and 103 (89.6\%) subjects in the Placebo group reported at least one unsolicited AE within 30 days post vaccination (Table 39 and Table 8.18).

Overall per subject, the most frequent unsolicited AEs within 30 days post vaccination were nausea ( 31 subjects or $26.5 \%$ ) and asthenia ( 30 subjects or $25.6 \%$ ) for the $\mathrm{HZ} / \mathrm{su}$ group, and also nausea and asthenia (both at 28 subjects or $24.3 \%$ ) for the Placebo group (Table 8.18).

Table 39 Global Summary of unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period (Total Vaccinated Cohort)

|  | Group |  |  |
| :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | Total |
| Number of subjects with at least one unsolicited symptom reported | 100 | 103 | 203 |
| Number of doses followed by at least one unsolicited symptom | 153 | 166 | 319 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term* | 415 | 398 | 813 |
| Number of unsolicited symptoms reported** | 430 | 410 | 840 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

In Table 8.20, Table 8.21 and Table 40, respectively, the following results are presented:

- the percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary SOC and PT within the 30-day (Days 0-29) postvaccination period (Table 8.20);
- the percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary SOC and PT within the 30-day (Days 0-29) post-vaccination period (Table 8.21);
- the global summary of grade 3 unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period (Table 40).
Overall, 18 (15.4\%) subjects in the HZ/su group and 15 (13.0\%) subjects in the Placebo group reported at least one grade 3 unsolicited AE within 30 days post vaccination (Table 8.20 and Table 40).

Overall per subject, the most frequent grade 3 unsolicited AEs within 30 days post vaccination were febrile neutropenia (4 subjects or 3.4\%) and neutropenia ( 3 subjects or $2.6 \%$ ) for the HZ/su group, and neutropenia ( 3 subjects or 2.6\%), febrile neutropenia (2 subjects or $1.7 \%$ ) and acute kidney injury ( 2 subjects or $1.7 \%$ ) for the Placebo group (Table 8.20).

Table 40 Global Summary of grade 3 unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period (Total Vaccinated Cohort)

|  | Group |  |  |
| :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | Total |
| Number of subjects with at least one unsolicited symptom reported | 18 | 15 | 33 |
| Number of doses followed by at least one unsolicited symptom | 22 | 15 | 37 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term | 23 | 22 | 45 |
| Number of unsolicited symptoms reported** | 23 | 22 | 45 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

In Table 8.22, Table 8.23 and Table 41, respectively, the following results are presented:

- the percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment, within the 30-day (Days 0-29) post-vaccination period (Table 8.22);
- the percentage of doses with unsolicited symptoms classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment, within the 30-day (Days 0-29) post-vaccination period (Table 8.23);
- the global summary of unsolicited signs and symptoms reported with causal relationship to vaccination as per investigator assessment, within the 30-day (Days 029) post-vaccination period (Table 41).

Overall, 10 (8.5\%) subjects in the HZ/su group and 9 (7.8\%) subjects in the Placebo group reported at least one unsolicited AE with causal relationship to vaccination as per investigator assessment, within 30 days post vaccination (Table 8.22 and Table 41); asthenia and injection site pruritus were both reported by 2 subjects (1.7\%) in the HZ/su group and injection site pain by 2 subjects (1.7\%) in the Placebo group. Other specified unsolicited AEs with causal relationship to vaccination as per investigator assessment were reported by no more than 1 subject in the HZ/su group and by no more than 1 subject in the Placebo group (Table 8.22).

Table 41 Global Summary of unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (Total Vaccinated Cohort)

|  | Group |  |  |
| :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | Total |
| Number of subjects with at least one unsolicited symptom reported | 10 | 9 | 19 |
| Number of doses followed by at least one unsolicited symptom | 11 | 11 | 22 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term* | 13 | 17 | 30 |
| Number of unsolicited symptoms reported** | 13 | 17 | 30 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

In Table 8.24 , Table 8.25 and Table 42 respectively, the following is presented:

- the percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary SOC and PT with causal relationship to vaccination, within the 30 -day (Days 0-29) post-vaccination period (Table 8.24);
- the percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary SOC and PT with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (Table 8.25);
- the global summary of grade 3 unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (Table 42).

Overall, there was 1 subject ( $0.9 \%$ ) in the $\mathrm{HZ} /$ su group with at least one grade 3 unsolicited AE with causal relationship to vaccination as per investigator assessment; the unsolicited AE reported was gastroenteritis. There were no subjects in the Placebo group with at least one grade 3 unsolicited AE with causal relationship to vaccination as per investigator assessment (Table 8.24).

Table 42 Global Summary of grade 3 unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (Total Vaccinated Cohort)

|  | Group |  |  |
| :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | Total |
| Number of subjects with at least one unsolicited symptom reported | 1 | 0 | 1 |
| Number of doses followed by at least one unsolicited symptom | 1 | 0 | 1 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term | 1 | 0 | 1 |
| Number of unsolicited symptoms reported** | 1 | 0 | 1 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

In Table 8.26, Table 8.27 and Table 8.28 respectively, the following results are presented:

- The percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary SOC and PT with medically attended visit, within the 30-day (Days 0-29) post-vaccination period (Table 8.26);
- the percentage of doses with unsolicited symptoms classified by MedDRA Primary SOC and PT with medically attended visit, within the 30-day (Days 0-29) postvaccination period (Table 8.27);
- the global summary of unsolicited signs and symptoms reported with medically attended visit, within the 30-day (Days 0-29) post-vaccination period (Table 8.28).

Overall, 31 (26.5\%) subjects in the HZ/su group and 33 (28.7\%) subjects in the Placebo group reported at least one unsolicited AEs with medically attended visit within 30 days post-vaccination (Table 8.26 and Table 8.28).
Overall per subject, the most frequent unsolicited AEs with medically attended visit within 30 days post vaccination were febrile neutropenia ( 4 subjects or $3.4 \%$ ) and asthenia and nausea (each 3 subjects or $2.6 \%$ ) for the HZ/su group, and vomiting (4 subjects or $3.5 \%$ ) and anaemia, neutropenia and constipation (each 3 subjects or 2.6\%) for the Placebo group (Table 8.26).

### 8.2.5. TVC: Serious adverse events

Data are presented for subjects included in the TVC.
The SAE Listing Table is in Section 12.1 and the SAE clinical narratives are in Section 12.3.

### 8.2.5.1. TVC: SAEs (any relationship), SAEs with causal relationship to vaccination, SAEs related to study participation, concurrent GSK medication/vaccine

The global summary of SAEs reported from the first vaccination up to 30 days post last vaccination is presented in Table 43.

The percentage of subjects reporting SAEs classified by MedDRA Primary SOC and PT, from first vaccination up to 30 days post last vaccination is presented in Table 8.32. During this period, the number (\%) of subjects with at least one SAE reported was 16 ( $13.7 \%$ ) in the $\mathrm{HZ} /$ su group and 14 ( $12.2 \%$ ) in the Placebo group.

The percentage of subjects reporting the occurrence of SAEs classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment from first vaccination up to 30 days post last vaccination is presented in Table 8.33. During this period, no subjects were reported with SAEs with causal relationship to vaccination as per investigator assessment.

Table 43 Global Summary of serious adverse events reported from the first vaccination up to 30 days post last vaccination (Total Vaccinated Cohort)

|  | Group |  |  |
| :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | Total |
| Number of subjects with at least one unsolicited symptom reported | 16 | 14 | 30 |
| Number of doses followed by at least one unsolicited symptom | 17 | 16 | 33 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term | 19 | 24 | 43 |
| Number of unsolicited symptoms reported** | 19 | 24 | 43 |

HZ/su = Herpes Zoster sub-unit vaccine
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

The global summary of SAEs reported from 30 days post last vaccination up to study end is presented in Table 44. The percentage of subjects reporting the occurrence of SAEs classified by MedDRA Primary SOC and PT from 30 days post last vaccination up to study end is presented in Table 8.34. During this period, the number (\%) of subjects with at least one SAE reported was $30(25.6 \%)$ in the HZ/su group and $31(27.0 \%)$ in the Placebo group.

No SAEs classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment from 30 days post last vaccination up to study end were reported (Table 8.35).

Table 44 Global Summary of serious adverse events reported from 30 days post last vaccination up to study end (Total Vaccinated Cohort)

|  | Group |  |
| :--- | :--- | :--- |
|  |  |  |
|  | HZ/su | Placebo |
| Total |  |  |
| Number of subjects with at least one unsolicited symptom reported | 30 | 31 |
| Number of doses followed by at least one unsolicited symptom | 30 | 31 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term | 54 | 40 |
| Number of unsolicited symptoms reported** | 60 | 40 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

The percentage of subjects reporting the occurrence of SAEs classified by MedDRA Primary SOC and PT from first vaccination up to study end is presented in Table 8.36. During this period, the number (\%) of subjects with at least one SAE reported was 36 $(30.8 \%)$ in the $\mathrm{HZ} /$ su group and $42(36.5 \%)$ in the Placebo group.

No SAEs classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment from first vaccination up to study end were reported (Table 8.37).

It is noted that prior to the first vaccination there were no reports of SAEs related to study participation or concurrent GSK medication/vaccine in the clinical database.

### 8.2.5.2. TVC: Fatal events

The percentage of subjects reported with fatal outcome up to study end is presented in Table 8.38. During this period, the number (\%) of subjects with fatal outcome reported was $12(10.3 \%)$ in the HZ/su group and $11(9.6 \%)$ in the Placebo group. None of the fatalities were considered causally related to vaccination as per investigator assessment.

### 8.2.5.3. TVC: Non-fatal events

Refer to Section 12.1 for the listing of all SAEs (TVC).

### 8.2.6. TVC: Adverse events leading to premature discontinuation of study vaccine and/or study

Up to the Month 2 visit (Visit 3), 3 subjects in the HZ/su group and 2 subjects in the Placebo group were withdrawn from the study due to an SAE; no subjects were withdrawn from the study due to a non-serious AE (see Section 6.2.1, Table 6.4).

Up to study end, 13 subjects in the HZ/su group and 12 subjects in the Placebo group were withdrawn from the study due to an SAE, of which 12 subjects in HZ/su group and 11 subjects in the Placebo group were withdrawn due to a fatal SAE. No subjects were withdrawn from the study due to a non-serious AE (see Section 6.2.1, Table 23).

The listing of subjects withdrawn from the study and/or from vaccination due to AEs, SAEs and solicited symptoms up to study end is shown in Table 8.269.

There were 3 subjects in the TVC that did not discontinue from the study but did not receive the second vaccination due to an $\mathrm{AE} / \mathrm{SAE}$ :

- 2 subjects in the HZ/su group and belonging to the PreChemo group came to Visit 2 but did not receive the second vaccination at investigator's discretion secondary to a non-serious AE (Table 8.269):
- tachycardia, considered related to vaccination per investigator's assessment;
- a suspected HZ episode, not considered related to vaccination per investigator's assessment.
- 1 subject in the HZ/su group and belonging to the OnChemo group did not come to Visit 2, secondary to a clinical condition (SAE, without causal relationship to vaccination as per investigator assessment.

Refer also to Section 6.2.1.

### 8.2.7. TVC: Adverse events of special interest

### 8.2.7.1. pIMDs

Data are presented for subjects included in the TVC.
The global summary of pIMDs reported from the first vaccination up to 30 days post last vaccination is presented in Table 45 . The percentage of subjects reporting the occurrence of pIMDs classified by MedDRA Primary SOC and PT from first vaccination up to 30 days post last vaccination is presented in Table 8.29. During this period, no subjects with pIMDs were reported.

The global summary of pIMDs reported from 30 days post last vaccination up to study end is presented in Table 46. The percentage of subjects reporting the occurrence of pIMDs classified by MedDRA Primary SOC and PT from 30 days post last vaccination up to the study end is presented in Table 8.30. Refer also to Table 8.270 giving further details regarding the pIMD reported: There was 1 pIMD (autoimmune thyroiditis), assessed as serious by investigator, in a Placebo group subject.

The percentage of subjects reporting the occurrence of pIMDs classified by MedDRA Primary SOC and PT from first vaccination up to study end is presented in Table 8.31.

Table 45 Global Summary of potential immune mediated diseases reported from the first vaccination up to 30 days post last vaccination (Total Vaccinated Cohort)

No records exist in this table

Table 46 Global Summary of potential immune mediated diseases reported from 30 days post last vaccination up to study end (Total Vaccinated Cohort)

|  | Group |  |  |
| :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | Total |
| Number of subjects with at least one unsolicited symptom reported | 0 | 1 | 1 |
| Number of doses followed by at least one unsolicited symptom | 0 | 1 | 1 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term | 0 | 1 | 1 |
| Number of unsolicited symptoms reported** | 0 | 1 | 1 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once


### 8.2.8. TVC: Concomitant medications/vaccinations

Data are presented for subjects included in the TVC.
The incidence of concomitant medication use during the 30-day (Days 0-29) postvaccination period by dose and overall is presented in Table 8.39.

Overall per subject, during the 30-day (Days 0-29) post-vaccination period, $96.6 \%$ of subjects in the HZ/su group and $98.3 \%$ of subjects in the Placebo group started to take any concomitant medication at least once. Steroids to prevent chemotherapy nausea and vomiting were taken by $88.9 \%$ subjects in the HZ/su group and $87.8 \%$ subjects in the Placebo group. No subjects started medication in anticipation of a study vaccine reaction (Table 8.39).

### 8.3. TVC: safety analysis in PreChemo/OnChemo groups

Data are presented for subjects of the PreChemo and OnChemo groups (PreChemo:OnChemo, stratified according 4:1 ratio, see Section 5.4.3.2.2) included in the TVC.

Treatment compliance and compliance in returning symptom sheets in the PreChemo and OnChemo groups is presented in Table 8.91 and Table 8.92 respectively.

The percentage of subjects having received only one dose was $15.6 \%$ and $4.4 \%$ in the $\mathrm{HZ} / \mathrm{su}$ and Placebo groups, respectively for the PreChemo group, and $11.1 \%$ and $4.2 \%$ in the HZ/su and Placebo groups, respectively, for the OnChemo group (Table 8.91).

The compliance in returning local and general symptom information for $\mathrm{HZ} / \mathrm{su}$ and Placebo groups, for both PreChemo and OnChemo groups, ranged from 94.9\% to 98.0\% for total (dose 1 and 2) (Table 8.92).

### 8.3.1. TVC: Overall incidence of adverse events in PreChemo/OnChemo groups

Data are presented for subjects of the PreChemo and OnChemo groups included in the TVC.

The incidence and nature of AEs (solicited and unsolicited), any grade and grade 3, reported during the 7 -day (Days 0-6) post-vaccination period following each dose and overall in the PreChemo and OnChemo groups is presented in Table 8.93 and Table 8.94 respectively.

Overall per subject, during the 7-day (Days 0-6) post-vaccination period, at least one (solicited and unsolicited) local or general symptom (any grade) was reported for $92.2 \%$ and $96.3 \%$ of subjects in the $\mathrm{HZ} /$ su group and for $79.1 \%$ and $83.3 \%$ of subjects in the Placebo group, for the PreChemo and OnChemo groups, respectively (Table 8.93).

Overall per subject, during the 7-day (Days 0-6) post-vaccination period, at least one grade 3 (solicited and unsolicited) local or general symptom was reported for $24.4 \%$ and $33.3 \%$ of subjects in the $\mathrm{HZ} /$ su group and for $14.3 \%$ and $33.3 \%$ of subjects in the Placebo group, for the PreChemo and OnChemo groups, respectively (Table 8.94).

### 8.3.2 TVC: Solicited local adverse events in PreChemo/OnChemo groups

Data are presented for subjects of the PreChemo and OnChemo groups included in the TVC.

The incidence of local symptoms (solicited only), any grade and grade 3, reported during the 7-day post-vaccination period (Day 0-6) following each dose and overall in the PreChemo and OnChemo groups is presented in Table 8.95 and Table 8.96 respectively.

Overall per subject, during the 7-day (Days 0-6) post-vaccination period, at least one solicited local symptom (any grade) was reported for $88.4 \%$ and $69.2 \%$ of subjects in the $\mathrm{HZ} /$ su group and for $4.7 \%$ and $12.5 \%$ of subjects in the Placebo group, for the PreChemo and OnChemo groups, respectively (Table 8.95).

For the PreChemo group, after dose 1 and dose 2, respectively, at least one solicited local symptom was reported for $84.9 \%$ and $54.1 \%$ of subjects in the HZ/su group, and for $2.3 \%$ and $3.6 \%$ of subjects in the Placebo group (Table 8.95).

For the OnChemoChemo group, after dose 1 and dose 2, respectively, at least one solicited local symptom was reported for $57.7 \%$ and $66.7 \%$ of subjects in the $\mathrm{HZ} / \mathrm{su}$ group, and for $4.2 \%$ and $9.1 \%$ of subjects in the Placebo group (Table 8.95).

Overall per subject, during the 7-day (Days 0-6) post-vaccination period, at least one grade 3 solicited local symptom was reported for $14.0 \%$ and $3.8 \%$ of subjects in the $\mathrm{HZ} / \mathrm{su}$ group and for $0.0 \%$ and $0.0 \%$ of subjects in the Placebo group for the PreChemo and OnChemo groups, respectively (Table 8.96).

For the PreChemo group, after dose 1 and dose 2, respectively, at least one grade 3 solicited local symptom was reported for $11.6 \%$ and $4.1 \%$ of subjects in the HZ/su group, and for $0.0 \%$ and $0.0 \%$ of subjects in the Placebo group.

For the OnChemoChemo group, after dose 1 and dose 2, respectively, at least one grade 3 solicited local symptom was reported for $0.0 \%$ and $4.2 \%$ of subjects in the HZ/su group, and for $0.0 \%$ and $0.0 \%$ of subjects in the Placebo group.

The incidence of solicited local symptoms reported during the 7-day (Days 0-6) postvaccination period by study vaccine following each dose and overall in the PreChemo and OnChemo groups is presented in Table 8.97.

For the PreChemo group, during the 7-day (Days 0-6) post-vaccination period overall, the most frequently reported solicited local symptom in the HZ/zu group was pain (any grade, overall per subject: $83.7 \%$ in HZ/su group versus $4.7 \%$ in Placebo group). Pain (any grade) after dose 1 was reported for $79.1 \%$ and $1.2 \%$ of subjects, and after dose 2 for $48.6 \%$ and $3.6 \%$ in the $\mathrm{HZ} /$ su group and Placebo group, respectively. Overall per subject, grade 3 pain was reported for $11.6 \%$ and $0.0 \%$ of subjects in the $\mathrm{HZ} /$ su group and Placebo group, respectively. Grade 3 pain after dose 1 was reported for $9.3 \%$ and $0.0 \%$ of subjects, and after dose 2 for $4.1 \%$ and $0.0 \%$ of subjects in the $\mathrm{HZ} /$ su group and Placebo group, respectively (Table 8.97).

For the OnChemo group, during the 7-day (Days 0-6) post-vaccination period overall, the most frequently reported solicited local symptom in the HZ/zu group was pain (any grade, overall per subject: $69.2 \%$ in HZ/su group versus $12.5 \%$ in Placebo group). Pain (any grade) after dose 1 was reported for $57.7 \%$ and $4.2 \%$ of subjects; and after dose 2 for $66.7 \%$ and $9.1 \%$ in the HZ/su group and Placebo group, respectively. Overall per subject, grade 3 pain was reported for $3.8 \%$ and $0.0 \%$ of subjects in the HZ/su group and Placebo group, respectively. Grade 3 pain after dose 1 was reported for $0.0 \%$ and $0.0 \%$ of subjects, and after dose 2 for $4.2 \%$ and $0.0 \%$ of subjects in the $\mathrm{HZ} /$ su group and Placebo group, respectively (Table 8.97).

The number of days with grade 3 local symptoms during the solicited post-vaccination period in the PreChemo and OnChemo groups is presented in Table 8.103.

### 8.3.3. TVC: Solicited general adverse events in PreChemo/OnChemo groups

Data are presented for subjects of the PreChemo and OnChemo groups included in the TVC.

The incidence of general symptoms (solicited only), any grade and grade 3, reported during the 7 -day post-vaccination period (Day 0-6) following each dose and overall in the PreChemo and OnChemo groups is presented in Table 8.95 and Table 8.96 respectively.

Overall per subject, during the 7-day (Days 0-6) post-vaccination period, at least one solicited general symptom (any grade) was reported for $79.1 \%$ and $88.5 \%$ of subjects in the HZ/su group and for $65.1 \%$ and $70.8 \%$ of subjects in the Placebo group, for the PreChemo and OnChemo groups, respectively (Table 8.95).

For the PreChemo group, after dose 1 and dose 2, respectively, at least one solicited general symptom was reported for $67.4 \%$ and $67.1 \%$ of subjects in the HZ/su group, and for $41.9 \%$ and $54.9 \%$ of subjects in the Placebo group.

For the OnChemoChemo group, after dose 1 and dose 2, respectively, at least one solicited general symptom was reported for $84.6 \%$ and $75.0 \%$ of subjects in the $\mathrm{HZ} / \mathrm{su}$ group, and for $66.7 \%$ and $68.2 \%$ of subjects in the Placebo group.

Overall per subject, during the 7-day (Days 0-6) post-vaccination period, at least one grade 3 solicited general symptom was reported for $19.8 \%$ and $30.8 \%$ of subjects in the $\mathrm{HZ} /$ su group and for $14.0 \%$ and $20.8 \%$ of subjects in the Placebo group for the PreChemo and OnChemo groups, respectively (Table 8.96).

For the PreChemo group, after dose 1 and dose 2, respectively, at least one grade 3 solicited general symptom was reported for $10.5 \%$ and $13.7 \%$ of subjects in the $\mathrm{HZ} / \mathrm{su}$ group, and for $7.0 \%$ and $8.5 \%$ of subjects in the Placebo group.

For the OnChemoChemo group, after dose 1 and dose 2, respectively, at least one grade 3 solicited general symptom was reported for $23.1 \%$ and $25.0 \%$ of subjects in the HZ/su group, and for $20.8 \%$ and $13.6 \%$ of subjects in the Placebo group.

The incidence of solicited general symptoms reported during the 7 -day (Days $0-6$ ) postvaccination period by study vaccine following each dose and overall in the PreChemo and OnChemo groups in Table 8.98.

For the PreChemo group, during the 7-day (Days 0-6) post-vaccination period overall, the most frequently reported solicited general symptom in the $\mathrm{HZ} / \mathrm{zu}$ group was fatigue (any grade, overall per subject: $66.3 \%$ in HZ/su group versus $60.5 \%$ in Placebo group); myalgia (any grade, overall per subject: $58.1 \%$ in $\mathrm{HZ} /$ su group versus $25.6 \%$ in Placebo group). Fatigue (any grade) after dose 1 was reported for $44.2 \%$ and $34.9 \%$ of subjects, and after dose 2 for $56.2 \%$ and $52.4 \%$ in the $\mathrm{HZ} /$ su group and Placebo group, respectively. Overall per subject, grade 3 fatigue was reported for $11.6 \%$ and $5.8 \%$ of subjects in the HZ/su group and Placebo group, respectively. Grade 3 fatigue after dose 1 was reported for $5.8 \%$ and $1.2 \%$ of subjects, and after dose 2 for $6.8 \%$ and $6.1 \%$ of subjects in the HZ/su group and Placebo group, respectively (Table 8.98).

For the OnChemo group, during the 7-day (Days $0-6$ ) post-vaccination period overall, the most frequently reported solicited general symptoms in the HZ/zu group was fatigue (any grade, overall per subject: $80.8 \%$ in $\mathrm{HZ} /$ su group versus $66.7 \%$ in Placebo group); gastrointestinal symptoms (any grade, overall per subject: $69.2 \%$ in HZ/su group versus $62.5 \%$ in Placebo group). Fatigue (any grade) after dose 1 was reported for $69.2 \%$ and $58.3 \%$ of subjects; and after dose 2 for $66.7 \%$ and $63.6 \%$ in the $\mathrm{HZ} /$ su group and Placebo group, respectively. Overall per subject, grade 3 fatigue was reported for $23.1 \%$ and $12.5 \%$ of subjects in the HZ/su group and Placebo group, respectively. Grade 3 fatigue after dose 1 was reported for $19.2 \%$ and $8.3 \%$ of subjects, and after dose 2 for $16.7 \%$ and $4.5 \%$ of subjects in the HZ/su group and Placebo group, respectively (Table 8.98).

The number of days with grade 3 general symptoms during the solicited post-vaccination period in the PreChemo and OnChemo groups is presented in Table 8.104.

The number and percentage of subjects who reported temperature by half degree measured via oral route, axillary route, tympanic route and reactal route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) in the PreChemo and OnChemo groups is presented in Table 8.99, Table 8.100 and Table 8.101 and Table 8.102 , respectively.

### 8.3.4. TVC: Unsolicited adverse events in PreChemo/OnChemo groups

Data are presented for subjects of the PreChemo and OnChemo groups included in the TVC.

In Table 8.105, Table 8.106 and Table 8.115 respectively, the following results are presented for the PreChemo and OnChemo groups:

- the percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary SOC and PT within the 30-day (Days 0-29) postvaccination period (Table 8.105);
- the percentage of doses with unsolicited symptoms classified by MedDRA Primary SOC and PT within the 30-day (Days 0-29) post-vaccination period (Table 8.106);
- the global summary of unsolicited signs and symptoms reported within the 30-day (Days $0-29$ ) post-vaccination period (Table 8.115).
In Table 8.107, Table 8.108 and Table 8.116, respectively, the following results are presented for the PreChemo and OnChemo groups:
- the percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary SOC and PT within the 30-day (Days 0-29) postvaccination period (Table 8.107);
- the percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary SOC and PT within the 30-day (Days 0-29) post-vaccination period (Table 8.108);
- the global summary of grade 3 unsolicited signs and symptoms reported within the 30-day (Days $0-29$ ) post-vaccination period (Table 8.116).

In Table 8.109, Table 8.110 and Table 8.117 respectively, the following results are presented for the PreChemo and OnChemo groups:

- the percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment, within the 30-day (Days 0-29) post-vaccination period (Table 8.109);
- the percentage of doses with unsolicited symptoms classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment, within the 30 -day (Days $0-29$ ) post-vaccination period (Table 8.110);
- the global summary of unsolicited signs and symptoms reported with causal relationship to vaccination as per investigator assessment, within the 30-day (Days 029) post-vaccination period (Table 8.117).

In Table 8.111, Table 8.112 and Table 8.118 respectively, the following results are presented for the PreChemo and OnChemo groups:

- the percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary SOC and PT with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (Table 8.111);
- the percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary SOC and PT with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (Table 8.112);
- the global summary of grade 3 unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (Table 8.113).

In Table 8.113, Table 8.114 and Table 8.119 respectively, the following results are presented for the PreChemo and OnChemo groups:

- the percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary SOC and PT with medically attended visit, within the 30-day (Days 0-29) post-vaccination period (Table 8.113);
- the percentage of doses with unsolicited symptoms classified by MedDRA Primary SOC and PT with medically attended visit, within the 30-day (Days 0-29) postvaccination period (Table 8.114);
- the global summary of unsolicited signs and symptoms reported with medically attended visit, within the 30-day (Days 0-29) post-vaccination period (Table 8.119).
For the PreChemo group, overall, 74 (82.2\%) subjects in the HZ/su group and 81 (89.0\%) in the Placebo group reported at least one unsolicited AE within 30 days post vaccination (Table 8.105). The most frequent unsolicited AEs within 30 days post vaccination were nausea ( 23 subjects or $25.6 \%$ in the the HZ/su group versus 23 subjects or $25.3 \%$ in the Placebo group) and asthenia ( 23 subjects or $25.6 \%$ in the the HZ/su group versus 25 subjects or $27.5 \%$ in the Placebo group).

For the PreChemo group, 13 (14.4\%) subjects in the HZ/su group, and 9 ( $9.9 \%$ ) subjects in the Placebo group reported at least one grade 3 unsolicited AE within 30 days post vaccination (Table 8.107).

For the OnChemo group, overall, 26 ( $96.3 \%$ ) subjects in the HZ/su group and 22 (91.7\%) in the Placebo group reported at least one unsolicited AE within 30 days post vaccination (Table 8.105). The most frequent unsolicited AEs within 30 days post vaccination were nausea ( 8 subjects or $29.6 \%$ in the the HZ/su group versus 5 subjects or $20.8 \%$ in the Placebo group) and asthenia ( 7 subjects or $25.9 \%$ in the the $\mathrm{HZ} /$ su group versus 3 subjects or $12.5 \%$ in the Placebo group). To note that dyspepsia was also reported by 5 subjects (20.8\%) in the Placebo group (versus 1 subject or $3.7 \%$ in the $\mathrm{HZ} /$ su group).

For the OnChemo group, 5 (18.5\%) subjects in the HZ/su group, and 6 (25.0\%) subjects in the Placebo group reported at least one grade 3 unsolicited AE within 30 days post vaccination (Table 8.107).

For the PreChemo group, overall, $10(11.1 \%)$ subjects in the $\mathrm{HZ} /$ su group and $7(7.7 \%)$ in the Placebo group reported at least one unsolicited AE with causal relationship to vaccination as per investigator assessment within 30 days post vaccination (Table 8.109). For the PreChemo group, 1 (1.1\%) subjects in the HZ/su group and $0(0.0 \%)$ subjects in the Placebo group reported at least one grade 3 unsolicited AE with causal relationship to vaccination as per investigator assessment within 30 days post vaccination (Table 8.111).

For the OnChemo group, overall, $0(0.0 \%)$ subjects in the HZ/su group and $2(8.3 \%)$ in the Placebo group reported at least one unsolicited AE with causal relationship to vaccination as per investigator assessment within 30 days post vaccination (Table 8.109). For the OnChemo group, no subjects in the HZ/su and Placebo group, respectively, reported any grade 3 unsolicited AE with causal relationship to vaccination as per investigator assessment within 30 days post vaccination (Table 8.111).

For the PreChemo and OnChemo groups, overall, respectively 19 (21.1\%) and 12 ( $44.4 \%$ ) subjects in the HZ/su group, and 28 (30.8\%) and 5 (20.8\%) subjects in the Placebo group reported at least one unsolicited AE with medically attended visit within 30 days post vaccination (Table 8.113).

### 8.3.5. TVC Serious adverse events in PreChemo/OnChemo groups

### 8.3.5.1. TVC: SAEs (any relationship), SAEs with causal relationship to vaccination in PreChemo/OnChemo groups

Data are presented for subjects of the PreChemo and OnChemo groups included in the TVC.

The global summary of SAEs reported from the first vaccination up to 30 days post last vaccination is presented for the PreChemo and OnChemo groups in Table 8.123. The percentage of subjects reporting SAEs classified by MedDRA Primary SOC and PT, from first vaccination up to 30 days post last vaccination is presented for the PreChemo and OnChemo groups in Table 8.124.

The percentage of subjects reporting the occurrence of SAEs classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment from first vaccination up to 30 days post last vaccination is presented for the PreChemo and OnChemo groups in Table 8.125. During this period, no subjects were reported with SAEs with causal relationship to vaccination as per investigator assessment.

The percentage of subjects reporting the occurrence of SAEs classified by MedDRA Primary SOC and PT from 30 days post last vaccination period up to study end is presented for the PreChemo and OnChemo groups in Table 8.126.

The percentage of subjects reporting the occurrence of SAEs classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment from 30 days post last vaccination up to study end is presented for the PreChemo and OnChemo groups in Table 8.127. During this period, no subjects were reported with SAEs with causal relationship to vaccination as per investigator assessment.

The percentage of subjects reporting the occurrence of SAEs classified by MedDRA Primary SOC and PT from first vaccination up to study end is presented for the PreChemo and OnChemo groups in Table 8.128.

The percentage of subjects reporting the occurrence of SAEs classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment from first vaccination up to study end is presented for the PreChemo and OnChemo groups in Table 8.129. During this period, no subjects were reported with SAEs with causal relationship to vaccination as per investigator assessment.

The number (\%) of subjects with at least one SAE reported from the first vaccination up to 30 -day post last vaccination, was $9(10.0 \%)$ and $7(25.9 \%)$ in the HZ/su group, and 10 (11.0\%) and $4(16.7 \%)$ in the Placebo group, for the PreChemo and OnChemo groups, respectively (Table 8.124).

The number (\%) of subjects with at least one SAE reported from 30-day post last vaccination up to study end, was 22 ( $24.4 \%$ ) and 8 (29.6\%) in the HZ/su group, and 25 ( $27.5 \%$ ) and $6(25.0 \%)$ in the Placebo group, for the PreChemo and OnChemo groups, respectively (Table 8.126).

The number (\%) of subjects with at least one SAE reported from first vaccination up to the study end, was 27 ( $30.0 \%$ ) and 9 (33.3\%) in the HZ/su group, and 34 (37.4\%) and 8 (33.3\%) in the Placebo group, for the PreChemo and OnChemo groups, respectively (Table 8.128).

### 8.3.5.2. TVC: Fatal events in PreChemo/OnChemo groups

The percentage of subjects with fatal outcome reported up to study end is presented for the PreChemo and OnChemo groups in Table 8.131. In the PreChemo group, 9 (10.0\%) fatalities in the $\mathrm{HZ} /$ su group and $10(11.0 \%)$ in the Placebo group, were reported up to the study end. In the OnChemo group, 3 (11.1\%) fatalities in the HZ/su group and 1 (4.2\%) in the Placebo group, were reported up to the study end. None of the fatalities were considered causally related to vaccination as per investigator assessment.

### 8.3.6. TVC: Adverse events leading to premature discontinuation of study vaccine and/or study in PreChemo/OnChemo groups

Up to the Month 2 visit (Visit 3), in the PreChemo group, 3 subjects in the HZ/su group and 2 subjects in the Placebo group were withdrawn from the study due to an SAE; no subjects were withdrawn from the study due to a non-serious AE; in the OnChemo group no subjects were withdrawn from the study due to an SAE or non-serious AE (see Section 6.2.2, Table 6.5).
Up to the Month 13 visit (Visit 5), in the PreChemo group, 10 subjects in the HZ/su group and 11 subjects in the Placebo group were withdrawn from the study due to an SAE, of which 9 and 10 subjects respectively were withdrawn due to a fatal SAE; no subjects were withdrawn from the study due to a non-serious AE. In the OnChemo group 3 subjects in the HZ/su group and 1 subject in the Placebo group were withdrawn from the study due to an SAE (all fatal SAEs); no subjects were withdrawn from the study due to a non-serious AE (see Section 6.2.2, Table 6.7).

Refer to Sections 6.2.1 and 8.2.6 for information regarding subjects withdrawn from vaccination due to an $A E / S A E$.

### 8.3.7. TVC: Adverse events of special interest in PreChemo/OnChemo groups

### 8.3.7.1. pIMDs in PreChemo/OnChemo groups

Data are presented for subjects of the PreChemo and OnChemo groups included in the TVC.

The global summary of pIMDs reported from the first vaccination up to 30 days post last vaccination is presented for the PreChemo and OnChemo groups in Table 8.130. The percentage of subjects reporting the occurrence of pIMDs classified by MedDRA Primary SOC and PT from first vaccination up to 30 days post last vaccination is presented for the PreChemo and OnChemo groups in Table 8.120. During this period, no subjects with pIMDs were reported.

The percentage of subjects reporting the occurrence of pIMDs classified by MedDRA Primary SOC and PT from 30 days post last vaccination up to study end is presented for the PreChemo and OnChemo groups in Table 8.121.

The number of subjects with at least one pIMD event reported from 30 days post last vaccination up to study end for both PreChemo and OnChemo groups, was $0(0.0 \%)$ in both $\mathrm{HZ} /$ su groups; and $0(0.0 \%)$ and $1(4.2 \%)$, respectively in the Placebo group (Table 8.121).

The percentage of subjects reporting the occurrence of pIMDs classified by MedDRA Primary SOC and PT from first vaccination up to study end is presented for the PreChemo and OnChemo groups in Table 8.122.

The number of subjects with at least one pIMD event reported from first vaccination up to study end for both PreChemo and OnChemo groups, was $0(0.0 \%)$ in both HZ/su groups; and $0(0.0 \%)$ and $1(4.2 \%)$, respectively in the Placebo group. The pIMD reported was "autoimmune thyroiditis" in the Placebo group for the OnChemo group (Table 8.122).

### 8.3.8. Concomitant medications/vaccinations in PreChemo/OnChemo groups

Data are presented for subjects of the PreChemo and OnChemo groups included in the TVC.

The incidence of concomitant medication use during the 30-day (Days 0-29) postvaccination period by dose and overall is presented for the PreChemo and OnChemo groups in Table 8.132.

### 8.4. TVC: safety analysis by age strata (18-49 YOA and $\geq 50$ YOA)

Data are presented by age strata (18-49 YOA and $\geq 50 \mathrm{YOA}$ ) for subjects included in the TVC.

Treatment compliance and compliance in returning symptom sheets is presented by age stratum in Table 8.175 and Table 8.176 respectively.

A total of $6.5 \%$ and $17.4 \%$ of subjects in the HZ/su group and $0.0 \%$ and $5.9 \%$ in the Placebo group, of the $18-49$ YOA and $\geq 50$ YOA strata, respectively, did not receive the second dose (Table 8.175).

The compliance in returning local and general symptom information for $\mathrm{HZ} / \mathrm{su}$ and Placebo groups, for both $18-49$ YOA and $\geq 50$ YOA strata, ranged from $93.9 \%$ to $100 \%$ for doses overall (dose 1 and 2) (Table 8.176).

### 8.4.1. TVC: Overall incidence of adverse events by age strata

Data are presented by age strata ( $18-49$ YOA and $\geq 50 \mathrm{YOA}$ ) for subjects included in the TVC.

The incidence and nature of AEs (solicited and unsolicited), any grade and grade 3, reported during the 7 -day (Days 0-6) post-vaccination period following each dose and overall is presented by age strata in Table 8.177 and Table 8.178 respectively.

Overall per subject, during the 7-day (Days 0-6) post-vaccination period, at least one (solicited and unsolicited) local or general symptom (any grade) was reported for $100 \%$ and $90.7 \%$ of subjects in the $\mathrm{HZ} /$ su group and for $83.3 \%$ and $78.8 \%$ of subjects in the Placebo group, for the $18-49$ YOA and $\geq 50$ YOA strata, respectively (Table 8.177).

Overall per subject, during the 7-day (Days 0-6) post-vaccination period, at least one grade 3 (solicited and unsolicited) local or general symptom was reported for $35.5 \%$ and $23.3 \%$ of subjects in the $\mathrm{HZ} / \mathrm{su}$ group and for $26.7 \%$ and $15.3 \%$ of subjects in the Placebo group, for the 18-49 YOA and $\geq 50 \mathrm{YOA}$ strata, respectively (Table 8.178).

### 8.4.2. TVC: Solicited local adverse events by age strata

Data are presented by age strata (18-49 YOA and $\geq 50 \mathrm{YOA}$ ) for subjects included in the TVC.

The incidence of local symptoms (solicited only), any grade and grade 3, reported during the 7 -day post-vaccination period (Day 0-6) following each dose and overall is presented by age strata in Table 8.179 and Table 8.180.

Overall per subject, during the 7-day (Days 0-6) post-vaccination period, at least one (solicited only) local symptom (any grade) was reported for $93.5 \%$ and $80.2 \%$ of subjects in the HZ/su group and for $20.0 \%$ and $1.3 \%$ of subjects in the Placebo group, for the 18 49 YOA and $\geq 50$ YOA strata, respectively (Table 8.179).

Overall per subject, during the 7-day (Days 0-6) post-vaccination period, at least one grade 3 (solicited only) local symptom was reported for $12.9 \%$ and $11.1 \%$ of subjects in the $\mathrm{HZ} / \mathrm{su}$ group and for $0.0 \%$ and $0.0 \%$ of subjects in the Placebo group, for the 18-49 YOA and $\geq 50$ YOA strata, respectively (Table 8.180).

The incidence of solicited local symptoms reported during the 7 -day (Days 0-6) postvaccination period by study vaccine following each dose and overall is presented by age strata in Table 8.181.

For the 18-49 YOA stratum, during the 7-day (Days 0-6) post-vaccination period overall, the most frequently reported solicited local symptom in the HZ/zu group was pain (any grade, overall per subject: $90.3 \%$ in $\mathrm{HZ} /$ su group versus $20.0 \%$ in Placebo group). Pain (any grade) after dose 1 was reported for $83.9 \%$ and $6.7 \%$ of subjects, and after dose 2 for $65.5 \%$ and $13.8 \%$ in the $\mathrm{HZ} /$ su group and Placebo group, respectively. Overall per subject, grade 3 pain was reported for $12.9 \%$ and $0.0 \%$ of subjects in the HZ/su group and Placebo group, respectively. Grade 3 pain after dose 1 was reported for $12.9 \%$ and $0.0 \%$ of subjects, and after dose 2 for $3.4 \%$ and $0.0 \%$ of subjects in the $\mathrm{HZ} /$ su group and Placebo group, respectively (Table 8.181).

For the $\geq 50$ YOA stratum, during the 7 -day (Days $0-6$ ) post-vaccination period overall, the most frequently reported solicited local symptom in the HZ/zu group was pain (any grade, overall per subject: $76.5 \%$ in HZ/su group versus $1.3 \%$ in Placebo group). Pain (any grade) after dose 1 was reported for $70.4 \%$ and $0.0 \%$ of subjects; and after dose 2 for $47.8 \%$ and $1.3 \%$ in the HZ/su group and Placebo group, respectively. Overall per subject, grade 3 pain was reported for $8.6 \%$ and $0.0 \%$ of subjects in the HZ/su group and Placebo group, respectively. Grade 3 pain after dose 1 was reported for $4.9 \%$ and $0.0 \%$ of subjects, and after dose 2 for $4.3 \%$ and $0.0 \%$ of subjects in the HZ/su group and Placebo group, respectively (Table 8.181). The number of days with local symptoms during the solicited post-vaccination period is presented by age strata in Table 8.259.

The number of days with grade 3 local symptoms during the solicited post-vaccination period is presented by age strata in Table 8.187.

The duration of solicited local symptoms (in days), not limited to the 7-day postvaccination period, following each dose and overall per dose, is presented by age strata in Table 8.260.

Information regarding the incidence and nature of local symptoms (solicited only) reported during the 7 -day (Days $0-6$ ) post-vaccination period and lasting beyond this period following each dose and overall, is presented by age strata in Table 8.267.

Information regarding the incidence and nature of grade 3 local symptoms (solicited only) reported during the 7 -day (Days $0-6$ ) post-vaccination period and lasting beyond this period following each dose and overall, is presented by age strata in Table 8.268.

Information regarding the different solicited local symptoms ongoing beyond the 7-day (Days $0-6$ ) post-vaccination period, by age strata, is presented in Table 8.261.

Refer also to Section 5.11.2 regarding Table 8.259, Table 8.260, Table 8.261, Table 8.267 and Table 8.268 (post-hoc analysis).

### 8.4.3. TVC: Solicited general adverse events by age strata

Data are presented by age strata (18-49 YOA and $\geq 50 \mathrm{YOA}$ ) for subjects included in the TVC.

The incidence of general symptoms (solicited only), any grade and grade 3, reported during the 7 -day post-vaccination period (Day 0-6) following each dose and overall is presented by age strata in Table 8.179 and Table 8.180.

Overall per subject, during the 7-day (Days 0-6) post-vaccination period, at least one (solicited only) general symptom (any grade) was reported for $87.1 \%$ and $79.0 \%$ of subjects in the HZ/su group and for $73.3 \%$ and $63.8 \%$ of subjects in the Placebo group, for the 18-49 YOA and $\geq 50$ YOA strata, respectively (Table 8.179).

Overall per subject, during the 7-day (Days 0-6) post-vaccination period, at least one grade 3 (solicited only) general symptom was reported for $32.3 \%$ and $18.5 \%$ of subjects in the $\mathrm{HZ} / \mathrm{su}$ group and for $23.3 \%$ and $12.5 \%$ of subjects in the Placebo group, for the 18 49 YOA and $\geq 50$ YOA strata, respectively (Table 8.180).

The incidence of solicited general symptoms reported during the 7-day (Days 0-6) postvaccination period by study vaccine following each dose and overall is presented by age stratum in Table 8.182.

For the 18-49 YOA stratum, during the 7-day (Days $0-6$ ) post-vaccination period overall, the most frequently reported solicited general symptom in the HZ/zu group was fatigue (any grade, overall per subject: 77.4\% in HZ/su group versus $66.7 \%$ in Placebo group); myalgia and gastrointestinal symptoms (any grade, overall per subject: myalgia: 58.1\% in $\mathrm{HZ} /$ su group versus $23.3 \%$ in Placebo group; gastrointestinal smptoms: $58.1 \%$ in $\mathrm{HZ} / \mathrm{su}$ group versus $53.3 \%$ in Placebo group). Fatigue (any grade) after dose 1 was reported for $54.8 \%$ and $46.7 \%$ of subjects, and after dose 2 for $62.1 \%$ and $62.1 \%$ in the $\mathrm{HZ} /$ su group and Placebo group, respectively. Overall per subject, grade 3 fatigue was reported for $25.8 \%$ and $16.7 \%$ of subjects in the $\mathrm{HZ} /$ su group and Placebo group, respectively. Grade 3 fatigue after dose 1 was reported for $16.1 \%$ and $6.7 \%$ of subjects, and after dose 2 for $13.8 \%$ and $10.3 \%$ of subjects in the $\mathrm{HZ} /$ su group and Placebo group, respectively (Table 8.182).

For the $\geq 50$ YOA stratum, during the 7 -day (Days $0-6$ ) post-vaccination period overall, the most frequently reported solicited general symptom in the HZ/zu group was fatigue (any grade, overall per subject: $66.7 \%$ in $\mathrm{HZ} /$ su group versus $60.0 \%$ in Placebo group); myalgia (any grade, overall per subject: $51.9 \%$ in $\mathrm{HZ} /$ su group versus $30.0 \%$ in Placebo group). Fatigue (any grade) after dose 1 was reported for $48.1 \%$ and $37.5 \%$ of subjects; and after dose 2 for $57.4 \%$ and $52.0 \%$ in the HZ/su group and Placebo group, respectively. Overall per subject, grade 3 fatigue was reported for $9.9 \%$ and $3.8 \%$ of subjects in the HZ/su group and Placebo group, respectively. Grade 3 fatigue after dose 1 was reported for $6.2 \%$ and $1.3 \%$ of subjects, and after dose 2 for $7.4 \%$ and $4.0 \%$ of subjects in the HZ/su group and Placebo group, respectively (Table 8.182).

The number and percentage of subjects who reported temperature by half degree measured via oral route, axillary route, tympanic route and rectal route during the 7-day (Days $0-6$ ) post-vaccination period following each dose (no conversion) is presented by age stratum in Table 8.183, Table 8.184, Table 8.185 and Table 8.186, respectively.

The number of days with general symptoms during the solicited post-vaccination period is presented by age strata in Table 8.262.

The number of days with grade 3 general symptoms during the solicited post-vaccination period is presented by age strata in Table 8.188.

The duration of solicited general symptoms (in days), not limited to the 7-day postvaccination period, following each dose and overall per dose, is presented by age strata in Table 8.263.

Information regarding the incidence and nature of general symptoms (solicited only) reported during the 7 -day (Days $0-6$ ) post-vaccination period and lasting beyond this period following each dose and overall is presented by age strata in Table 8.267.

Information regarding the incidence and nature of grade 3 general symptoms (solicited only) reported during the 7 -day (Days $0-6$ ) post-vaccination period and lasting beyond this period following each dose and overall is presented by age strata in Table 8.268.

Information regarding the different solicited general symptoms ongoing beyond the 7-day (Days 0-6) post-vaccination period is presented by age strata in Table 8.264.

Refer to Section 5.11.2 regarding Table 8.262, Table 8.263 and Table 8.264 (post-hoc analysis).

### 8.4.4. TVC: Unsolicited adverse events by age strata

Data are presented by age strata ( $18-49 \mathrm{YOA}$ and $\geq 50 \mathrm{YOA}$ ) for subjects included in the TVC.

In Table 8.189, Table 8.190 and Table 8.199 respectively, the following results are presented by age strata:

- the percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary SOC and PT within the 30-day (Days 0-29) postvaccination period (Table 8.189);
- the percentage of doses with unsolicited symptoms classified by MedDRA Primary SOC and PT within the 30-day (Days 0-29) post-vaccination period (Table 8.190);
- the global summary of unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period (Table 8.199).
In Table 8.191, Table 8.192 and Table 8.200, respectively, the following results are presented by age strata:
- the percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary SOC and PT within the 30-day (Days 0-29) postvaccination period (Table 8.191);
- the percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary SOC and PT within the 30-day (Days 0-29) post-vaccination period (Table 8.200);
- the global summary of grade 3 unsolicited signs and symptoms reported within the 30-day (Days $0-29$ ) post-vaccination period (Table 8.200).
In Table 8.193, Table 8.194 and Table 8.201, respectively, the following results are presented by age strata:
- the percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment, within the 30-day (Days 0-29) post-vaccination period (Table 8.193);
- the percentage of doses with unsolicited symptoms classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment, within the 30 -day (Days 0-29) post-vaccination period (Table 8.194);
- the global summary of unsolicited signs and symptoms reported with causal relationship to vaccination as per investigator assessment, within the 30-day (Days 029) post-vaccination period (Table 8.202).

In Table 8.195, Table 8.196 and Table 8.202 respectively, the following results are presented by age strata:

- the percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary SOC and PT with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (Table 8.195);
- the percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary SOC and PT with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (Table 8.196);
- the global summary of grade 3 unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days $0-29$ ) post-vaccination period (Table 8.202).
In Table 8.197, Table 8.198 and Table 8.203 respectively, the following results are presented by age strata:
- the percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary SOC and PT with medically attended visit, within the 30-day (Days 0-29) post-vaccination period (Table 8.197);
- the percentage of doses with unsolicited symptoms classified by MedDRA Primary SOC and PT with medically attended visit, within the 30-day (Days 0-29) postvaccination period (Table 8.198);
- the global summary of unsolicited signs and symptoms reported with medically attended visit, within the 30-day (Days 0-29) post-vaccination period (Table 8.203).

For the 18-49 YOA stratum, overall, 25 (80.6\%) subjects in the HZ/su group and 27 ( $90.0 \%$ ) in the Placebo group reported at least one unsolicited AE within 30 days post vaccination (Table 8.189). Overall per subject, the most frequent unsolicited AEs within 30 days post vaccination were asthenia ( 13 subjects or $41.9 \%$ in the the $\mathrm{HZ} /$ su group versus 4 subjects or $13.3 \%$ in the Placebo group) and nausea ( 12 subjects or $38.7 \%$ in the the $\mathrm{HZ} /$ su group versus 9 subjects or $30.0 \%$ in the Placebo group).

For the 18-49 YOA stratum, 3 (9.7\%) subjects in the HZ/su group, and 4 (13.3\%) subjects in the Placebo group reported at least one grade 3 unsolicited AE within 30 days post vaccination (Table 8.191).

For the $\geq 50$ YOA stratum, overall, 75 (87.2\%) subjects in the HZ/su group and 76 ( $89.4 \%$ ) in the Placebo group reported at least one unsolicited AE within 30 days post vaccination (Table 8.189). Overall per subject, the most frequent unsolicited AEs within 30 days post vaccination were nausea ( 19 subjects or $22.1 \%$ in the the HZ/su group versus 19 subjects or $22.4 \%$ in the Placebo group) and asthenia ( 17 subjects or $19.8 \%$ in the the $\mathrm{HZ} /$ su group versus 24 subjects or $28.2 \%$ in the Placebo group).

For the $\geq 50$ YOA stratum, 15 (17.4\%) subjects in the HZ/su group and 11 (12.9\%) subjects in the Placebo group reported at least one grade 3 unsolicited AE within 30 days post vaccination (Table 8.191).

For the 18-49 YOA stratum, overall, 4 (12.9\%) subjects in the HZ/su group and 2 (6.7\%) in the Placebo group reported at least one unsolicited AE with causal relationship to vaccination as per investigator assessment within 30 days post vaccination (Table 8.193).

For the $18-49$ YOA stratum, $1(3.2 \%)$ subjects in the HZ/su group and $0(0.0 \%)$ subjects in the Placebo group reported at least one grade 3 unsolicited AE with causal relationship to vaccination as per investigator assessment within 30 days post vaccination (Table 8.195).

For the $\geq 50$ YOA stratum, overall, $6(7.0 \%)$ subjects in the $\mathrm{HZ} /$ su group and $7(8.2 \%)$ in the Placebo group reported at least one unsolicited AE with causal relationship to vaccination as per investigator assessment within 30 days post vaccination (Table 8.193).

For the $\geq 50 \mathrm{YOA}$ stratum, no subjects in the HZ/su and Placebo group, respectively, reported any grade 3 unsolicited AE with causal relationship to vaccination as per investigator assessment within 30 days post vaccination (Table 8.195).

For the 18-49 YOA and $\geq 50$ YOA strata, overall, respectively 9 (29.0\%) and 22 (25.6\%) subjects in the HZ/su group, and 8 (26.7\%) and 25 (29.4\%) subjects in the Placebo group reported at least one unsolicited AE with medically attended visit within 30 days post vaccination (Table 8.197).

### 8.4.5. TVC Serious adverse events by age strata

### 8.4.5.1. TVC: SAEs (any relationship), SAEs with causal relationship to vaccination by age strata

Data are presented by age strata ( $18-49 \mathrm{YOA}$ and $\geq 50 \mathrm{YOA}$ ) for subjects included in the TVC.

The global summary of SAEs reported from the first vaccination up to 30 days post last vaccination is presented by age strata in Table 8.208. The percentage of subjects reporting SAEs classified by MedDRA Primary SOC and PT, from first vaccination up to 30 days post last vaccination is presented by age strata in Table 8.207.

The percentage of subjects reporting the occurrence of SAEs classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment from first vaccination up to 30 days post last vaccination is presented by age strata in Table 8.209. During this period, no subjects were reported with SAEs with causal relationship to vaccination as per investigator assessment.

The percentage of subjects reporting SAEs classified by MedDRA Primary SOC and PT, from 30 days post last vaccination up to study end is presented by age strata in Table 8.210 .

The percentage of subjects reporting the occurrence of SAEs classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment from 30 days post last vaccination up to study end is presented by age strata in Table 8.211. During this period, no subjects were reported with SAEs with causal relationship to vaccination as per investigator assessment.

The percentage of subjects reporting SAEs classified by MedDRA Primary SOC and PT, from first vaccination up to study end is presented by age strata in Table 8.212.

The percentage of subjects reporting the occurrence of SAEs classified by MedDRA Primary SOC and PT with causal relationship to vaccination as per investigator assessment from first vaccination up to study end is presented by age strata in Table 8.213. During this period, no subjects were reported with SAEs with causal relationship to vaccination as per investigator assessment.

The number (\%) of subjects with at least one SAE reported from the first vaccination up to 30 -day post last vaccination, was 3 ( $9.7 \%$ ) and 13 (15.1\%) in the HZ/su group, and 2 ( $6.7 \%$ ) and 12 ( $14.1 \%$ ) in the Placebo group, for the $18-49$ YOA and $\geq 50$ YOA strata, respectively (Table 8.207).

The number (\%) of subjects with at least one SAE reported from 30-day post last vaccination up to study end, was $4(12.9 \%)$ and $26(30.2 \%)$ in the HZ/su group, and 7 ( $23.3 \%$ ) and $24(28.2 \%)$ in the Placebo group, for the $18-49$ YOA and $\geq 50$ YOA strata, respectively (Table 8.210).

The number (\%) of subjects with at least one SAE reported from first vaccination up to the study end, was 5 (16.1\%) and 31 (36.0\%) in the HZ/su group, and 9 (30.0\%) and 33 ( $38.8 \%$ ) in the Placebo group, for the $18-49$ YOA and $\geq 50$ YOA strata, respectively (Table 8.212).

### 8.4.5.2. TVC: Fatal events by age strata

The percentage of subjects with fatal outcome reported up to study end is presented by age strata in Table 8.215.

In the $18-49$ YOA stratum, $1(3.2 \%)$ fatalities in the $\mathrm{HZ} /$ su group and $2(6.7 \%)$ in the Placebo group, were reported up to the study end. In the $\geq 50$ YOA stratum, 11 (12.8\%) fatalities in the HZ/su group and 9 (10.6\%) in the Placebo group, were reported up to the study end (Table 8.215).

### 8.4.6. TVC: Adverse events leading to premature discontinuation of study vaccine and/or study by age strata

Up to the Month 2 visit (Visit 3), in the 18-49 YOA stratum, no subjects were withdrawn from the study due to an SAE or AE. In the $\geq 50 \mathrm{YOA}$ stratum, 3 subjects in the $\mathrm{HZ} / \mathrm{su}$ group and 2 subjects in the Placebo group were withdrawn from the study due to an SAE; no subjects were withdrawn from the study due to a non-serious AE (see Section 6.2.3, Table 6.6).

Up to the Month 13 visit (Visit 5), in the 18-49 YOA stratum, 1 subject in the HZ/su group and 2 subjects in the Placebo group were withdrawn from the study due to an SAE. In the $\geq 50 \mathrm{YOA}$ stratum, 12 subjects in the HZ/su group and 10 subjects in the Placebo group were withdrawn from the study due to an SAE; no subjects were withdrawn from the study due to a non-serious AE (see Section 6.2.3, Table 6.8).

Refer to Sections 6.2.1 and 8.2.6 for information regarding subjects withdrawn from vaccination due to an AE/SAE.

### 8.4.7. TVC: Adverse events of special interest by age strata

### 8.4.7.1. plMDs by age strata

Data are presented by age strata (18-49 YOA and $\geq 50 \mathrm{YOA}$ ) for subjects included in the TVC.

The global summary of pIMDs reported from the first vaccination up to 30 days post last vaccination is presented by age strata the in Table 8.214. The percentage of subjects reporting the occurrence of pIMDs classified by MedDRA Primary SOC and PT from first vaccination up to 30 days post last vaccination is presented by age strata in Table 8.204. During this period, no subjects with pIMDs were reported.

The percentage of subjects reporting the occurrence of pIMDs classified by MedDRA Primary SOC and PT from 30 days post last vaccination up to study end is presented by age strata in Table 8.205.

The number of subjects with at least one pIMD reported from 30 days post last vaccination up to study end, for both $18-49 \mathrm{YOA}$ and $\geq 50 \mathrm{YOA}$ strata, was $0(0.0 \%)$ in both $\mathrm{HZ} /$ su groups; and $0(0.0 \%)$ and $1(1.2 \%)$, respectively in the Placebo group (Table 8.205).

The percentage of subjects reporting the occurrence of pIMDs classified by MedDRA Primary SOC and PT from first vaccination up to study end is presented by age strata in Table 8.206.

The number of subjects with at least one pIMD event reported from first vaccination up to study end, for both 18-49 YOA and $\geq 50$ YOA strata, was $0(0.0 \%)$ in both $\mathrm{HZ} / \mathrm{su}$ groups; and $0(0.0 \%)$ and $1(1.2 \%)$, respectively in the Placebo group (Table 8.206).

### 8.4.8. Concomitant medications/vaccinations by age strata

Data are presented by age strata (18-49 YOA and $\geq 50 \mathrm{YOA}$ ) for subjects included in the TVC.

The incidence of concomitant medication use during the 30-day (Days 0-29) postvaccination period by dose and overall is presented by age strata in Table 8.216.

### 8.5. ATP cohort for safety: safety analysis, overall

To complement the analysis of safety, overall, on the TVC, an analysis of safety was also performed on the ATP cohort for Safety up to 30 days post last vaccination (active phase results) and the ATP cohort for Safety up to study end.

The results regarding the analysis of safety data overall, performed on the ATP cohort for safety (overall incidence of solicited and unsolicited symptoms, solicited symptoms, unsolicited AEs, SAEs, AE leading to withdrawal, pIMDs, concomitant medications/vaccinations) are presented from Table 8.40 to Table 8.90.

The results in the ATP cohort for safety were similar to that of the TVC.

### 8.6. ATP cohort for safety: safety analysis by PreChemo/OnChemo groups

To complement the analysis of safety in the PreChemo and OnChemo groups on the TVC, an analysis of safety was also performed on the ATP cohort for Safety up to 30 days post last vaccination (active phase results) and the ATP cohort for Safety up to study end.

The results regarding the analysis of safety data in the PreChemo and OnChemo groups, performed on the ATP cohort for safety (overall incidence of solicited and unsolicited symptoms, solicited symptoms, unsolicited AEs, SAEs, AE leading to withdrawal, pIMDs, concomitant medications/vaccinations) are presented from Table 8.133 to Table 8.174, and in Table 8.272.

The results in the ATP cohort for safety were similar to that of the TVC.

### 8.7. ATP cohort for safety: safety analysis by age strata

To complement the analysis of safety by age strata, on the TVC, an analysis of safety was also performed on the ATP cohort for Safety up to 30 days post last vaccination (active phase results) and the ATP cohort for Safety up to study end.

The results regarding the analysis of safety data by age strata, performed on the ATP cohort for safety (overall incidence of solicited and unsolicited symptoms, solicited symptoms, unsolicited AEs, SAEs, AE leading to withdrawal, pIMDs, concomitant medications/vaccinations) are presented from Table 8.217 to Table 8.258.

The results in the ATP cohort for safety were similar to that of the TVC.

### 8.8. Pregnancy

No subject became pregnant.

### 8.9. Important safety information received after the data lock point (database freeze date)

No relevant additional safety information was available after the data lock point.

### 8.10. Safety summary

The primary analysis for safety was based on the TVC.
A descriptive summary of safety data obtained at end of study analysis for the TVC is provided in this section. No safety concern was identified.

## All subjects

Results obtained for all subjects included in the TVC are presented. A total of $90.5 \%$ of subjects in the TVC received the second dose.

## Solicited symptoms

A higher percentage of subjects reported solicited local and general AEs (any grade, grade 3) during the 7 -day post-vaccination period in the HZ/su group compared to the Placebo group. In the HZ/su group, the most frequent solicited local symptom observed was pain; the most frequent solicited general symptom was fatigue, followed by myalgia. In the Placebo group, the percentage of subjects with general symptoms was also high. Of note, the HZ/su and placebo subjects in this study had an an underlying disease and were to receive/ received chemotherapy. Note that the following data will be "overall per subject (dose 1 and dose considered)" unless otherwise indicated.

- Any AE during the 7-day (Days 0-6) post-vaccination period:
- At least one solicited or unsolicited AE (local or general) (any grade) was reported for $93.2 \%$ and $80.0 \%$ of subjects in the HZ/su and Placebo group, respectively.
- At least one local AE (solicited or unsolicited) was reported for $80.3 \%$ and $7.8 \%$ of subjects in the HZ/su and Placebo group, respectively. At least one general AE (solicited or unsolicited) was reported for $84.6 \%$ and $80.0 \%$ of subjects in the HZ/su and Placebo group, respectively.
- $\quad$ Solicited local symptoms during the 7-day (Days 0-6) post-vaccination period:
- At least one solicited local symptom was reported for $83.9 \%$ and $6.4 \%$ of subjects in the HZ/su and Placebo group, respectively. The most frequently reported solicited local symptom in the HZ/zu group was pain (any grade: 80.4\% in the HZ/su group versus $6.4 \%$ in the Placebo group).

After dose 1 and dose 2, respectively, at least one solicited local symptom was reported for $78.6 \%$ and $57.1 \%$ of subjects in the $\mathrm{HZ} /$ su group, and for $2.7 \%$ and $4.8 \%$ of subjects in the Placebo group.

- At least one grade 3 solicited local symptom was reported for $11.6 \%$ and $0.0 \%$ of subjects in the HZ/su and Placebo group, respectively. Grade 3 pain was reported for $9.8 \%$ and $0.0 \%$ of subjects in the $\mathrm{HZ} /$ su group and Placebo group, respectively.
After dose 1 and dose 2, respectively, at least one grade 3 solicited local symptom was reported for $8.9 \%$ and $4.1 \%$ of subjects in the HZ/su group, and for none of the subjects in the Placebo group.
- $\quad$ Solicited general symptoms during the 7-day (Days 0-6) post-vaccination period:
- At least one solicited general symptom was reported for $81.3 \%$ and $66.4 \%$ of subjects in the HZ/su and Placebo group, respectively. The most frequently reported solicited general symptoms in the HZ/su group was fatigue (any grade, overall/subject: $69.6 \%$ in HZ/su group versus $61.8 \%$ in Placebo group) and myalgia (any grade: $53.6 \%$ in HZ/su group versus $28.2 \%$ in Placebo group). Fatigue assessed by the investigator as related to vaccination, was reported for $17.0 \%$ and $12.7 \%$ of subjects in the HZ/su group and Placebo group, respectively. Myalgia assessed by the investigator as related to vaccination was reported for $26.8 \%$ and $4.5 \%$ of subjects in the HZ/su group and the Placebo group, respectively.

After dose 1 and dose 2, respectively, at least one solicited general symptom was reported for $71.4 \%$ and $69.1 \%$ of subjects in the HZ/su group, and for $47.3 \%$ and $57.7 \%$ of subjects in the Placebo group.

- At least one grade 3 solicited general symptom was reported for $22.3 \%$ and $15.5 \%$ of subjects in the HZ/su and Placebo group, respectively. Grade 3 fatigue was reported for $14.3 \%$ and $7.3 \%$ of subjects in the HZ/su group and Placebo group, respectively. Grade 3 myalgia was reported for $10.7 \%$ and $3.6 \%$ of subjects in the HZ/su group and the Placebo group, respectively. Grade 3 fatigue assessed by the investigator as related to vaccination, was reported for $2.7 \%$ and $0.9 \%$ of subjects in the $\mathrm{HZ} /$ su group and Placebo group, respectively. Grade 3 myalgia assessed by the investigator as related to vaccination was reported for $6.3 \%$ and $0.0 \%$ of subjects in the HZ/su group and the Placebo group, respectively. It is noted that grade 3 shivering assessed by the investigator as related to vaccination was reported for $3.6 \%$ and $0.0 \%$ in the $\mathrm{HZ} / \mathrm{su}$ and Placebo group, respectively.
After dose 1 and dose 2, respectively, at least one grade 3 solicited general symptom was reported for $13.4 \%$ and $16.5 \%$ of subjects in the HZ/su group, and for $10.0 \%$ and $9.6 \%$ of subjects in the Placebo group.


## Unsolicited AEs

Numbers and percentages of subjects with unsolicited AEs were overall balanced between between HZ/su and Placebo groups.

- Unsolicited AEs during the 30-day (Days 0-29) post-vaccination period:
- Overall, 100 ( $85.5 \%$ ) subjects in the HZ/su group and 103 ( $89.6 \%$ ) subjects in the Placebo group reported at least one unsolicited AE. Overall per subject, the most frequent unsolicited AEs within 30 days post vaccination were nausea (31 subjects or $26.5 \%$ ) and asthenia ( 30 subjects or $25.6 \%$ ) for the HZ/su group, and also nausea and asthenia (both at 28 subjects or $24.3 \%$ ) for the Placebo group.
- Overall, 18 ( $15.4 \%$ ) subjects in the HZ/su group and 15 (13.0\%) subjects in the Placebo group reported at least one grade 3 unsolicited AE. Overall per subject, the most frequent grade 3 unsolicited AEs within 30 days post vaccination were febrile neutropenia ( 4 subjects or $3.4 \%$ ) and neutropenia ( 3 subjects or $2.6 \%$ ) for the HZ/su group, and neutropenia ( 3 subjects or $2.6 \%$ ), febrile neutropenia ( 2 subjects or $1.7 \%$ ) and acute kidney injury ( 2 subjects or $1.7 \%$ ) for the Placebo group.
- Overall, 10 ( $8.5 \%$ ) subjects in the HZ/su group and 9 (7.8\%) subjects in the Placebo group reported at least one unsolicited AE with causal relationship to vaccination as per investigator assessment.
- Overall, there was 1 subject ( $0.9 \%$ ) in the HZ/su group with at least one grade 3 unsolicited AE with causal relationship to vaccination as per investigator assessment; the unsolicited AE reported was gastroenteritis. There were no subjects in the Placebo group with at least one grade 3 unsolicited AE with causal relationship to vaccination as per investigator assessment.
- Overall, 31 (26.5\%) subjects in the HZ/su group and 33 (28.7\%) subjects in the Placebo group reported at least one unsolicited AE with medically attended visit.


## SAEs, (S)AEs leading to withdrawal, pIMDs

Numbers and percentages of subjects with fatalities, SAEs, (S)AEs leading to withdrawal from study and pIMDs were overall balanced between HZ/su and Placebo group.

- SAEs:
- From the first vaccination up to study end, the number (\%) of subjects with fatal outcome reported was $12(10.3 \%)$ in the $\mathrm{HZ} /$ su group and $11(9.6 \%)$ in the Placebo group. None of the fatalities were considered causally related to vaccination as per investigator assessment.
- From the first vaccination up to 30 days post last vaccination, the number (\%) of subjects with at least one SAE reported was 16 (13.7\%) in the HZ/su group and $14(12.2 \%)$ in the Placebo group. From 30 days post last vaccination up to study end, the number (\%) of subjects with at least one SAE reported was 30 ( $25.6 \%$ ) in the $\mathrm{HZ} /$ su group and $31(27.0 \%)$ in the Placebo group. From first vaccination up to study end, the number (\%) of subjects with at least one SAE reported was $36(30.8 \%)$ in the $\mathrm{HZ} /$ su group and 42 (36.5\%) in the Placebo group. During the study, no subjects were reported with SAEs with causal relationship to vaccination as per investigator assessment.
- SAEs, AEs leading to withdrawal:
- Up to the Month 2 visit (Visit 3), 3 subjects in the HZ/su group and 2 subjects in the Placebo group were withdrawn from the study due to an SAE, no subjects were withdrawn from the study due to a non-serious AE.
- Up to study end, 13 subjects in the HZ/su group and 12 subjects in the Placebo group were withdrawn from the study due to an SAE, of which 12 and 11 subjects respectively were withdrawn due to fatalities. No subjects were withdrawn from the study due to a non-serious AE.
- pIMDs:
- From first vaccination up to 30 days post last vaccination, no subjects with pIMDs were reported.
- From 30 days post last vaccination up to study end, and from first vaccination up to study end, there was 1 pIMD (autoimmune thyroiditis), considered as serious per investigator assessment, in a subject from the Placebo group.


## Pregnancies:

- No pregnancies were reported.


## Subjects in the PreChemo and OnChemo groups

Results were obtained for subjects included in the PreChemo and OnChemo groups, respectively. It is noted that the results obtained for the OnChemo group represent data from a relatively small number of subjects compared to the PreChemo group (according to the stratification ratio PreChemo:OnChemo 4:1).

## Solicited symptoms

Results regarding solicited local symptoms (any grade, grade 3) reported during the 7-day (Days $0-6$ ) post-vaccination period in the PreChemo and OnChemo groups were generally consistent with the results obtained for all subjects.

Results regarding solicited general symptoms (any grade, grade 3) in the PreChemo and OnChemo groups were generally consistent with the results obtained for all subjects.

## Unsolicited AEs

Results regarding unsolicited AEs reported during the 30-day (Days 0-29) postvaccination period in the PreChemo and OnChemo groups were generally consistent with the results obtained for all subjects.

SAEs, (S)AEs leading to withdrawal, pIMDs
Results regarding SAEs and(S)AEs leading to withdrawal in the PreChemo and OnChemo groups reported during the study were generally consistent with the results obtained for all subjects. One pIMD, assessed as serious by investigator, occurred in a Placebo OnChemo subject.

## Subjects in the 18-49 YOA and $\geq 50$ YOA strata

Results were obtained for subjects included in the $18-49 \mathrm{YOA}$ and $\geq 50 \mathrm{YOA}$ strata, respectively. It is noted that the results obtained for the 18-49 YOA stratum represent data from a relatively small number of subjects compared to the $\geq 50 \mathrm{YOA}$ stratum.

## Solicited symptoms

Results regarding solicited local symptoms (any grade, grade 3) reported during the 7-day (Days $0-6$ ) post-vaccination period in the $18-49$ YOA and $\geq 50$ YOA strata were generally consistent with results obtained for all subjects.

Results regarding solicited general symptoms (any grade, grade 3) in the 18-49 YOA and $\geq 50$ YOA strata were generally consistent with results obtained for all subjects.

## Unsolicited AEs

Results regarding unsolicited AEs reported during the 30-day (Days 0-29) postvaccination period in the $18-49$ YOA and $\geq 50$ YOA strata were generally consistent with results obtained for all subjects.

SAEs, (S)AEs leading to withdrawal, pIMDs
Results regarding SAEs and (S)AEs leading to withdrawal in the 18-49 YOA and $\geq 50$ YOA strata reported during the study were generally consistent with results obtained for all subjects. One pIMD, assessed as serious by investigator, occurred in a Placebo OnChemo subject in the $\geq 50 \mathrm{YOA}$ stratum.

## CONFIDENTIAL

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## 9. OVERALL CONCLUSIONS

This study in subjects with solid tumours receiving/to receive chemotherapy evaluated the $\mathrm{HZ} / \mathrm{su}$ vaccine in terms of immunogenicity and safety.

## Immunogenicity

The focus of the study was to examine the immunological response to HZ/su given in different immunisation schedules to subjects receiving/to receive chemotherapy which would compromise their immune systems. The confirmatory immunogenicity objectives were assessed sequentially in order of ascending rank until an objective was not met. The confirmatory objectives were assessed at the first analysis step. The active phase results on CMI were different at end of study analysis compared to first analysis. Even so, there was no impact on study conclusions.

- The confirmatory primary objective of the study was met as the lower limit of the $95 \%$ CI of the GM ratio (HZ/su PreChemo Group over Placebo PreChemo group) in anti-gE Ab concentrations at Month 2 (post second vaccination) was 17.9. Therefore, the success criterion (greater than 3) was demonstrated. The adjusted GM ratio was 23.2 ( $95 \% \mathrm{CI}: 17.9-30.0 ; \mathrm{P}<0.0001$ ).
- The first confirmatory secondary objective of the study was met as the lower limit of the $95 \%$ CI of the VRR for anti-gE Ab concentrations in the HZ/su PreChemo group at Month 2 (post second vaccination) was $85.0 \%$. Therefore, the success criterion (at least $60 \%$ ) was demonstrated. The VRR was $93.8 \%$ ( $95 \%$ CI: $85.0-98.3$ ).
- The second confirmatory secondary objective of the study was met as the lower limit of the $95 \%$ CI of the GM ratio (HZ/su PreChemo group over Placebo PreChemo group) in gE-specific CD4[2+] T-cell frequencies (3.79) at Month 2 (post second vaccination) was 3.79. Therefore, the success criterion (greater than 1) was demonstrated. The observed GM ratio was 13.67 ( $95 \% \mathrm{CI}: 3.79-49.38 ; \mathrm{P}=0.0002$ ).

Descriptive results obtained with the end of study analysis: the observed GM ratio at Month 2 was 9.94 ( $95 \%$ CI: 3.63 -27.19).

- The third confirmatory secondary objective of the study was not met as the lower limit of the $95 \%$ CI of the VRR for gE-specific CD4[2+] T-cell frequencies in the $\mathrm{HZ} /$ su PreChemo group ( $33.5 \%$ ) at Month 2 (post second vaccination) was $33.5 \%$. Therefore, the success criterion (at least 50\%) was not demonstrated. The observed VRR was 57.9\% (95\% CI: 33.5 - 79.7).
Descriptive results obtained with the end of study analysis: the observed VRR at Month 2 was 50.0\% (95\% CI: 28.2 - 71.8).
Results from descriptive analyses showed in HZ/su subjects (overall, and in the PreChemo and OnChemo groups) humoral immune responses 1 month post first vaccination and 1 month post second vaccination. Persistence of 12 months post second vaccination humoral response was also observed.

Results from descriptive analyses in the PreChemo group showed that CMI responses to $\mathrm{HZ} /$ su were above the pre-vaccination level 1 month post first vaccination; a stronger immune response was observed 1 month post second vaccination. Additionally, the persistence of gE-specific CMI at 1 year post second vaccination in PreChemo HZ/su subjects was observed.

## Safety

Results from descriptive analyses did not reveal a safety concern.
In subjects with solid tumours receiving chemotherapy, a higher percentage of subjects reported solicited local and general AEs (any grade, grade 3) during the 7-day postvaccination period in the HZ/su group compared to the Placebo group. In the Placebo group, the percentage of subjects with solicited general symptoms was also high. Numbers and percentages of subjects with unsolicited AEs reported during the 30-day post-vaccination period and numbers and percentages of subjects with respectively fatalities, SAEs and (S)AEs leading to study withdrawal reported during the study were generally well balanced between HZ/su and Placebo group. During the study, no subjects were reported with SAEs with causal relationship to vaccination as per investigator assessment. There was 1 pIMD , considered as serious per investigator assessment, in a subject from the Placebo group.

Reactogenicity and safety results obtained for the PreChemo and OnChemo groups and for the $18-49$ YOA and $\geq 50$ YOA strata were generally consistent with the overall results for all subjects in this study.

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## 11. STUDY REPORT AUTHORS /CONTRIBUTING AUTHORS

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## 12. SERIOUS ADVERSE EVENTS / OTHER SIGNIFICANT ADVERSE EVENTS / PREGNANCY

There were no pregnancies reported in the study.

### 12.1. SAE Listing

The listing of all SAEs for the TVC is presented in Table 8.271.
The listing of all SAEs for the ATP cohort for safety up to study end is presented in Table 8.274 .

## 12.2. plMDs listing

The details of potential immune-mediated disorders (pIMDs) reported as identified by predefined list of preferred terms and/or by investigator assessment up to study end are presented for the TVC respectively in Table 8.270.

The details of potential immune-mediated disorders (pIMDs) reported as identified by predefined list of preferred terms and/or by investigator assessment up to study end are presented for the ATP cohort for safety up to study end are presented in Table 8.273.

### 12.3. Clinical narratives for SAEs (including serious pIMDs)

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B, Oxaliplatin, Fluorouracil
Serious Events: Febrile neutropenia, Clostridium difficile infection, Mucosal inflammation, Diarrhoea, Hypokalaemia, Hyponatraemia

Narrative: This 68 -year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 1st dose of Herpes zoster vs Placebo (intramuscular) on 12th February 2014, for prophylaxis.

Co-suspect products included OXALIPLATIN for adenocarcinoma of colon and fluorouracil unknown for adenocarcinoma of colon.

Concurrent medical conditions included adenocarcinoma of colon and dihydropyrimidine dehydrogenase deficiency. Concomitant products included omeprazole (Omeprazol), metoclopramide (Primperan (Metoclopramide)), insulin human, fentanyl, mepivacaine, paracetamol and omeprazole.

On PPD 33 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 mucositis. Serious criteria included hospitalization. Additional event(s) included severe - grade 3 diarrhea on 17th March 2014 with serious criteria of hospitalization, severe - grade 3 febrile neutropenia on 23rd March 2014 with serious criteria of hospitalization, GSK medically significant and life threatening, severe - grade 3 clostridium difficile infection on 23 rd March 2014 with serious criteria of hospitalization and GSK medically significant, severe - grade 3 hypokalemia on 23rd March 2014 with serious criteria of hospitalization and severe - grade 3 hyponatremia on 23rd March 2014 with serious criteria of hospitalization. The subject was treated with filgrastim, cilastatin + imipenem (Imipenem + Cilastatin), ciprofloxacin, nystatin (Mycostatin) and metronidazole (Flagyl (Metronidazole)). Herpes zoster vs Placebo was interrupted (Dechallenge was positive). Rechallenge with Herpes zoster vs Placebo was unknown. The outcome of mucositis was recovered/resolved on 8th April 2014. The outcome(s) of the additional event(s) included febrile neutropenia (recovered/resolved on 25th March 2014), diarrhea (recovered/resolved on 3rd April 2014), hypokalemia (recovered/resolved on 4th April 2014), hyponatremia (recovered/resolved on 4th April 2014) and clostridium difficile infection (recovered/resolved on 7th April 2014).

The investigator considered that there was no reasonable possibility that the mucositis, diarrhea, febrile neutropenia, clostridium difficile infection, hypokalemia and hyponatremia may have been caused by Herpes zoster vs Placebo. Other possible cause(s) of the mucositis included concurrent medication. Other possible cause(s) of the febrile neutropenia included concurrent medication.

Relevant Tests: ANALYTICAL TEST MICROBIOLOGICAL ON 1/ABR/2014: POSITIVE TO ANTIGEN AND TOXIN A AND B OF CLOSTRIDIUM DIFFICILE BY

## Confidential

## Unblinded Report - With Suspect Products and Serious Events

INMUNOCHROMATOGRAPHIC TECHNIQUES Diagnostic results (unless otherwise stated, normal values were not provided): On 23rd March 2014, Blood potassium result was $2.6 \mathrm{mmol} / \mathrm{L}$ (normal low: 3.5, normal high: 5.5), Blood sodium result was $129 \mathrm{mmol} / \mathrm{L}$ (normal low: 132, normal high: 146), Neutrophil count result was 14.6 \% (normal low: 40, normal high: 75), Neutrophil count result was $400 / \mathrm{mm} 3$, SODIUM result was $129 \mathrm{mmol} / \mathrm{L}$ (normal low: 132, normal high: 146) and White blood cell count result was $2520 / \mathrm{mm} 3$ (normal low: 3500, normal high: 11000). On 25th March 2014, Blood potassium result was $3.6 \mathrm{mmol} / \mathrm{L}$ (normal low: 3.5, normal high: 5.5), Blood sodium result was $136 \mathrm{mmol} / \mathrm{L}$ (normal low: 132, normal high: 146), Neutrophil count result was 25.0 \% (normal low: 40, normal high: 75), Neutrophil count result was $1700 / \mathrm{mm} 3$, SODIUM result was $136 \mathrm{mmol} / \mathrm{L}$ (normal low: 132, normal high: 146) and White blood cell count result was $6640 / \mathrm{mm} 3$ (normal low: 3500, normal high: 11000). On 28th March 2014, Blood potassium result was $3.8 \mathrm{mmol} / \mathrm{L}$ (normal low: 3.5, normal high: 5.5) and Neutrophil count result was $7.3 \times 10 \mathrm{e} 3 / \mathrm{mcL}$. On an unknown date, Body temperature result was 38.5 C .

Investigator comments:
The 23/MAR/2014 The patient was admitted to the emergency department because of vomiting, and diarrhea ( 6 times/day) since a week ago and fever (Max 38.5 C) in this day ,being subjected to hematology test (among others) that led to the diagnosis of febrile neutropenia grade IV. (It's clinically confirmed that his life was threatened due a Febrile Neutropenia IV grade").Also, with mild adominal pain , Hypokalemia and Hyponatremia and ileitis symptoms.
He is treated with antibiotics and G-CSF. He is still hospitalized on 25/MAR/2014. He was transferred to regular floor at 20:14 of the day 24/MAR/2014.

All the adverse events was : Diarrhea grade III, Mucositis grade III, Hyponatremia grade III, Hypopotassemia grade III and Febrile Neutropenia grade IV ( Diarrhea and Mucositis since 17/Mar/2014 ) All ( unless, the Clostridium infection, and the Hyponatremia and Hypopotassemia that was related to diarrhea) are secundary effect both, Oxaliplatin and 5-FU.

The patient has a deficiency of the enzyme dihydropyrimidine dehydrogenase (DPD) This is the reason why the patient has high toxicity to the Flouroracilo (mainly) and the oxaliplatin

- End of Febrile Neutropenia diagnosis : 25 / MAR / 2014
- The patient was isolated on 1 / APR / 2014 because a diagnosed infection of Clostridium Difficile.
- End of Diarrhea diagnosis : 3 / APR / 2014
- End of Hyponatremia and Hypokalemia diagnosis : 4 / ABR / 2014
- The isolate was removed on 7 / APR / 2014 because the health improvement, - End of the infection of Clostridium
- End of Mucositis grade III : 8 / APR / 2014.

Hospital discharge for heath improvement performed on 9/APR/2014.
Prescribed medication at discharge : MEPIVACAINA, CIFLOXACINE , PARACETAMOL if Dysphagia , and METRONIDAZOL

Other possible cause(s) of the febrile neutropenia and mucositis included and concurrent medication Oxaliplatin and Fluorouracil started on 12 February 2014, 39 days before febrile neutropenia and 28 days before mucositis.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study

## Confidential Unblinded Report - With Suspect Products and Serious Events

Unblinding date is 10 Feb17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Diarrhoea, Clostridium difficile infection, Malnutrition
Narrative: This 68 -year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 1st dose of Herpes zoster vs Placebo (intramuscular) on 12th February 2014, for prophylaxis.

Concurrent medical conditions included adenocarcinoma of colon and dihydropyrimidine dehydrogenase deficiency. Concomitant products included METOCLOPRAMIDE (PRIMPERAM), PARACETAMOL, ENOXAPARIN (CLEXANE), METAMIZOLE, DEXAMETHASONE (FORTECORTIN (DEXAMETASONA)), HUMAN BIOSYNTHETIC INSULIN (HUMULIN REGULAR INSULIN), BENZOXONIUM CHLORIDE, HYDROCORTISONE, TYROTHRICIN (COHORTAN), OMEPRAZOLE (OMEPRAZOL) and ALBUMIN NORMAL HUMAN SERUM (ALBUMIN HUMAN).

On PPD $\quad 66$ days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 diarrhea. Serious criteria included hospitalization. Additional event(s) included severe - grade 3 clostridium difficile infection on 29th April 2014 with serious criteria of hospitalization and GSK medically significant and severe - grade 3 malnutrition on 14th May 2014 with serious criteria of hospitalization. The subject was treated with CIPROFLOXACIN, METRONIDAZOLE (FLAGYL (METRONIDAZOLE)), POTASSIUM CHLORIDE, LEVOFLOXACIN, RIFAXIMIN, VANCOMYCIN, AMINO ACIDS NOS, CARBOHYDRATES, ELECTROLYTES NOS (ISOPLASMAL G), AMINO ACIDS NOS, CARBOHYDRATES, ELECTROLYTES NOS, FAT EMULSIONS (OLICLINOMEL), PROTEINS NOS (PROTEIN) and NUTRITIONAL SUPPLEMENT NOS (FRESUBIN). Herpes zoster vs Placebo was discontinued (Dechallenge was negative). The outcome of diarrhea was recovered/resolved on 20th May 2014. The outcome(s) of the additional event(s) included clostridium difficile infection (recovered/resolved on 20th May 2014) and malnutrition (recovered/resolved on 27th May 2014).

The investigator considered that there was no reasonable possibility that the diarrhea, clostridium difficile infection and malnutrition may have been caused by Herpes zoster vs Placebo.

Relevant Tests: 29/APR/2014 MICROBIOLOGY TEST (CDI TOXIN):
Toxin Clostridium difficile: POSITIVE
Antigen detection by immunochromatography: POSITIVE
Toxin detection by immunochromatography : POSITIVE
Toxin detection by PCR : POSITIVE

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

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13/MAY/2014 MICROBIOLOGY TEST (CDI TOXIN) :
Difficile Clostridium Detection:
Antigen detection: POSITIVE
Toxin detection: POSITIVE
Detection of Clostridium difficile Toxin B by PCR: POSITIVE.
20/MAY/2014 MICROBIOLOGY TEST (CDI TOXIN) :
Clostridium difficile toxin: NEGATIVE
22/MAY/2014 MICROBIOLOGY TEST (CDI TOXIN) :
Clostridium difficile toxin: NEGATIVE
23/MAY/2014 MICROBIOLOGY TEST (CDI TOXIN) :
Clostridium difficile toxin: NEGATIVE
Investigator Comments:
The 28/APR/2014 the patient comes to the emergency room due to diarrhea, nausea and abdominal pain
(related to Leukocytosis and Clostridium difficile infection). Only the Diarrhea and the infection was
severe. Patient was with diarrhea since 19apr2014.
He is hospitalized on 29/APR/2014.
Clostridium difficile infection is detected on 29/APR/2014
The patient was treated for a very severe protein malnutrition from 14/MAY/2014 (first evidence of protein
malnutrition)
End of Clostridium difficile infection on 20/MAY/2014
End of Diarrhea condition on 20/MAY/2014
End of hospital treatment for protein malnutrition on 27/MAY/2014
The patient was discharged on 27/MAY/2014 with a good clinical evolution.
Aditional important information (follow up)
The 13/JUN/2014 was proposed the possibility of patient withdrawal from the study because of their past
clinical status
but having greatly improved the clinical condition of the patient, and with its active willingness to continue
in the present study, it was decided to keep in the study.
On the other hand, the administration of the second dose of the vaccine will be definitely not administered
by medical decision.
Case unblinded due to end of study
Unblinding date is 10Feb17
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Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Device related sepsis, Bacteraemia
Narrative: This 76-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised,

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observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 1st dose of Herpes zoster vs Placebo (intramuscular) on 27th May 2013, for prophylaxis.

Concomitant products included paracetamol.
On PPD 51 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 central line sepsis. Serious criteria included hospitalization and GSK medically significant. Additional event(s) included severe - grade 3 bacteremia on 17th July 2013 with serious criteria of hospitalization and GSK medically significant. The subject was treated with vancomycin, cloxacillin, ENOXAPARIN (CLEXANE), PARACETAMOL, amoxicillin, clavulanate potassium (Augmentine) and meropenem. Herpes zoster vs Placebo was interrupted. The outcome of central line sepsis was recovered/resolved on 29th July 2013. The outcome(s) of the additional event(s) included bacteremia (recovered/resolved on 29th July 2013).

The investigator considered that there was no reasonable possibility that the central line sepsis and bacteremia may have been caused by Herpes zoster vs Placebo.

Relevant Tests: X-ray, blood sample, ECG, urine and blood cultives. Staphylococcus aureus found Diagnostic results (unless otherwise stated, normal values were not provided): On 19th July 2013, Blood creatine result was $1.37 \mathrm{mg} / \mathrm{dL}$ (normal low: 0. , normal high: 1.3 ), C-reactive protein result was $22.3 \mathrm{mg} / \mathrm{L}$ (normal low: 0, normal high: 5), Haemoglobin result was $11.6 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5), Lymphocyte count result was $0.76 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1, normal high: 3.5), Neutrophil count result was $4.77 \times 10 \mathrm{e} 9 / \mathrm{L}$ (normal low: 1.7 , normal high: 7.5 ) and Red blood cell count result was $3.6 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4.6, normal high: 5.7). On 21st July 2013, Blood creatine result was $1.44 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6 , normal high: 1.3), C-reactive protein result was $48.1 \mathrm{mg} / \mathrm{L}$ (normal low: 0, normal high: 5), Creatinine renal clearance result was $47.69 \mathrm{ml} / \mathrm{min}$ (normal low: 65, normal high: 150), Haematocrit result was 36.2 \% (normal low: 40, normal high: 54), Haemoglobin result was $12.6 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5), Lymphocyte count result was $0.69 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1, normal high: 3.5), Mean platelet volume result was 6.4 fL (normal low: 7.5 , normal high: 11), Monocyte count result was 20.7 \% (normal low: 4, normal high: 12), Neutrophil count result was $1.51 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5) and Red blood cell count result was $3.87 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4.6, normal high: 5.7). On 23rd July 2013, Blood calcium result was $8 \mathrm{mg} / \mathrm{dL}$ (normal low: 8.7, normal high: 10.3), Blood creatine result was $1.09 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6 , normal high: 1.3), C-reactive protein result was $10.2 \mathrm{mg} / \mathrm{L}$ (normal low: 0 , normal high: 5), Creatinine renal clearance result was $65.77 \mathrm{ml} / \mathrm{min}$ (normal low: 65, normal high: 150), Haematocrit result was 33.7 \% (normal low: 40, normal high: 54), Haemoglobin result was $11.7 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5), Lymphocyte count result was $1,42 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1, normal high: 3.5), Mean platelet volume result was 6.16 fL (normal low: 7.5, normal high: 11), Neutrophil count result was $1.34 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5 ), Red blood cell count result was 3.64 x10E6/mcL (normal low: 4.6, normal high: 5.7) and White blood cell count result was 3.87 x10e3/mcL (normal low: 4, normal high: 11). On 24th July 2013, Blood calcium result was $8.5 \mathrm{mg} / \mathrm{dL}$ (normal low: 8.7, normal high: 10.3), Blood creatine result was $1.31 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6 , normal high: 1.3), Creatinine renal clearance result was $53.19 \mathrm{ml} / \mathrm{min}$ (normal low: 65, normal high: 150), Haematocrit result was 33.9 \% (normal low: 40, normal high: 54), Haemoglobin result was $11.6 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5 ) and Red blood cell count result was 3.68 x10E6/mcL (normal low: 4.6, normal high: 5.7). On 25th July 2013, Blood creatine result was $1.41 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6, normal high: 1.3), Creatinine renal clearance result was $48.86 \mathrm{ml} / \mathrm{min}$ (normal low: 65, normal high: 150), Haematocrit result was 33.7 \% (normal low: 40, normal high: 54), Haemoglobin result was $11.4 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5),

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Lymphocyte count result was $3.88 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1, normal high: 3.5), Mean platelet volume result was 6.07 fL (normal low: 7.5 , normal high: 11) and Monocyte count result was $1.18 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 0.2, normal high: 1). On 25th July 2013, Red blood cell count result was $3.64 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4.6, normal high: 5.7). On 26th July 2013, Haematocrit result was 35 \% (normal low: 40, normal high: 54), Haemoglobin result was $12.2 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5), Monocyte count result was $1.62 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 0.2 , normal high: 1 ), Neutrophil count result was $3.2 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5), Platelet count result was $492 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 140, normal high: 450) and Red blood cell count result was $3.79 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4.6, normal high: 5.7). On 29th July 2013, Blood creatine result was $1.2 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6, normal high: 1.3), Creatinine renal clearance result was $58.86 \mathrm{ml} / \mathrm{min}$ (normal low: 65, normal high: 150), Haematocrit result was 37.9 \% (normal low: 40, normal high: 54), Haemoglobin result was $12.8 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5), Neutrophil count result was 45,2 \% (normal low: 40, normal high: 60), Platelet count result was 487 x10e3/mcL (normal low: 140, normal high: 450), Red blood cell count result was $4.04 \times 10 E 6 / \mathrm{mcL}$ (normal low: 4.6, normal high: 5.7) and White blood cell count result was $7.97 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11). On 5th August 2013, Blood lactate dehydrogenase result was 268 u/L (normal low: 140, normal high: 240), Blood urea result was $74 \mathrm{mg} / \mathrm{dL}$ (normal low: 15, normal high: 45), Blood urea result was 34.5 $\mathrm{mg} / \mathrm{dL}$ (normal low: 7, normal high: 21), Haematocrit result was 38.9 \% (normal low: 36, normal high: 48), Haemoglobin result was $13.1 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 18), Platelet count result was 278 x10e3/mcL (normal low: 140, normal high: 450), Protein total result was $8.8 \mathrm{~g} / \mathrm{dL}$ (normal low: 6.4, normal high: 8.3), Red blood cell count result was $4.16 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4.60, normal high: 5.70 ) and White blood cell count result was $8.05 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11).

Investigator Comments:
Patient came from other hospital were antibiotic treatment was initiated with Vancomicine + Meropenem past July 18th.
Patient came to hospital ( ER) after 12 hours with fever (38 celsius) and chills on 19-Jul-2013. Patient refers that past July 17th presented pain and erytema on central line catheter. On July 18th presented fever
This was related to a sistemic infection due to his central line catheter and was hospitalized past July 19th A blood culture was done showing Staphylococcus aureus. Thrombosis related to catheter was excluded, therefore catheter tip was removed and $S$. aureus was also detected here.
The final diagnosis was Septicemia by S. aureus on Central line catheter, also with a secondary bacteriemia. None of these events were related to investigational product.
24Jul2013:No incidentes, asymptomatic
Antibiotic treatment facilitates the recovery of the patient showing a good progression, fever disappears. Subject refers a clinical stable situation and was discharged with an excellent general condition on 29-Jul-2013.

Case unblinded due to end of study
Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Suspect Products: Vaccine placebo<br>Serious Events: Neutropenia, Anaemia, Respiratory tract infection, Thrombocytopenia


#### Abstract

Narrative: This 69-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 22nd July 2013, for prophylaxis.


Concomitant products included radium, metoclopramide (Primperan), pantoprazole (Pantoprazol), tranexamic acid and furosemide.

On PPD 259 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 neutropenia. Serious criteria included death, hospitalization and GSK medically significant. Additional event(s) included severe - grade 3 anemia on 7th April 2014 with serious criteria of death and hospitalization, severe - grade 3 respiratory infection on 7th April 2014 with serious criteria of death, hospitalization and GSK medically significant and moderate - grade 2 thrombocytopenia on 7th April 2014 with serious criteria of death and hospitalization. The subject was treated with blood transfusion, auxiliary products (Blood Concentrate), filgrastim (Neupogen), meropenem, morphine, hydrocortisone sodium phosphate (Actocortina), midazolam, ipratropium bromide (Atrovent) and dexamethasone. The outcome of neutropenia was fatal on PPD 2014. The outcome(s) of the additional event(s) included anemia (fatal on PPD 2014), respiratory infection (fatal on PPD 2014) and thrombocytopenia (fatal on PPD PPD 2014). The subject died on PPD 2014. The reported cause of death was dyspnea, neutropenia, anemia and pneumonia. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the neutropenia, anemia, respiratory infection and thrombocytopenia may have been caused by Herpes zoster vs Placebo.

Relevant Tests: Angio-CT performed on 08Apr2014 showed a left opacity with air bronchogram that confirmed a respiratory infection. Diagnostic results (unless otherwise stated, normal values were not provided): On 7th April 2014, Haemoglobin result was $9.9 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 18), Neutrophil count result was $0.93 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5) and Platelet count result was $91 \times 10 e 3 / \mathrm{mcL}$ (normal low: 140, normal high: 450). On 8th April 2014, Haemoglobin result was 7.7 g/dL (normal low: 13, normal high: 17.5), Neutrophil count result was $0.15 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5 ) and Platelet count result was $72 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 140, normal high: 450). On 9th April 2014, Haemoglobin result was $10.9 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5), Neutrophil count result was $0.29 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5 ) and Platelet count result was $59 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 140, normal high: 450).

Investigator Comments:
On 7th April 2014, patient attended to Emergency Room referring cough with hemoptysis (starting the symptons on the same day). A few hours later it is diagnosed a severe (grade IV) respiratory infection secondary to a grade IV neutropenia, reason for which patient is hospitalized on April 8th at early morning. Patient also had dyspnea starting one day prior hospitalization and not clinically severe.
Since 7th April 2014, according to analytic results, patient also had grade III anemia and grade II thrombocytopenia.
Previously, on March, patient began treatment with radium 223 (on 25Mar2014).
The events have occurred in the context of the Radium 223, but PI can not ensure the causality between these events and the radiotherapy. There could also be related to the progression of the main disease

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diagnosed on 7th February 2014 (reason for which patient started treatment with Radium 223). In any case the SAEs are not related to the investigational product.
Patient died in the hospital on PPD 2014.
Event awareness and notification day was 26May2014.
Additional details:
The subject withdrawn from study due to the SAEs neutropenia, anemia and respiratory infection.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding date is 10 Feb 17
The subject developed neutropenia 259 days after receiving Herpes zoster vs Placebo and anemia, thrombocytopenia and respiratory infection subsequently and died due to these events. The events are due to progression of the underlying disease. Causal association with vaccine seems unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Cardiac arrest


#### Abstract

Narrative: This 53-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 1st July 2013, for prophylaxis.

On PPD 99 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 cardiac arrest. Serious criteria included hospitalization and GSK medically significant. The subject was treated with epinephrine (Adrenaline) and clamoxyl (nos) (Clamoxyl). The outcome of cardiac arrest was recovered/resolved on 9th October 2013.

The investigator considered that there was no reasonable possibility that the cardiac arrest may have been caused by Herpes zoster vs Placebo.

Investigator Comments : Patient with a cardiorespiratoty failure while she was on day hospital due to choking while she was drinking a soda drink ( possible aspiration Bronchial associated). Patient was hospitlized on 08OCT2013 cyanotic (cantral and periferic) with mild hypokalemy, mild hypophosphatemia, a paralysed of right vocal


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cord and a moderate protein malnutrition .
8Oct2013: Patient was afebril, stable, asymptomatic, no chest pain, no palpitations, no other symptoms. Patient was kept at the hospital during 48 hours for observation and then she was discharged with oxigenotherapy, with a significant improvement of the respiratory tract,. The antibiotic therapy was due to prophilaxis due to purulent secretions.
A fibroscopy was performed 9OCT2013) result: pharangeal paralisis with vocal right cort in right paramedian position.

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD

Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Acute kidney injury, Hydronephrosis, Anaemia, Prostate cancer
Narrative: This 87-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 22nd July 2013, for prophylaxis.

Concomitant products included metamizole, risperidone (Risperdal), metoclopramide (Primperan), prednisone, dexamethasone and tramadol.

On PPD 7 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 bilateral hydronephrosis. Serious criteria included hospitalization and GSK medically significant. Additional event(s) included severe - grade 3 acute renal failure on 16th August 2013 with serious criteria of hospitalization and GSK medically significant, severe - grade 3 anemia on 16th August 2013 with serious criteria of hospitalization and severe - grade 3 progression of prostate cancer on 16th August 2013 with serious criteria of hospitalization and GSK medically significant. The subject was treated with amoxicillin, clavulanate potassium (Augmentin), ceftriaxone, blood transfusion, auxiliary products (Blood Concentrate), furosemide, enoxaparin (Clexane), pantoprazole (Pantoprazol), lorazepam, haloperidol, paracetamol, ondansetron and macrogol, potassium chloride, sodium bicarbonate, sodium chloride (Movicol). The outcome of bilateral hydronephrosis was recovered/resolved on 6th September 2013. The outcome(s) of the additional event(s) included acute renal failure (recovered/resolved on 8th September 2013), anemia (not recovered/not resolved) and progression of prostate cancer (not recovered/not resolved).

The investigator considered that there was no reasonable possibility that the bilateral hydronephrosis, acute renal failure, anemia and progression of prostate cancer may have been caused by Herpes zoster

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## Unblinded Report - With Suspect Products and Serious Events

vs Placebo. Diagnostic results (unless otherwise stated, normal values were not provided): On 26th August 2013, Blood creatinine result was $3.18 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6 , normal high: 1.3), Blood potassium result was $3.3 \mathrm{mmol} / \mathrm{L}$ (normal low: 3.5, normal high: 5.5), Blood urea result was $80 \mathrm{mg} / \mathrm{dL}$ (normal low: 15, normal high: 45), Blood urea result was $37.3 \mathrm{mg} / \mathrm{dL}$ (normal low: 7, normal high: 21), Creatinine renal clearance result was $18.55 \mathrm{ml} / \mathrm{min}$ (normal low: 65, normal high: 150), Haematocrit result was 24.9 \% (normal low: 40, normal high: 54), Haemoglobin result was $8.1 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5), Protein total result was $6.1 \mathrm{~g} / \mathrm{dL}$ (normal low: 6.4, normal high: 8.3), Red blood cell count result was 2.57 x10E6/mcL (normal low: 4.6, normal high: 5.7) and White blood cell count result was $21.4 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11). On 27th August 2013, Blood creatine result was $3.03 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6 , normal high: 1.3), Creatinine renal clearance result was $19.62 \mathrm{ml} / \mathrm{min}$ (normal low: 65, normal high: 150), Haematocrit result was 30.2 \% (normal low: 40, normal high: 54), Haemoglobin result was $9.8 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5), Neutrophil count result was $17.7 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5 ) and White blood cell count result was $21.4 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11). On 28th August 2013, Blood creatine result was $3.02 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6 , normal high: 1.3) and Creatinine renal clearance result was $19.69 \mathrm{ml} / \mathrm{min}$ (normal low: 65, normal high: 150). On 29th August 2013, Blood creatine result was $4.21 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6 , normal high: 1.3), Creatinine renal clearance result was $13.42 \mathrm{ml} / \mathrm{min}$ (normal low: 65, normal high: 150), Haematocrit result was 29.5 \% (normal low: 40, normal high: 54), Haemoglobin result was $9.5 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5), Neutrophil count result was $18.8 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7 , normal high: 7.5 ), Red blood cell count result was $3.12 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4.6, normal high: 5.7) and White blood cell count result was $21.2 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11). On 30th August 2013, Blood creatine result was $4.18 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6, normal high: 1.3), Blood urea result was $102 \mathrm{mg} / \mathrm{dL}$ (normal low: 15, normal high: 45), Creatinine renal clearance result was $13.53 \mathrm{ml} / \mathrm{min}$ (normal low: 65, normal high: 150), Haematocrit result was 29.1 \% (normal low: 40, normal high: 54), Haemoglobin result was $9.4 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5), Neutrophil count result was $14.1 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7 , normal high: 7.5 ), Red blood cell count result was 3.06 x10E6/mcL (normal low: 4.6, normal high: 5.7 ) and White blood cell count result was $17.3 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11). On 2nd September 2013, Blood creatine result was $2.1 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6, normal high: 1.3), Creatinine renal clearance result was $29.95 \mathrm{ml} / \mathrm{min}$ (normal low: 65, normal high: 150), Haematocrit result was 31.4 \% (normal low: 40, normal high: 54), Haemoglobin result was 10.3 g/dL (normal low: 13, normal high: 17.5) and Red blood cell count result was $3.32 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4.6, normal high: 5.7). On 5th September 2013, Haematocrit result was 24.8 \% (normal low: 40, normal high: 54) and Haemoglobin result was $7.7 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5). On 6th November 2013, Haematocrit result was 35.4 \% (normal low: 40, normal high: 54), Haemoglobin result was $12.1 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5) and Red blood cell count result was $3.64 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4.6, normal high: 5.7). On 7th February 2014, Haematocrit result was 26.2 \% (normal low: 40, normal high: 54), Haemoglobin result was 8.2 g/dL (normal low: 13, normal high: 17.5) and Red blood cell count result was $2.9 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4.6, normal high: 5.7). On 2nd September 2014, Blood potassium result was $2.9 \mathrm{mmol} / \mathrm{L}$ (normal low: 3.5, normal high: 5.5).

Investigator Comments:
Patient came to ER Service on August 26th 2013 expressing symptons such as nausea, fatigue, abdominal pain. Later, the patient was hospitalized on 27-Aug-2013 after being diagnosed with acute renal failure grade IV associated with a previous urinary track infection due to an obstruction with right hydronephrosis grade IV (secondary to a vesicle infiltration of prostatic origin) detected on 26May2013 and left hydronephrosis grade III detected on 29Jul2013, kidney was oedematous. Patient also had a multifactorial anemia (grade III) and a proteic desnutrition. These AEs were due to the tumour (prostatic cancer) and they started 10 days prior to the visit to ER Service.

Patient presented good evolution and a mild cardiac insufiency treated with diuretics. During the hospitalization a CT scan was performed showing progressive disease (pulmonar progression).

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On 26Aug2013 according analytic results moderate piuria and bacteriuria were diagnosed, none of them were related to investigational product.

On 06Sep2013 patient was afebrile and assymptomatic, without any pain nor any other symptom.
Patient was discharched on September 8th 2013 with antibiotic therapy and sent to a paliative care unit who continue the following (under medical decision, chemotherapy was no longer administered). Patient withdrawn from study the same 08Sep2013.

By Feb. 7th 2014 the patient continue having anemia.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.
The subject was withdrawn from the study due to SAE bilateral hydronephrosis, acute renal failure, and anemia.

Case unblinded due to end of study Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Gastroenteritis, Hepatic encephalopathy, Oral candidiasis, Malnutrition, Dysphagia, Anaemia, Odynophagia, Oesophagitis, Acute kidney injury

Narrative: This 68-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 24th July 2013, for prophylaxis.

On PPD 21 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 hepatic encephalopathy. Serious criteria included death, hospitalization and GSK medically significant. Additional event(s) included moderate - grade 2 anemia on 28th August 2013 with serious criteria of death and hospitalization, severe - grade 3 acute gastroenteritis on 3rd September 2013 with serious criteria of death and hospitalization, moderate - grade 2 protein-calorie malnutrition on 6th September 2013 with serious criteria of death and hospitalization, moderate - grade 2 acute renal failure on 6th September 2013 with serious criteria of death, hospitalization and GSK medically significant, moderate - grade 2 oral candidiasis on 9th September 2013 with serious criteria of death and hospitalization, moderate - grade 2 dysphagia on 9th September 2013 with serious criteria of death and

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hospitalization, moderate - grade 2 odynophagia on 9th September 2013 with serious criteria of death and hospitalization and moderate - grade 2 esophagitis on 9th September 2013 with serious criteria of death and hospitalization. The subject was treated with meropenem, tramadol, paracetamol, enoxaparin (Clexane), blood transfusion, auxiliary products (Blood Concentrate), nystatin (Mycostatin), fluconazole (Diflucan), macrogol + potassium chloride + sodium bicarbonate + sodium chloride (Movicol), fentanyl (Durogesic), metoclopramide (Primperam), fluconazole, prednisone and dexamethasone (Fortecortin). The outcome of hepatic encephalopathy was fatal on PPD
2013. The outcome(s) of the additional event(s) included acute gastroenteritis (fatal on PPD 2013), oral candidiasis (fatal on $\begin{array}{lll}\text { PPD } & \text { 2013), protein-calorie malnutrition (fatal on PPD } & \text { 2013), dysphagia (fatal on } \\ \text { PPD } & \text { 2013), anemia (fatal on PPD }\end{array}$ 2013), esophagitis (fatal on PPD 2013) and acute renal failure (fatal on PPD 2013). The subject died on PPD 2013. The reported cause of death was gastroenteritis, hepatic encephalopathy, candidiasis of mouth, protein-calorie malnutrition, dysphagia, anemia, odynophagia, esophagitis and acute renal failure. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the hepatic encephalopathy, anemia, acute gastroenteritis, protein-calorie malnutrition, acute renal failure, oral candidiasis, dysphagia, odynophagia and esophagitis may have been caused by Herpes zoster vs Placebo. Diagnostic results (unless otherwise stated, normal values were not provided): On 28th August 2013, Aspartate aminotransferase result was $167 \mathrm{u} / \mathrm{L}$ (normal low: 4, normal high: 50), Blood alkaline phosphatase result was 1557 u/L (normal low: 53, normal high: 128), Blood creatinine result was $1.5 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6, normal high: 1.3), Blood glucose result was $115 \mathrm{mg} / \mathrm{dL}$ (normal low: 70, normal high: 110), Blood urea result was $82 \mathrm{mg} / \mathrm{dL}$ (normal low: 15, normal high: 45), Haematocrit result was 34.5 \% (normal low: 36, normal high: 48), Haemoglobin result was $11.3 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 18), Neutrophil count result was $9.32 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7 , normal high: 7.5 ), Red blood cell count result was 4.10 x10E6/mcL (normal low: 4.6, normal high: 5.7 ) and White blood cell count result was $12.7 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11). On 6th September 2013, Alanine aminotransferase result was $99 \mathrm{u} / \mathrm{L}$ (normal low: 5, normal high: 40), Blood calcium result was $7.5 \mathrm{mg} / \mathrm{dL}$ (normal low: 8.7, normal high: 10.3), Blood creatinine result was $2.65 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6, normal high: 1.3), Blood urea result was 111 mg/dL (normal low: 15, normal high: 45), Haematocrit result was 28.4 \% (normal low: 40, normal high: 54), Haemoglobin result was $9.4 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5), Monocyte count result was 1.1 $x 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 0.2 , normal high: 1), Neutrophil count result was $9.2 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5), Protein total result was $5.2 \mathrm{~g} / \mathrm{dL}$ (normal low: 6.4, normal high: 8.3), Red blood cell count result was $3.4 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4.6, normal high: 5.7 ) and White blood cell count result was $13 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11). On 8th September 2013, Alanine aminotransferase result was 107 u/L (normal low: 5, normal high: 40), Blood calcium result was $8.1 \mathrm{mg} / \mathrm{dL}$ (normal low: 8.7, normal high: 10.3), Blood creatinine result was $0.98 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6 , normal high: 1.3 ), Blood urea result was $60 \mathrm{mg} / \mathrm{dL}$ (normal low: 15, normal high: 45), Haematocrit result was 27.6 \% (normal low: 40, normal high: 54), Haemoglobin result was $8.7 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5), Monocyte count result was $0.9 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 0.2 , normal high: 1), Neutrophil count result was $6.8 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5), Red blood cell count result was $3.22 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4.6, normal high: 5.7) and White blood cell count result was $9.7 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11). On 9th September 2013, Alanine aminotransferase result was 108 u/L (normal low: 5, normal high: 40), Blood alkaline phosphatase result was 1075 u/L (normal low: 53, normal high: 128), Blood creatinine result was $0.81 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6 , normal high: 1.3 ), Blood urea result was $42 \mathrm{mg} / \mathrm{dL}$ (normal low: 15, normal high: 45), Haematocrit result was 27.6 \% (normal low: 40, normal high: 54), Haemoglobin result was 8.9 g/dL (normal low: 13, normal high: 17.5), Monocyte count result was $0.7 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 0.2, normal high: 1), Neutrophil count result was $4.8 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5) and Protein total result was $4.8 \mathrm{~g} / \mathrm{dL}$ (normal low: 6.4, normal high: 8.3). On 9th September 2013, Red blood cell count result was $3.28 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4.6 , normal high: 5.7 ) and White blood cell count result was 7.7

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x10e3/mcL (normal low: 4, normal high: 11). On 11th September 2013, Alanine aminotransferase result was 114 u/L (normal low: 5, normal high: 40), Blood alkaline phosphatase result was 1106 u/L (normal low: 53, normal high: 128), Blood bilirubin result was $1.71 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.2, normal high: 1.2), Blood urea result was $49 \mathrm{mg} / \mathrm{dL}$ (normal low: 15, normal high: 45), Blood urea result was $22.8 \mathrm{mg} / \mathrm{dL}$ (normal low: 7, normal high: 21), Haematocrit result was 32.6 \% (normal low: 40, normal high: 54), Haemoglobin result was $10.6 \mathrm{~g} / \mathrm{dL}$ (normal low: 13, normal high: 17.5 ), Monocyte count result was $0.9 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 0.2 , normal high: 1), Neutrophil count result was $5.6 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5), Protein total result was $5 \mathrm{~g} / \mathrm{dL}$ (normal low: 6.4, normal high: 8.3) and Red blood cell count result was $3.87 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4.6, normal high: 5.7).

Investigator Comments : Patient was hospitalized on 06-Sep-2013 due to diarrhea that started 3 days prior to the hospitalization, Even though the ethiology of the event was not clear at first moment, an empiric antibiotic treatment is then started which helps the patient to get an improvement of the health condition. Later the diagnosis showed that all the clinical ethiology of the events were related to the main disease.
A few days later, muguet candidiasis was diagnosed and so a topical treatment was started.
During the following days of hospitalization, patient presented a worsening of the overall health condition. On PPD 2013 the death was certified.
All the events described in Screen 1 are related to the progression of the main disease.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding date is 10 Feb 17
The subject developed hepatic encephalopathy 21 days after receiving Herpes zoster or placebo and oral candidiasis, protein-calorie malnutrition, dysphagia, anemia, dysphagia and other events subsequently and died due to these events. The events are related to progression of the underlying disease or anticancer therapies.Causal association with vaccine is unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD

Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Colorectal cancer
Narrative: This 64-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 23rd July 2013, for prophylaxis.

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Concurrent medical conditions included colorectal carcinoma.
On PPD 144 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 colorectal carcinoma. Serious criteria included death and GSK medically significant. The outcome of colorectal carcinoma was fatal on PPD 2014. The subject died on PPD
2014. The reported cause of death was colorectal carcinoma. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the colorectal carcinoma may have been caused by Herpes zoster vs Placebo.

Investigator Comments:
On 14-Dec-2013 patients family confirms the worsening of the general condition (patient is at home but visited by a palliative care service). Patient died at home due to progresive disease on PPD 2014. No further information.

Additional details:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.
Subject withdrawn from study due to this event.
Case unblinded due to end of study
Unblinding Date is 10-FEB-17
The subject developed progression of colorectal cancer 144 days after receiving Herpes zoster vs Placebo and died due to this disease. The event is considered as due to progression of underlying disease. Causality with the vaccine seems unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Anal abscess

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subject was treated with amoxicillin (Amoxycillin) and dexketoprofen trometamol (Enantyum). The outcome of perianal abscess was recovered/resolved on 12th March 2014.

The investigator considered that there was no reasonable possibility that the perianal abscess may have been caused by Herpes zoster vs Placebo.

Investigator Comments : Patient went to the hospital on 11 Nov2013 with a very intense perianal pain since 3 days ago and, on 12Nov2013, was hospitalized after a perianal abcess was diagnosted which required a drainage and antibiotics for treatment. Patient was discharged from hospital on 19Nov2013 with a stable clinical condition and the drainage was removed on 26Dec2013. The perianal abcess was fully resolved on 12Mar2014.
the patient has been treated with perianal care with baths perianal area
Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD

Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Staphylococcal infection

> Narrative: This 41-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 5th August 2013, for prophylaxis.

> On PPD 124 days after receiving Herpes zoster vs Placebo, the subject developed moderate - grade 2 bacterial infection due to staphylococcus aureus. Serious criteria included hospitalization and GSK medically significant. The subject was treated with amoxicillin + clavulanate potassium (Augmentine), levofloxacin (Levofloxacine), enoxaparin (Clexane), vancomycin, cloxacillin, gentamicin (Gentamicine), piperacillin + tazobactam, metamizole magnesium (Nolotil), paracetamol and cefalexin (Cefalexina). The outcome of bacterial infection due to staphylococcus aureus was recovered/resolved on 16th December 2013.

> The investigator considered that there was no reasonable possibility that the bacterial infection due to staphylococcus aureus may have been caused by Herpes zoster vs Placebo.

> Relevant Tests: A blood culture was performed. S. Aureus oxacillin sensitive was found. Diagnostic results

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#### Abstract

(unless otherwise stated, normal values were not provided): On 7th December 2013, Alanine aminotransferase result was 62 u/L (normal low: 5, normal high: 40), Blood glucose result was $127 \mathrm{mg} / \mathrm{dL}$ (normal low: 70, normal high: 110), Blood urea result was $44 \mathrm{mg} / \mathrm{dL}$ (normal low: 15, normal high: 45), Creactive protein result was $6.6 \mathrm{mg} / \mathrm{L}$ (normal low: 0.0, normal high: 5.0), Haemoglobin result was $10.6 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 16), Lymphocyte count result was 3.8 \% (normal low: 16, normal high: 45), Lymphocyte count result was $0.2 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1, normal high: 3.5), Monocyte count result was $0.1 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 0.2, normal high: 1 ), Neutrophil count result was 93.7 \% (normal low: 42, normal high: 74) and Red blood cell count result was $3.5 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4, normal high: 5.5). On 9th December 2013, Alanine aminotransferase result was 108 u/L (normal low: 5, normal high: 40), Creactive protein result was $200.5 \mathrm{mg} / \mathrm{L}$ (normal low: 0, normal high: 5), Haemoglobin result was $9.1 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 18), Lymphocyte count result was $0.36 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1, normal high: 3.5), Monocyte count result was $0.19 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 0.2 , normal high: 1), Neutrophil count result was 86.40 \% (normal low: 42, normal high: 74), Protein total result was $4.9 \mathrm{~g} / \mathrm{dL}$ (normal low: 6.4, normal high: 8.3) and Red blood cell count result was $2.99 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4, normal high: 5.5). On 10th December 2013, C-reactive protein result was $138.3 \mathrm{mg} / \mathrm{L}$ (normal low: 0, normal high: 5), Haemoglobin result was $9 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 16), Lymphocyte count result was 0.8 x10e3/mcL (normal low: 1, normal high: 3.5), Red blood cell count result was 2.83 x10E6/mcL (normal low: 4, normal high: 5.5) and White blood cell count result was $3.94 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11). On 12th December 2013, C-reactive protein result was $48.6 \mathrm{mg} / \mathrm{L}$ (normal low: 0, normal high: 5), Haematocrit result was 27.9 \% (normal low: 36, normal high: 47), Haemoglobin result was $9.8 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 16), Lymphocyte count result was $1.35 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1, normal high: 3.5), Neutrophil count result was $3.82 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5), Red blood cell count result was $3.10 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4, normal high: 5.5) and White blood cell count result was $5.74 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11). On 13th December 2013, Blood glucose result was 82 $\mathrm{mg} / \mathrm{dL}$ (normal low: 70 , normal high: 110), Eosinophil count result was $0.95 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 0 , normal high: 2), Haemoglobin result was $9.7 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 16), Mean cell haemoglobin result was 31.9 pg (normal low: 27, normal high: 31), Neutrophil count result was 4.1 $x 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5), Red blood cell count result was $3.04 \times 10 \mathrm{E} 6 / \mathrm{mcL}$ (normal low: 4, normal high: 5.5) and White blood cell count result was $7.54 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11). On 16th December 2013, C-reactive protein result was $15.2 \mathrm{mg} / \mathrm{L}$ (normal low: 0, normal high: 5), Eosinophil count result was $0.81 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 0 , normal high: 5) and Haemoglobin result was $11 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 16). On 16th December 2013, Neutrophil count result was 5.16 $x 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.7, normal high: 7.5), Platelet count result was $468 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 140, normal high: 450) and Red blood cell count result was 3.51 x10E6/mcL (normal low: 4, normal high: 5.5).


Investigator Comments : Patient was hospitalized due to febrile syndrome on December 8th 2013. The symptons started 24h prior to hospitalization On December 9th, a blood culture was performed and S. Aureus oxacillin sensitive was found and treated, so the final diagnosis that embrace all the symptons, including fever, was Infection by S. aureus related to catheter. Also refers Anemia mild, related to chemotherapy (Patient was currently under chemotherapy treatment). After this results, the catheter was removed and patient observed a good general clinical evolution.
On December 16th, patient was discharged.
Case unblinded due to end of study
Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Subject ID:<br>PPD

Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Thrombocytopenia, Acute kidney injury, Constipation


#### Abstract

Narrative: This 84-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 1st dose of Herpes zoster vs Placebo (intramuscular) on 16th September 2013, for prophylaxis.

Concomitant products included red blood cells, concentrated (Red Blood Cells Concentrate), furosemide, ferrous sulphate (Iron Sulphate), lorazepam and cefuroxime.

On PPD 6 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 constipation. Serious criteria included hospitalization. Additional event(s) included severe - grade 3 thrombocytopenia on 27th September 2013 with serious criteria of hospitalization and severe - grade 3 acute renal failure on 1st October 2013 with serious criteria of hospitalization and GSK medically significant. The subject was treated with sodium dihydrophosphate, sodium phosphate dibasic (Enema (Disodium Hydrophosphate + Sodium Dihydrophosphate)), macrogol, potassium chloride, sodium bicarbonate, sodium chloride (Movicol) and piperacillin, tazobactam (Piperacillin + Tazobactam). The outcome of constipation was recovered/resolved on 4th October 2013. The outcome(s) of the additional event(s) included thrombocytopenia (recovered/resolved on 7th October 2013) and acute renal failure (recovered/resolved on 8th October 2013).

The investigator considered that there was no reasonable possibility that the constipation, thrombocytopenia and acute renal failure may have been caused by Herpes zoster vs Placebo.


Relevant Tests: 3Oct2013: Urocultive:Enterococcus faecalis
2Oct2013:Abdominal ultrasound: Linfocele in surgical bed
Diagnostic results (unless otherwise stated, normal values were not provided): On 27th September 2013, Platelet count result was $55 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 140, normal high: 450). On 1st October 2013, Blood creatinine result was $1,61 \mathrm{mg} / \mathrm{dL}$ (normal low: 0,60, normal high: 1,30), Blood urea result was $84 \mathrm{mg} / \mathrm{dL}$ (normal low: 15, normal high: 45) and Platelet count result was $16 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 140, normal high: 450). On 3rd October 2013, Blood creatinine result was $1,41 \mathrm{mg} / \mathrm{dL}$ (normal low: 0,60, normal high: 1,30 ) and Platelet count result was $47 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 140, normal high: 450). On 4th October 2013, Blood creatinine result was $1,40 \mathrm{mg} / \mathrm{dL}$ (normal low: 0,60 , normal high: 1,30 ), Blood urea result was $58 \mathrm{mg} / \mathrm{dL}$ (normal low: 15, normal high: 45) and Platelet count result was $91 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 140, normal high: 450). On 7th October 2013, Blood creatinine result was $1,20 \mathrm{mg} / \mathrm{dL}$ (normal low: 0,60, normal high: 1,30), Blood urea result was $32 \mathrm{mg} / \mathrm{dL}$ (normal low: 15, normal high: 45) and Platelet count result was $241 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 140, normal high: 450).

Investigator Comments:

## Confidential

## Unblinded Report - With Suspect Products and Serious Events

Patient came to the hospital (Emergency room) with abdominal pain, thoracic pain and acute renal failure and he was hospitalized on 2 Oct2013 showing with all this nausea and vomits. The abdominal pain is probably due to constipation. Patient also had a grade 4 platelet count decrease and grade 2 anemia( . An urocultive was performed and Enterococcus faecalis was isolated.
An abdominal ultrasound was made and $65-70 \mathrm{~mm}$ cavity was found that was compatible with a lynphocele in surgical bed : a complete drainage and enema were done past 2Oct2013 . Lynphocele was the cause of all these Serious Adverse events, not related with Investigational product. Past 4Oct2013 Another enema was administered and Constipation was resolved. No nausea and no vomits.Patient was asymptomatic
The patient was discharged past 80ct2013 with the events resolved and with antibiotherapy Because all the toxicity, chemotherapy is stopped and the patient withdrawn his informed consent from this clinical trial (16Oct2013).

Additional details:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Pleural effusion

Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 08 April 2013, he received the 1st dose of Varicella Zoster vaccine gE ( 50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical condition at the time of the event included chronic obstructive pulmonary disease.
On PPD 21 days after the 1st dose of Blinded vaccine, this 78-year-old subject developed pleural effusion. The subject was hospitalised and the event was life-threatening. The subject was treated with acetylcysteine, hyoscine butylbromide, morphine, Dormicum, haloperidol, fentanyl, salbutamol sulphate, frusemide, meropenem, unknown, lorazepam, ipratropium bromide, heparin sodium, clopidogrel, diltiazem hydrochloride and omeprazole. The subject died on PPD 2013 due to pleural effusion. An autopsy was not performed. The investigator considered that there was no reasonable possibility that the pleural effusion may have been caused by investigational product.

Investigator Comments :
The patient came to emergency room due to malaise. Not refered fever or cough. The Investigator team

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

decided that the patient must be hospitalizad on 29 APRIL 2013. The patient didnt respond to the tretament administered. Finally, the patient died on PPD 2013. The SAE is related with the disease/tumor.

This case contains an event assessed by the investigator as related to the anti-cancer therapy and/or disease/tumour.

Case unblinded due to end of study
Unblinding Date is 10-FEB-17
The subject developed pleural effusion 21 days after receiving 1st dose of blinded vaccine Herpes zoster vs placebo and died 5 days later due to this. The event is considered related to anti-cancer therapy and disease or tumour.Causal association with vaccine unlikley. Based on unblinding information,the vaccine given to subject was placebo.

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Febrile neutropenia, Kidney infection

Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 13 May 2013, she received the 1st dose of Varicella Zoster vaccine gE ( 50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

The subject's past medical history included acute myocardial infarction. Medical conditions at the time of the event included diabetes mellitus type 2 and hypertension arterial. Concomitant medications included Insulin.

On PPD 19 days after the 1st dose of Blinded vaccine, this 73-year-old subject developed kidney infection. On 03 June 2013, she developed febrile neutropenia. The subject was hospitalized and the events were life-threatening. The subject was treated with paracetamol, metoclopramide hydrochloride, ondansetron hydrochloride, filgrastim, piperacillin sodium, frusemide, aspirin, tramadol hydrochloride, dipyrone, amikacin, levofloxacin, ciprofloxacin, imipenem, metoclopramide, low molecular weight heparin, lorazepam, lactulose, non-gsk propranolol hydrochloride, omeprazole and dexamethasone. The events resolved on 18 July 2013. The investigator considered that there was no reasonable possibility that the febrile neutropenia and kidney infection may have been caused by investigational product. The subject was withdrawn from the study due to the event.

Investigator Comments :
The patient came to emergency room due to fever on 03 June 2013. She had vomits during 48 hours, without diarrhea. On 01 Jun 2013 the patient presented renal infection. This event was severe. Not related with the products investigational. This event was resolved on 18 Jul 2013.

## Confidential Unblinded Report - With Suspect Products and Serious Events

Finally, the patient was hospitalized in oncology.
During the first 24h of hospitalization the patient suffered septic shock requiring admission to ICU due to neutropenic enteritis. In ICU, the patient required prolonged intubation due to respiratory distress syndrome. Likewise, presented respiratory and digestive bleeding due to thrombocytopenia postchemotherapy.
The patient was stabilized and moved to the ward on 18/Jul/2013.
The patient withdrew consent to participate in the study on 16/Jul/2013.
The SAEs were related with disease tumor.
The patient was hospitalized on 03 Jun 2013 and the date discharged was on 18 Jul 2013.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Autoimmune thyroiditis
Narrative: This 52-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 29th July 2013, for prophylaxis.

On PPD 252 days after receiving Herpes zoster vs Placebo, the subject developed mild - grade 1 autoimmune thyroiditis. Serious criteria included GSK medically significant and clinically significant/intervention required. The subject was treated with thiamazole (Tirodril). The outcome of autoimmune thyroiditis was recovering/resolving.

The investigator considered that there was no reasonable possibility that the autoimmune thyroiditis may have been caused by Herpes zoster vs Placebo.

Relevant Tests: apr2014 ecography was performed for this patient and trhe result was positive to autoimmune tiroidism

Investigator Comments
on apr2014 ecography was performed for this patient and trhe result was positive to autoimmune tiroidism.

## Confidential Unblinded Report - With Suspect Products and Serious Events

the patient started on apr2014 with medication for this event (tirodril).
During this time the patient is coming to endocrine medical office for control of this disease.
The patient continued stable and without changes in the medication.
The value of the tirotropin in the analitic 07apr2014 was $0.01 \mathrm{IU} / \mathrm{ml}$.
The patient had not experienced similar event in the past. The family diagnosed with autoinmune disorde is unknown. The patient had not any infection. the patient had not test during this period. it is a chronic condition.

There wasn t a genetic predisposition, family history, or syndrome. It was a thyroid disease.
This case contains an event assessed by the investigator as a serious possible immune mediated disorder (pIMD).

Case unblinded due to end of study
Unblinding Date is 10-FEB-17
The subject developed autoimmune thyroiditis 252 days after receiving Herpes zoster vs Placebo and was recovering from the event. The event is considered as a serious possible immune mediated disorder (pIMD). Due to the lack of information regarding any positive family history for any autoimmune or other genetic and environmental causes of autoimmune thyroiditis, the causal association of the event with the vaccine seems unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Pyrexia
Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 27 June 2013 and 29 July 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD 16 days after the 1st dose of Blinded vaccine, this 51-year-old subject developed fever unknown origin. The subject was hospitalised. The subject was treated with paracetamol, ketoprofen, pantoprazole, heparin, lorazepam, Piperacillin + tazobactam, lactobacillus acidophilus and meropenem. The event resolved on 26 July 2013. The investigator considered that there was no reasonable possibility that the fever unknown origin may have been caused by investigational product.

## Confidential Unblinded Report - With Suspect Products and Serious Events

Investigator Comments :
The patient came to emergency room due to fever (38.5C) on 15Jul2013. The doctors decide hospitalised to the patient for antibiotic treatment.
The patient has completed three weeks of antibiotic treatment satisfactorily.
She received discharged on 29Jul2013 after receiving the second cycle of chemotherapy and the second dose of vaccine.
The finally diagnosed was fever unknown origin.
Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Respiratory failure
Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 01 July 2013 and 06 August 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE $(50 \mathrm{mcg})$ adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD 44 days after the 2nd dose of Blinded vaccine, this 85-year-old subject developed respiratory insufficiency. The subject was hospitalised. The subject was treated with heparin sodium, paracetamol, metamizole magnesium, lorazepam, fentanyl, omeprazole, Fortecortin, nicoumalone, tramadol hydrochloride, dipyrone and red blood cells. The event resolved on 25 September 2013. The investigator considered that there was no reasonable possibility that the respiratory insufficiency may have been caused by investigational product.

Investigator Comments:
The patient come to emergy room due to respiratory insufficiency on 19sep2013. The saturation was $86 \%$. Finally the patient was hospitalized to discard possible pulmonary Thromboembolism on 19sep2013.The patient during admission had anaemia (7.80) and was administred two bags of red cells, resolving the anemia. She present inguinal pain and in the RX pelvis saw that she had pelvic fracture.During admisson realized at gamma V/P and the resuld was a pulmonary thrombolism. With the treatment for pain and medication for the control of pulmonary Thromboembolism the patient has presented a very good evolution anf finally she was discharged on 25Sep2013.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding Date is $10-$ FEB-17

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Anaemia, Respiratory failure
Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 01 July 2013 and 06 August 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE $(50 \mathrm{mcg})$ adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD 64 days after the 2nd dose of Blinded vaccine, this 85-year-old subject developed respiratory insufficiency. On 10 October 2013, she developed anemia. The subject was hospitalised. The subject was treated with heparin sodium, red blood cells, paracetamol, levofloxacin, ipratropium bromide, acetylcysteine, ibuprofen, tramadol hydrochloride and budesonide. Anemia resolved on 12 October 2013. Respiratory insufficiency resolved on 13 October 2013. The investigator considered that there was no reasonable possibility that the anemia and respiratory insufficiency may have been caused by investigational product.

Investigator Comments :
The patient came to emergency room due to dyspnea. In the emergency room conducted analytical and saw that she was anemic and respiratory insufficcience. The last event started on 09Oct2013.
The patient was hospitalized due anemia and respiratory insufficicience on 100ct2013. Two packed red cells were transfused and treatment for dyspnea was administered.
She had good evolution and was discharged on 130 ct2013.
Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Metastases to central nervous system, Febrile neutropenia
Narrative: This 68-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised,

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## Unblinded Report - With Suspect Products and Serious Events

observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 26th August 2013, for prophylaxis.

On PPD 259 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 brain metastases. Serious criteria included hospitalization and GSK medically significant. Additional event(s) included moderate - grade 2 febrile neutropenia on 27th August 2014 with serious criteria of hospitalization and GSK medically significant. The subject was treated with prednisone and piperacillin sodium + tazobactam sodium (Tazocel). The outcome of brain metastases was not recovered/not resolved. The outcome(s) of the additional event(s) included febrile neutropenia (recovered/resolved on 5th September 2014).

The investigator considered that there was no reasonable possibility that the brain metastases and febrile neutropenia may have been caused by Herpes zoster vs Placebo.

Investigator Comments:
The patient started with cerebral edema as first symptoms on 12May2014. He was admitted at the hospital on 27 Aug2014 due to poor general status and progressive neurological deterioration due to his disease progression. After to the improvemet in the clinical evolution of the neutropenia febrile, it was decided to discharge the patient on 5Sep2014.

During the hospitalization antibiotherapy (tazocel) was administered to treat the neutropenia febrile.
Regarding the brain metastasis, the last information we have in the medical records is that on 15SEp2014 due to very poor general status (the patient is confined to bed) and it is decided to treat him in the palliative unit (no more information available in the medical records).

Additional details:
Subject withdrawn from the study due to event brain metastases.
Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Skin haemorrhage
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 10 July 2013 and 20 August 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE

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## Unblinded Report - With Suspect Products and Serious Events

$(50 \mathrm{mcg})$ adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.


#### Abstract

On PPD same day after the 2nd dose of Blinded vaccine, this 36-year-old subject developed skin bleeding. The subject was hospitalised. The subject was treated with red blood cells, tranexamic acid, metamizole magnesium, meropenem, fentanyl, paracetamol, morphine, Augmentin, ketoprofen, platelet concentrate, Inacid, midazolam, methotrimeprazine, diazepam, folic acid, Urbason, ranitidine hydrochloride, dexchlorpheniramine maleate, bromazepam, lactulose, fluconazole, hydrocortisone sodium phosphate, pantoprazole, frusemide and Movicol. The subject died on PPD 2013 due to skin bleeding. An autopsy was not performed. The investigator considered that there was no reasonable possibility that the skin bleeding may have been caused by investigational product.

Investigator Comments : The patient come to emergency room due to hemorrhage. In the emergency room saw in the analytica anemia. The patient was hospitalized for treatmet of anemia and hemorrhage on 20aug2013. radiotherapy is given between 19 Sep and October 2, 2013. After second dose but not is related. Finally the patient was died on PPD 2013 . This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study Unblinding Date is 10-FEB-17 The subject developed skin haemorrhage same day after recieivng 2nd dose of blinded vaccine Herpes zoster vs placebo and died due to this 2 months later. The event is considered related to anti-cancer therapy or disease/tumour.Causal association with vaccine is unlikely.Based on unblinded information,the study vaccine recieved by subject is Vaccine placebo.


Study Number: 116427
Study Center ID: PPD
Subject ID: P
PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Febrile neutropenia
Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 22 July 2013 and 03 September 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine $\mathrm{gE}(50 \mathrm{mcg})$ adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD 25 days after the 1st dose of Blinded vaccine, this 52-year-old subject developed febrile neutropenia. The subject was hospitalised. The subject was treated with meropenem, vancomycin, filgrastim, dipyrone, paracetamol, Augmentin, omeprazole, bromazepam and fusidate

## Confidential Unblinded Report - With Suspect Products and Serious Events

sodium. The event resolved on 31 August 2013. The investigator considered that there was no reasonable possibility that the febrile neutropenia may have been caused by investigational product .

Investigator Comments :
The patient came to emergency room on 17 Aug2013 due to fever of 38.1 C for 24 hours. Finally the patient was hospitalized for antibiotic treatment and control of neutropenia on 17Aug2013. The patient has completed antibiotic treatment and no longer has fever. She was discharged on 23Aug2013. Fucidine was administered due to overrinfected lesion in the left parasternal region related to insect bite.

Case unblinded due to end of study
Unblinding date is 10 Feb17Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Sepsis
Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 22 August 2013 and 24 September 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE ( 50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical conditions at the time of the event included cervix carcinoma.
On PPD 2013, four days after the 2nd dose of Blinded vaccine, this 64-year-old subject died due to sepsis. An autopsy was not performed. The investigator considered that there was no reasonable possibility that the sepsis may have been caused by investigational product.

Investigator Comments :
On 15th of October 2013 patient s son came to doctor office and explained that his mother died on PPD 2013. Apparently by a probable septic shock.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding Date is $10-$ FEB-17
The subject developed sepsis 4 days after receiving Herpes zoster vs placebo and died due to this. The event is considered related to anti-cancer therapies or underlying disease .Causal association with vaccine unlikely.

Study Number: 116427

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Study Center ID: PPD<br>Subject ID: PPD<br>Randomization Number:<br>Case ID: PPD<br>Suspect Products: Hz/su + AS01B<br>Serious Events: Bladder cancer

Narrative: This 65-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 1st October 2013, for prophylaxis.

Concurrent medical conditions included bladder carcinoma.
On PPD 142 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 bladder carcinoma. Serious criteria included death, hospitalization and GSK medically significant. The subject was treated with morphine hydrochloride, paracetamol, oxycodone hydrochloride (Oxycontin), omeprazole, dexamethasone (Fortecortin), gabapentin, levofloxacin, meropenem, platelets, human blood (Transfusion Of Platelets), red blood cells (Red Cell Transfusion), midazolam, amikacin, dexketoprofen trometamol (Enantyum), furosemide, tamsulosin, filgrastim (Neupogen), filgrastim (Nivestim) and fentanyl. The outcome of bladder carcinoma was fatal on PPD 2014. The subject died on PPD 2014. The reported cause of death was bladder carcinoma. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the bladder carcinoma may have been caused by Herpes zoster vs Placebo. Diagnostic results (unless otherwise stated, normal values were not provided): On 20th February 2014, Neutrophil count result was $0.30 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.50, normal high: 7.50 ) and Platelet count result was $22 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 150, normal high: 450).

Investigator Comments:
The patient came to emergency room due to back pain on 20feb2014. He did not referred fever or traumatism.
The patient was hospitalized in oncology service.
He was disorientated and with fever(40C) before the hospitalization.
The patient received several platelets transfusion and red cells transfusions.
His general status is bad.
During the next days, the patient did not improved his status. The doctor decided informed to the family about the patient critical situation.
Finally the patientt was sedated. He died on PPD 2014.
The patient was hospitalized on 20feb2014 and he not was discharged because he died on PPD 2014.
Additional details:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

## Confidential Unblinded Report - With Suspect Products and Serious Events

The Subject withdrawn from study due to this SAE:BLADDER CARCINOMA PROGRESSION
Case unblinded due to end of study
Unblinding Date is 10-FEB-17
The subject developed disease progression of the underlying bladder carcinoma 142 days after receiving Herpes zoster vs Placebo and died due to this disease. The event is due to the progression of the past illness. Causality with vaccine seems unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Pulmonary embolism
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 11 April 2013 and 21 May 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical conditions at the time of the event included catheterization venous and colon neoplasia.
On PPD 76 days after the 2nd dose of Blinded vaccine, this 48-year-old subject developed pulmonary embolism. The subject was hospitalised. The subject was treated with enoxaparin. The event resolved on 18 September 2013. The investigator considered that there was no reasonable possibility that the pulmonary embolism may have been caused by investigational product.

Investigator Comments :
After cycle 6 of chemotherapy control TAC was performed and the results as trombosis around of catheter inserted on Apr2013 and embolism pulmonar no symphtomatic.
Pulmonar Embolism was diagnosed in 07Aug2013 (day of the hospitalization). In april 2013, a catheter was inserted and probably this was the cause of the trombo, but not is the start date of the event. Patient was hospitalizaed and enoxaparine treatment was administrated during hospitalization (80mg/12) without complicationa.
Patient was discharged in a good conditions on 09Aug2013 with same medication. In control visit (18sep2013) the event is considered resolved and patiets will continue with enoxaparina prophylactic treatment.
SAE EMBOLISM PULMONARY was due to disease/tumour.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study

## Confidential Unblinded Report - With Suspect Products and Serious Events

## Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Epiglottitis
Narrative: This 72-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 13th January 2014, for prophylaxis.

On PPD 219 days after receiving Herpes zoster vs Placebo the subject developed moderate - grade 2 epiglottitis. Serious criteria included hospitalization and GSK medically significant. The subject was treated with ceftriaxone (Ceftriaxona), methylprednisolone and cefditoren. The outcome of epiglottitis was recovered/resolved on 2nd September 2014.

The investigator considered that there was no reasonable possibility that the epiglottitis may have been caused by Herpes zoster vs Placebo.

Investigator Comments :
The 20Aug2014, the subject presented odynophagia and cough with stridor. The patients went to ER where was diagnosed of upper respiratory tract acute infection with epiglottitis. Requires hospitalization with good clinical improvement after the treatment with antibiotics and corticoids. The patient admission the day August 282014 and was discharged on day 2 September 2014
ILEOSTOMY CLOSURE: After completing adjuvant chemotherapy regimen, elective surgery is performed for reconstruction of intestinal transit with ileostomy closure. No complications. Good course.
As this event was planned at the beginning of the study, it is not considered an SAE and it is recorded in general medical history section.
FAQUECTOMY: No hospitalization required. Not considered an SAE.
Case unblinded due to end of study
Unblinding date is 10 Feb17

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Pulmonary embolism
Narrative: This 45-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 16th July 2013, for prophylaxis.

Concomitant products included dexketoprofen (Dexketoprofeno), omeprazole and paracetamol.
On PPD 207 days after receiving Herpes zoster vs Placebo, the subject developed moderate - grade 2 pulmonary thromboembolism. Serious criteria included hospitalization and GSK medically significant. The subject was treated with bemiparin sodium (Hibor) and ENOXAPARIN. The outcome of pulmonary thromboembolism was recovered/resolved on 23rd September 2015.

The investigator considered that there was no reasonable possibility that the pulmonary thromboembolism may have been caused by Herpes zoster vs Placebo.

Relevant Tests: transthoracic echo:
Sessile mass within the right atrium attached to the back wall thereof and intermediate echogenicity of $2.4 \times 2.1 \mathrm{~cm}$ that permece equal in size and echo caracterisitcas regarding February 11, 2014. Occupation not appreciated by the mass inside VCI. This mass does not affect functionally to tricuspid valve. Consider among dignosticas options: tumor (myxoma), thrombus (not less likely solution), other (wart).
Biventicular size and preserved systolic function.
Study vavlular average.
Diagnostic results (unless otherwise stated, normal values were not provided): On 8th February 2014, Platelet count result was $116.00 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 150.0, normal high: 400.0).

Investigator Comments:
The patient comes to emergency with dyspnea on 08 February 2014.
In March 2014 entered in oncology and PET image suggestive of right atrial thrombus adjacent to port a cath in echocardiography. In AP thrombus confirms no other findings.
After testing the diagnostic trial is:
Pulmonary embolism
Right atrial thrombus passing through the tricuspid valve Mild thrombocytompenia.
Go to the heath center for dysphnea 3 days os evolution.
The following test were performed:
Echocardiography on 17/02/2014
Sessile mass within the right atrium attached to the back wall thereof and
intermediate echogenicity of $2.4 \times 2.1 \mathrm{~cm}$ that permece equal in size and echo caracterisitcas regarding

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February 11, 2014. Occupation not appreciated by the mass inside inferior vena cava. This mass does not affect
functionally to tricuspid valve. Consider among dignosticas options: tumor (myxoma), thrombus
(not less likely solution), other (wart).
Biventicular size and preserved systolic function.
Study vavlular average.
Doppler ultrasound on 02/10/2014
The patient discharged on 04/03/2014.
Case unblinded due to end of study
Unblinding Date is $10-\mathrm{FEB}-17$
The subject developed pulmonary thromboembolism 207 days after receiving Herpes zoster vs Placebo and recovered. After due analysis GSK accepts and agrees with the causality assessment of the Serious Adverse Event by the Principal Investigator as unrelated to participation in the study.

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Adenocarcinoma of colon
Narrative: This 75-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 1st dose of Herpes zoster vs Placebo (intramuscular) on 5th August 2013, for prophylaxis.

Concurrent medical conditions included diabetes mellitus, hypertension and hypercholesterolemia. Concomitant products included omeprazole (Omeprazol), hydroxyzine, macrogol, phytomenadione, metamizole, calcium polystyrene sulfonate, dexamethasone, enoxaparin, metamizole magnesium (Nolotil), metoclopramide, morphine (Morfina), ondansetron, paracetamol, tramadol, phytomenadione (Fitomenadiona), hydroxyzine hydrochloride (Hidroxicina), prednisone and morphine.

On PPD 4 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 adenocarcinoma of colon stage iv. Serious criteria included death, hospitalization and GSK medically significant. The subject was treated with vitamins nos (Vitamin). Herpes zoster vs Placebo was discontinued. The outcome of adenocarcinoma of colon stage iv was fatal on PPD 2013. The subject died on PPD 2013. The reported cause of death was adenocarcinoma of colon stage iv. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the adenocarcinoma of colon stage iv may have been caused by Herpes zoster vs Placebo.

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Relevant Tests: TAC on 20/Aug/2013: Disease Progression Diagnostic results (unless otherwise stated, normal values were not provided): On 19th August 2013, BILIRUBIN TOTAL result was $8.60 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.3, normal high: 1.1). On 31st August 2013, BILIRUBIN TOTAL result was $24.80 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.3, normal high: 1.1). On 2nd September 2013, BILIRUBIN TOTAL result was $24.80 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.3, normal high: 1.1).

Investigator Comments:
The patient had bilirrubina total 8.60 and had general discomfort, choluria and acholia. He was in emergency (19 August 2013) and then in hospital admission (20Aug2013)
Event due to disease progression 20 August 2013.
Discharged date 30 Aug 2013 and patient come back home Inpatient hospitalization on 31 August 2013 due to anuria and hyperbilirrubinemia related to disease progression not related to investigational product. Discharged date 03 September2013 Inpatient hospitalization 03 September 2013 due to disease progression. Patient has been hospitalizated in palliative care service in other hospital.
Hospitalized hospital patient in hospital stay long 03 September.
Finally died there on PPD 2013 at 18:10
The patient leaves the trial on September 9 by malaise and decision of the investigator.
Income and adverse events are caused by the progression of the disease (Stage IV colon adenocarcinoma)

Additional details:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.
Subject withdrawn from study due to this event.
Case unblinded due to end of study
Unblinding Date is 10-FEB-17
The subject developed adenocarcinoma of colon stage IV related to disease progression 4 days after receiving 1st dose of Herpes zoster vs placebo and died due to this later. Very short time to onset for a carcinoma stage IV to develop and the event is considered due to anti cancer therapy or disease/tumour.Hence,causal association with vaccine seems unlikely.Based on unblinding information, the vaccine recieved by the subject was Herpes zoster.

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Cardiac failure
Narrative: This 75-year-old female subject was enrolled in a blinded study titled A phase II/III,

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## Unblinded Report - With Suspect Products and Serious Events

randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 27th January 2015, for prophylaxis.

Concurrent medical conditions included hypertension, hypercholesterolemia and diabetes.
On PPD 163 days after receiving Herpes zoster vs Placebo, the subject developed moderate grade 2 cardiac failure. Serious criteria included hospitalization and GSK medically significant. The subject was treated with furosemide, red blood cells, concentrated (Red Cells Concentrated), amlodipine (Amlodipino), doxazosin, losartan, metoclopramide, ondansetron and paracetamol. The outcome of cardiac failure was recovered/resolved on 5th November 2015.

The investigator considered that there was no reasonable possibility that the cardiac failure may have been caused by Herpes zoster vs Placebo. Diagnostic results (unless otherwise stated, normal values were not provided): On 29th July 2015, Blood creatinine result was $2.26 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.5, normal high: 0.9), Blood creatinine result was $1.53 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.5 , normal high: 0.9 ), Blood urea result was $112 \mathrm{mg} / \mathrm{dL}$ (normal low: 21, normal high: 50), Blood urea result was $123 \mathrm{mg} / \mathrm{dL}$ (normal low: 21, normal high: 50) and Haemoglobin result was $7.20 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 16). On 31st July 2015, Blood creatinine result was $1.71 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.5 , normal high: 0.9 ), Blood urea result was $108 \mathrm{mg} / \mathrm{dL}$ (normal low: 21, normal high: 50) and Haemoglobin result was $10.60 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 16). On 4th August 2015, Blood creatinine result was $1.57 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.5, normal high: 0.9), Blood urea result was $98 \mathrm{mg} / \mathrm{dL}$ (normal low: 21, normal high: 50) and Haemoglobin result was $10.30 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 16). On 10th August 2015, Haemoglobin result was $9.60 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 16).

Investigator comment
the patient comes to the emergency room on 29 July 2015 for progressive lower limb edema for 20 days month with progressive dyspnea and 2 weeks of evolution.
The patient is admitted to hospital ward for case study and evolution.
Analytical, arterial blood gases, electrocardiogram, echocardiogram and ultrasound.
The ecocradiograma no relevant findings. Furosemide treatment is started and edeama lowe limbs disappear within 48 hours

Patient shows normochromic, normocytic anemia and 2 pool os plateletd are administered.
Due to Maintained renal failure of probable pre reanl origin (renal function previous to the hospitalization is normal) and poorly controlled blood pressure is measured at nephrology. Discharged is decided once improves kidney funtion and blood pressure control

Discharged date: 10 August 2015
event related to tumor disease
Additional information:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumour

## Confidential Unblinded Report - With Suspect Products and Serious Events

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Neutropenia
Narrative: This 40-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 24th February 2015, for prophylaxis.

On PPD 144 days after receiving Herpes zoster vs Placebo, the subject developed moderate grade 2 neutropenia. Serious criteria included hospitalization and GSK medically significant. The outcome of neutropenia was recovered/resolved on 21st July 2015.

The investigator considered that there was no reasonable possibility that the neutropenia may have been caused by Herpes zoster vs Placebo.

Investigator Comments:
The patient reports that it has been entered for neutropenia. The next day will bring reports Information not available atually. (10/12/2015)

Additional details:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD
Randomization Number:

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Case ID: PPD<br>Suspect Products: Hz/su + AS01B<br>Serious Events: Cholangiocarcinoma


#### Abstract

Narrative: This 70-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 2nd March 2015, for prophylaxis.

The subject's past medical history included angioedema. Concurrent medical conditions included hypertension, cholangiocarcinoma and thyroidectomy total. Concomitant products included levothyroxine sodium (Levotiroxina Sodica) and enalapril.

> On PPD 249 days after receiving Herpes zoster vs Placebo, the subject developed moderate - grade 2 extrahepatic cholangiocarcinoma. Serious criteria included hospitalization and GSK medically significant. The subject was treated with metamizole, paracetamol, piperacillin, tazobactam (Piperacillin + Tazobactam), glucose (Serum Glucose), omeprazole and piperacillin. The outcome of extrahepatic cholangiocarcinoma was not recovered/not resolved. > The investigator considered that there was no reasonable possibility that the extrahepatic cholangiocarcinoma may have been caused by Herpes zoster vs Placebo.


Diagnostic results (unless otherwise stated, normal values were not provided):
On 20th November 2015, Blood bilirubin result was $3.30 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.30 , normal high: 1.1). On 21st November 2015, Blood bilirubin result was $3.30 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.30, normal high: 1.1). On 23rd November 2015, Blood bilirubin result was $4.00 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.30, normal high: 1.1). On 27th November 2015, Blood bilirubin result was $2.70 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.30 , normal high: 1.1).

Investigator Comments :
70 year old woman who comes to the emergency exit pericatheter pus on 06Nov2015
No fever refersrekates increased abdominal discomfort, good oral tolerance, nausea or vomiting, no jaundice, dark urine or not acolia

Diagnostic trials
Stage IV extrahepatic cholangiocarcinoma
Acute cholangitis related to prior in a patient with biliary drainage catheter
Intrahepatic dilatation of bile duct in relation to the previous
Sign in charge of Medixal Oncology acute cholangitis in relation to biliary diversion catheter
The patient discharged on 11 November 2015 for clinical stability, analytical and hemodynamics.
Admnission date is on 06 November 2015

## Confidential Unblinded Report - With Suspect Products and Serious Events

20 November 2015: Referred patient consultations Medical Oncology worsening liver function and increased bilirubin imaging test to assess and if necessary revise biliary drainage.

Patient presenting with jaundice, remaining hemodynamically stable throughout their stay in the Hospital. Upon arrival you have not completed antibiotic with which he was an itinerant. Cultures were taken and piperacillin / tazobactam is started empirically to cover possible biliary focus and / or skin in a patient with recent placement of biliary drainage.
During admission, abdominal ultrasound is done indicating dilatation of the intra- and extrahepatic bile duct so bile drainage is exchanged, checking positioning and permeability contrast and fluoroscopy, objectifying way to duodenum on 27 November.
Given prior to discharge and growth of E . faecium antibiotic linezolid given the low sensitivity of the germ to other oral antibiotics it was modified.
It is discharged afebrile, hemodynamically stable and clear analytical improvement with high bilirubin of $2.7 \mathrm{mg} / \mathrm{dL}$.

Date of discharged: 27 November 2015
REASON FOR HIGH
Stability clinical, hemodynamic and significant clinical improvement.
reason for hospitalization: hyperbilirubinemia on 20 November 2015
SAE related tumor disease
Not recovered (11/01/17)Died PPD 16.
Additional details:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD

Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Sepsis, Cholangitis acute
Narrative: This 70-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 2nd March 2015, for prophylaxis.

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Concurrent medical conditions included hypothyroidism, hypertension and drug allergy. Concomitant products included levothyroxine sodium (Eutirox).

On PPD 1 year and 7 days after receiving Herpes zoster vs Placebo, the subject developed moderate - grade 2 sepsis. Serious criteria included hospitalization and GSK medically significant. Additional event(s) included moderate - grade 2 cholangitis acute on 8th March 2016 with serious criteria of hospitalization and GSK medically significant. The subject was treated with piperacillin (Piperacilina), omeprazole (Omeprazol), paracetamol and dexamethasone. The outcome of sepsis was not recovered/not resolved. The outcome(s) of the additional event(s) included cholangitis acute (not recovered/not resolved).

The investigator considered that there was no reasonable possibility that the sepsis and cholangitis acute may have been caused by Herpes zoster vs Placebo.
Diagnostic results (unless otherwise stated, normal values were not provided): On 14th March 2016, Alanine aminotransferase result was 54.00 u/L (normal low: 6.0, normal high: 40.0), Aspartate aminotransferase result was 73.00 u/L (normal low: 6.0, normal high: 40.0), Blood bilirubin result was 4.80 $\mathrm{mg} / \mathrm{dL}$ (normal low: 0.3, normal high: 1.1) and Gamma-glutamyltransferase result was $656.00 \mathrm{u} / \mathrm{L}$ (normal low: 6.0, normal high: 36.0).

Investigator Comments :
Patient who comes emergency room by persistent and abundant bilious exuded by external biliary drainage.
Refers dysthermia and shivering sensation, but without fever have measurable. Abdominal usual pain related cholangitis. It has not increased pain.
Colurica urine the clearer the last 4-5 days, no acolia. Previous weeks
Symptoms begin on March 8. Attended the emergency on March 14
Hospitalization for suspected infection in biliary drainage area.
Sepsis admitted for acute cholangitis after reviewing drain on 08/03/16. Discharge on 21 March 2016.
After starting antibiotic therapy with piperacillin tazobactam for 4 days improves liver function and bilirubin.
The patient has perfect general condition and is afebrile we decided discharged home.
SAE related to disease tumor.
Not recovered (05 April 2016)
Not recovered adverse event (10 Januanry 2017)
The patient died on PPD 2016
Additional details:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Case ID: PPD<br>Suspect Products: Vaccine placebo, DEXAMETHASONE<br>Serious Events: Hepatitis C


#### Abstract

Narrative: This 54-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 1st dose of Herpes zoster vs Placebo (intramuscular) on 22nd July 2013, for prophylaxis.

Co-suspect products included dexamethasone for vomiting. On PPD 45 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 viral hepatitis c. Serious criteria included hospitalization and GSK medically significant. The outcome of viral hepatitis c was recovered/resolved on 20th September 2013.

The investigator considered that there was no reasonable possibility that the viral hepatitis c may have been caused by Herpes zoster vs Placebo. Other possible cause(s) of the viral hepatitis c included concurrent medication.


On 5th September 2013, 2 days after receiving concomitant drug DEXAMETHASONE , the subject developed severe - grade 3 viral hepatitis c

Relevant Tests: Abdominal ultrasound performed on 17 sep 2013 without relevant findings Serology test for hepatitis done on 17sep2013 with the following results:

1. Antihepatitis $A$ antibody (lgM): not significant
2. Hepatitis $B$ surface antigen: not significant
3. Antihepatitis B core antibody: not significant
4. Antihepatitis B core antibody ( $\operatorname{lgM}$ ): not significant
5. Antihepatitis B surface antibody: minor to $10 \mathrm{UI} / \mathrm{L}$ (normal range: 0-10 UI/L)
6. Antihepatitis C antibody (lgG): present

Diagnostic results (unless otherwise stated, normal values were not provided): On 17th September 2013, Alanine aminotransferase result was 730 IU/L (normal low: 0, normal high: 40), Aspartate aminotransferase result was 120 IU/L (normal low: 0, normal high: 40), Hepatitis C antibody positive result was POSITIF and Ultrasound abdomen result was NORMAL unknown. On 20th September 2013, Alanine aminotransferase result was 434 IU/L (normal low: 0, normal high: 40) and Aspartate aminotransferase result was 77 IU/L (normal low: 0, normal high: 40). On 1st October 2013, Alanine aminotransferase result was 286 IU/L (normal low: 0, normal high: 40) and Aspartate aminotransferase result was 57 IU/L (normal low: 0, normal high: 40).

## Investigator Comments :

The patient came to medical visit on 17/sep/2013 showing increased levels of ALT and AST in blood test. The patient presented mild asthenia, mild renal failure and severe nausea and vomiting (these events did not meet SAE criteria). Although the abdominal ultrasound result, done on that same day, was normal, the patient was hospitalized on 17/sep/2013 to control the ALT and AST levels and also to perform further tests.
A serology test was performed (17/sep/2013) showing presence of anti hepatitis $C$ antibodies. With these findings and due to the fact the patient was taking steroids for vomiting and nauseas caused by

## Confidential Unblinded Report - With Suspect Products and Serious Events

chemotherapy, the PI considers that the patient suffered a hepatitis $C$ reactivation without liver dysfunction because of steroids, not related to study vaccine. Slnce there is an improvement of transaminases levels and his general status, the patient was discharged on 20/sep/2013

Case unblinded due to end of study Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Head and neck cancer

Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 22 July 2013 and 09 September 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical conditions at the time of the event included head and neck cancer.
On PPD four months after the 2nd dose of Blinded vaccine, this 55-year-old subject developed disease progression (head and neck cancer). The subject was hospitalised. The subject was treated with ketoprofen, cephazolin sodium, ondansetron hydrochloride, pantoprazole, Augmentin, paracetamol and omeprazole. The event was unresolved at time of reporting. The investigator considered that there was no reasonable possibility that the disease progression (head and neck cancer) may have been caused by investigational product.

Investigator Comments:
The patient experienced an abscess in the back which was biopsied and the report confirmed head and neck metastases in skin. So, the patient was hospitalized on 30/jan/2014 in order to resect this tumour lesion. Since the patient clinical evolution was good, he was discharged on 03/feb/2014

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Death

Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 10 September 2013 he received the 1st dose of Varicella Zoster vaccine gE ( 50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD 2013, 37 days after the 1st dose of Blinded vaccine, this 63-year-old subject died. An autopsy was not performed. The investigator considered that there was no reasonable possibility that the death nos may have been caused by investigational product.

Investigator Comments:
The patient s sister-in-law phoned the site to report his death home on PPD 2013. She told PI that the patient was having a shower, when the patient experimented diziness with severe dyspnea and he fainted. Although emergency number was called, the patient had already died. The PI considers that the death can be related to pulmonary thromboembolism or cardiac arrythmia but these have not been checked. The day before his death, the patient did not have any symptoms.

Case unblinded due to end of study Unblinding Date is 10-FEB-17
The subject died 37 days after receiving Herpes zoster vs placebo. The cause of death can be considered to be pulmonary thromboembolism or cardiac arrythmia. Causal association with vaccine is difficult to assess as limited information is provided for adequate causality assessment.Based on unblnding information,the vaccine received by subject was Herpes zoster vaccine.

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Bronchial obstruction

Narrative: This 63-year-old male subject was enrolled in a blinded study titled A phase IIIIII, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 16th December 2013, for prophylaxis.

## Confidential Unblinded Report - With Suspect Products and Serious Events

Concurrent medical conditions included squamous cell carcinoma of lung.
On PPD 266 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 bronchial obstruction. Serious criteria included hospitalization and GSK medically significant. The outcome of bronchial obstruction was recovered/resolved on 14th November 2014.

The investigator considered that there was no reasonable possibility that the bronchial obstruction may have been caused by Herpes zoster vs Placebo.

Relevant Tests: Thorax CT (8/sep/2014): necrotic mass in upper right lobe related to cancer relapse Thorax CT (22/oct/2014): increased of necrotic mass in upper right lobe, suspictious of tumor progression fibrobroncoscopy (23oct2014): tumoral mass obsctructing the right bronchus partially
fibrobroncoscopy was done on 07nov2014 a necrotic mass which was obstructing the bright bronchus
Investigator Comments:
During the previous hospitalization, a fibrobroncoscopy was done on 07nov2014 where a necrotic mass which was obstructing the bright bronchus (more than $90 \%$ ). Due to this finding, criotherapy was performed to resect the mass on 14/nov2014 with a partially desobstruction and good sympthomatic evolution. After less than 24 hours of observation, the patient was discharged on 15nov2014. Obviously, this mass is related to the tumor.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Pneumonia
Narrative: This 63-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 16th December 2013, for prophylaxis.

Concurrent medical conditions included squamous cell carcinoma of lung. Concomitant products included pantoprazole (Pantoprazol), saccharomyces boulardii and enoxaparin.

## Confidential Unblinded Report - With Suspect Products and Serious Events

On PPD 266 days after receiving Herpes zoster vs Placebo the subject developed severe - grade 3 pneumonia. Serious criteria included hospitalization and GSK medically significant. The subject was treated with amikacin sulphate (Amikacina), linezolid, paracetamol, fluconazole, prednisone (Prednisona), amoxicillin trihydrate, clavulanate potassium (Amoxicilina/Clavulanico), omeprazole (Omeprazol), meropenem, Flucticasona+Salmeterol, enoxaparin and saccharomyces boulardii. The outcome of pneumonia was recovered/resolved on 22nd October 2014.

The investigator considered that there was no reasonable possibility that the pneumonia may have been caused by Herpes zoster vs Placebo.

Relevant Tests: Thorax xray (22sep2014): atelectasis with associatted infiltrate upper right lobe Thorax CT (22sep2014): right pleural effussion and micronodes with infection/inflamatory etiology. possible pneumonia with abscess
Thorax CT (01Oct2014): good clinical evolution
Fibrobronchoscopy (23sep2014): lesion in right bronchial system obsctructing partially. No sign of fistula
Pleural effusion culture (24sep2014). negative
Endobronchial aspirant culture (24sep2014): negative
Sputum culture (23sep2014). Candida albicans isolated.
Blood culture: negative
Stool culture and toxine Chlostridium difficile: negative
Thorax CT (22oct2014): confirmation of improve of infection/inflamatory etiology
Diagnostic results (unless otherwise stated, normal values were not provided): On 22nd September 2014, C-reactive protein result was $392,4 \mathrm{mg} / \mathrm{L}$ (normal low: 0 , normal high: 5) and Neutrophil count result was $8.018 / \mathrm{mcL}$ (normal low: 1500, normal high: 7500). On 23rd September 2014, Neutrophil count result was 4350 /mcL (normal low: 1500, normal high: 7500).

Investigator Comments :
Patient with lung cancer comes to site due to dyspnea, malaise, cough and expectorations (first episoide of them was 2 weeks ago) and fever (since 18sep2014) On 22sep2014 a thorax x-ray and blood test are performed whit signs of pneumonia. For that reason, patient was hospitalized on 22/sep/2014 for treatment and further. 72 hours after the admission, fever was resolved and dyspnea decreased.
Treatment with antibiotherapy was started. Fluconazol was adminsitred since Candida albicans was isoletd in a sputum culture.
Due to the treament taken, his status improved since 04/oct/2014 so he was discharged on 07oct2014 keeping with antibiotherapy for 14 days after the end of hospitalization.
This event is related to his underlying disease.
Additional details:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Enteritis
Narrative: This 60-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 18th March 2014, for prophylaxis.

On PPD 282 days after receiving Herpes zoster vs Placebo, the subject developed moderate - grade 2 ileitis. Serious criteria included hospitalization. The subject was treated with hyoscine butylbromide (Butilescopolamina), metamizole sodium (Metamizol), piperacillin (Piperacilina), tazobactam, levofloxacin (Levofloxacino) and metronidazole (Metronidazol). The outcome of ileitis was recovered/resolved on 31st December 2014.

The investigator considered that there was no reasonable possibility that the ileitis may have been caused by Herpes zoster vs Placebo.

Relevant Tests: Thorax-abdomen-pelvis CT scan (26/dec/2014). findings related to cecoileitis.
Diagnostic results (unless otherwise stated, normal values were not provided): On 24th December 2014, Blood creatine result was $1.23 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6 , normal high: 1.3 ), C-reactive protein result was $23.9 \mathrm{mg} / \mathrm{dL}$ (normal low: 0, normal high: 5.0) and Neutrophil count result was $960 / \mathrm{mm} 3$ (normal low: 1500, normal high: 7500). On 29th December 2014, Blood creatine result was $1.29 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.6 , normal high: 1.3), C-reactive protein result was $13.9 \mathrm{mg} / \mathrm{dL}$ (normal low: 0, normal high: 5.0) and Neutrophil count result was 1207 /mm3 (normal low: 1500, normal high: 7500).

Investigator Comments:
The patient came to emergency room on 25 dec 2014 since he experienced fever, diarrhea and vomiting which does not stop with taking codeisan. A thorax-abdomen-pelvis was done on 26/dec/2014 where signs of cecoileitis can be assessed apart form progresion of his colorectal cancer. The patient received analgesic treatment and antibiotics as prophylaxis. The patient was discharged on 31/dec/2014. This event could be related to evolution of the disease.

Additional details:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

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Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Mouth ulceration
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 19 April 2013 and 03 June 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.
On PPD 119 days after the 2nd dose of Blinded vaccine, this 59-year-old subject developed buccal mucosa ulceration. The subject was hospitalised. The subject was treated with tramadol hydrochloride, Amoxicillin-clavulanic acid, metamizole magnesium, paracetamol, filgrastim, platelet concentrate, metoclopramide hydrochloride, insulin, lorazepam, ketoprofen and Movicol. The event resolved on 07 October 2013. The investigator considered that there was no reasonable possibility that the buccal mucosa ulceration may have been caused by investigational product.
Investigator Comments :
patient went to emergency room service on 30sept2013 due to bucal pain, without fever, nauseas, vomits or abdominal pain. after medication patient was better, with the third molar tooth infected. patient was discharged on 03oct2013, and malignity has been ruled out
Case unblinded due to end of study
Unblinding Date is 10-FEB-17
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Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Myocardial infarction
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 19 April 2013 and 03 June 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical condition at the time of the event included hypercholesterolemia.

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On PPD five months after the 2nd dose of Blinded vaccine, this 59-year-old subject developed cardiac infarction. The subject was hospitalised. The subject was treated with captopril, heparin, ivabradine hydrochloride, spironolactone, frusemide, carvedilol, enalapril and omeprazole. The event resolved on 18 November 2013. The investigator considered that there was no reasonable possibility that the cardiac infarction may have been caused by investigational product.

Investigator Comments:
Patient went on 01nov2013 to the emergency room service due to dysonea, ortopnea, cough and edemas in lower limbs. Patient was diagnosed cardiac infart killip II. Patient was discharged on 18nov2013.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Lung neoplasm malignant
Narrative: This 71-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 28th June 2013, for prophylaxis.

On PPD 128 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 lung cancer. Serious criteria included death, hospitalization and GSK medically significant. The subject was treated with amoxicillin, clavulanate potassium (Augmentin), fluconazole, filgrastim (Neupogen), lidocaine, meropenem, OMEPRAZOLE (OMEPRAZOL), methylprednisolone (Urbason), paracetamol, metamizole magnesium (Nolotil), enoxaparin, lorazepam, dexketoprofen, hydrocortisone sodium phosphate (Actocortina), dopamine, ipratropium bromide (Atrovent), metoclopramide (Primperan), hyoscine butylbromide (Buscapina), midazolam maleate (Dormicum), MORPHINE and HALOPERIDOL. | The outcome of lung cancer was fatal on PPD 2013. The subject died on PPD 2013. |
| :--- | :--- | The reported cause of death was lung cancer. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the lung cancer may have been caused by Herpes zoster vs Placebo.

Relevant Tests: Hemoculture 5Nov2013: sterile after 5 days of incubation.

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Uroculture 5Nov2013: less than $10.000 \mathrm{col} / \mathrm{ml}$. Diagnostic results (unless otherwise stated, normal values were not provided): On 6th November 2013, Neutrophil count result was $0.2 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.8, normal high: 7.5). On 7th November 2013, Neutrophil count result was $0.0 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.8, normal high: 7.5). On 8th November 2013, Neutrophil count result was $0.0 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.8, normal high: 7.5). On 9th November 2013, Neutrophil count result was $1.5 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.8, normal high: 7.5).

Investigator Comments:
The patient was admitted in the Hospital on 05 nov2013 due to odynophagia, hyperoxia and cough, increased greenish yellow sputum with dyspnea and fever in the last 48 hours.
Generalized musculoskeletal pain.
Concomitant to febrile neutropenia grade IV, he had also mucositis grade III, and consolidative pneumonia.
After antibiotic treatment broad-spectrum and oxygen therapy the patient had not improved the overall status, and finally he died onPPD 2013.
Patient had progression disease, so neutropenia febrile could be a sympt of it.
Additional details:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.
Subject withdrawn from study due to this event.
Case unblinded due to end of study
Unblinding Date is 10-FEB-17
The subject developed lung neoplasm malignant 128 days after receiving Herpes zoster vs Placebo and died due to this after 7 days. The event is related to the progression of pre-existing condition. Causal association with the vaccine seems unlikely

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Musculoskeletal chest pain
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 28 May 2013 and 09 July 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD 69 days after the 2nd dose of Blinded vaccine, this 78-year-old subject developed costal pain. The subject was hospitalised. The subject was treated with Targin, levofloxacin, candesartan cilexetil, ipratropium bromide, meropenem, vancomycin, digoxin, Amoxicillin-clavulanic acid, nebivolol hydrochloride, haloperidol, salbutamol sulphate, megestrol acetate, primidone, enoxaparin, pregabalin,

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## Unblinded Report - With Suspect Products and Serious Events

Movicol, lorazepam, budesonide, nystatin, zolpidem, cloperastine hydrochloride, methylprednisolone, morphine, ketoprofen, paracetamol, midazolam, dipyrone, ketorolac trometamol, hyoscine butylbromide, diclofenac, venlafaxine hydrochloride and metoclopramide. The event resolved on 04 February 2014. The investigator considered that there was no reasonable possibility that the costal pain may have been caused by investigational product.

Investigator Comments:
Patient went to the emergency room service on 16 Nov 2013 due to hemitorax pain, from 2 months approximately, also dyspnea increased and vomits during the last days (exact start date not available). The diagnosis was right costal pain probably secondary to infiltration costal tumour.
Endoscopy and torax radiography were done, with normal results.
Patient was derived on 05dec2013 to the palliative unit care. On 04feb2014 patient is discharged from palliative unit care.
During the hospitalization patient had: left shoulder pain, bacteriemia, respiratory infection, dyspnea of minimum efforts, supraventricular tachyarrhythmia, hypertension, depression, anorexia, paresis and delirium. Hemoculture performed on 04dec2013 was positive .
The only information we have until now is that patient was discharged on 04Feb2014. At visit 5 we will confirm if the stop date of this SAE is the same as the discharge date.
Visit 5 will not be done as this patient is consent withdrawal on 15Jul2014.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Seizure
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 07 June 2013 and 10 July 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical conditions at the time of the event included epileptic crisis.
On PPD three days after the 2nd dose of Blinded vaccine, this 71-year-old subject developed seizure. The subject was hospitalised. The subject was treated with levetiracetam, Augmentin, meropenem, clonazepam, hydrocortisone sodium phosphate, vancomycin, haloperidol, lacosamide, levofloxacin and Movicol. The event resolved on 25 July 2013. The investigator considered that there was

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## Unblinded Report - With Suspect Products and Serious Events

no reasonable possibility that the seizure may have been caused by investigational product.
Investigator Comments :
On 13jul2013 patient went to emergency room service due to shock, loss of consciousness, vomiting and seizures,Viral encephalitis was discarded
Diagnosis is focal seizures crisis subintrantes generalized, in patient with a history of epilepsy after head trauma, with sensitive and hemiparesis right afasia.
The evolution of patient is good. During hospitalization the patient had also febrile syndrome. On 05aug2013 patient is moved to palliative unit care
This sae has been updated after check medical files, it has been confirmed that this sae is no pimd. On 23Aug2013 the patient was discharged according to his clinical stability.

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B, Paclitaxel, Carboplatine
Serious Events: Febrile neutropenia
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 05 July 2013 and 29 August 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE $(50 \mathrm{mcg})$ adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical conditions at the time of the event included lung cancer.
On PPD 12 days after the 1st dose of Blinded vaccine and two days after a dose of Paclitaxel and Carboplatine (treatment for lung cancer), this 74-year-old subject developed febrile neutropenia. The subject was hospitalised. The subject was treated with Augmentin, ciprofloxacin, filgrastim, metoclopramide hydrochloride, granisetron hydrochloride, paracetamol, enoxaparin, omeprazole, gabapentin, amitriptyline hydrochloride, oxycodone hydrochloride, lignocaine hydrochloride and metronidazole. The event resolved on 30 July 2013. The investigator considered that there was no reasonable possibility that the febrile neutropenia may have been caused by investigational product and that the event was possibly due to the concomitant medications, paclitaxel (manufacturer Bristol-Myers Squibb) and carboplatin (manufacturer Non-GSK).

Investigator Comments :
Patient went to emergency room service on 20 July 2013 due to diarrhea, fever and vomiting.
Patient diagnose was febrile neutropenia related to the anti-cancer therapies.
Concomitant to this event, the patient had mucositis grade 2, anemia grade 2, and thrombocytopenia grade 3. Mucositis, anemia and thrombocytopenia were not considered as SAE.

## Confidential Unblinded Report - With Suspect Products and Serious Events

On 30 July 2013 patient was discharged after overall recovery.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Respiratory tract infection
Narrative: This 74-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 29th August 2013, for prophylaxis.

On PPD 157 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 respiratory infection. Serious criteria included death, hospitalization and GSK medically significant. The subject was treated with azithromycin, meropenem (Meronem), ipratropium bromide (Atrovent), enoxaparin (Clexane), omeprazole (Omeprazol), methylprednisolone (Urbason), paracetamol, candesartan, gabapentin (Neurontin), oxycodone hydrochloride (Oxycontin), naproxen, macrogol, potassium chloride, sodium bicarbonate, sodium chloride (Movicol), ibuprofen, metoclopramide (Primperan), lorazepam, hydrocortisone sodium phosphate (Actocortina), amlodipine, dexamethasone, dexketoprofen trometamol (Enantyum), morphine, sodium citrate, midazolam and hyoscine butylbromide (Buscapina). The outcome of respiratory infection was fatal on PPD 2014. The subject died on PPD 2014. The reported cause of death was respiratory infection. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the respiratory infection may have been caused by Herpes zoster vs Placebo.

Relevant Tests: TORAX RADIOGRAPHY: 7FEB2014: interstitial infiltrate UPPER LIMBS RADIOGRAPHY: 12FEB2014: metastasic lesions TORAX RADIOGRAPHY: 12FEB2014: improvement of the interstitial infiltrate Diagnostic results (unless otherwise stated, normal values were not provided): On 7th February 2014, C-reactive protein result was $22.4 \mathrm{mg} / \mathrm{dL}$ (normal low: 0.0, normal high: 0.5).

Investigator Comments

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Patient went to the emergency room service on 07feb2014, due to previous five days with cough with expectorations, dyspnea of minimun effort the last two days and associated with fever on 07Feb2014.

Patient was diagnosed respiratory infection, with no improvement, and died on PPD 2014.
Start date (admision) of SAE is 2 feb2014 and end date (discharge) is PPD 2014
Additional information
Subject withdrawn from study due to this event RESPIRATORY INFECTION.
Case unblinded due to end of study
Unblinding Date is $10-$ FEB-17
The subject developed respiratory tract infection 157 days after receiving Herpes zoster vs Placebo and died due to this disease. Due to the biological nature of the event, the causality with the vaccine seems unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B, Capecitabine
Serious Events: Gastroenteritis, Respiratory tract infection


#### Abstract

Narrative: This 68-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 1st dose of Herpes zoster vs Placebo (intramuscular) on 27th May 2013, for prophylaxis.

Co-suspect products included Capecitabine for chemotherapy. On PPD 9 days after receiving Herpes zoster vs Placebo, the subject developed moderate grade 2 gastroenteritis. Serious criteria included hospitalization. Additional event(s) included moderate grade 2 respiratory infection on 16th June 2013 with serious criteria of hospitalization and GSK medically significant. The subject was treated with metamizole, LOPERAMIDE HYDROCHLORIDE (FORTASEC), METOCLOPRAMIDE (PRIMPERAN), MEROPENEM, METRONIDAZOLE (METRONIDAZOL), AMOXICILLIN + CLAVULANIC ACID (Amoxicillin-clavulanic acid), VANCOMYCIN, CEFIXIME, AMOXICILLIN, CLAVULANIC ACID (AMOXICILLIN-CLAVULANIC ACID), PARACETAMOL, LEVOFLOXACIN, OMEPRAZOLE (OMEPRAZOL) and Levofloxacin. The outcome of gastroenteritis was recovered/resolved on 21st June 2013. The outcome(s) of the additional event(s) included respiratory infection (recovered/resolved on 1st July 2013).

The investigator considered that there was no reasonable possibility that the gastroenteritis and


## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

respiratory infection may have been caused by Herpes zoster vs Placebo. Other possible cause(s) of the gastroenteritis included concurrent medication.

Relevant Tests: 8.Jun. 2103 - abdominal X Rays: Result: nonspecific luminogram After this abdominal X Ray, several thorax and abdominal X Rays were performed in order to follow the diagnosis
18.Jun.2013: Test on stool: Normal result
19.Jun.2013: Test on stool: Normal result
18.Jun.2013: CT Scan for abdomen and pelvis: Abnormal due to gastroenteritis and colorrectal carcinoma. Diagnostic results (unless otherwise stated, normal values were not provided): On 10th June 2013, Neutrophil count result was $0.9 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 1.8 , normal high: 7.4 ) and White blood cell count result was $1.6 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11.3).

Investigator Comments:
Patient came to emergency room on 8 June. 2013 due to diarrhea, vomiting and abdominal pain. Gastroenteritis was diagnosed and he was hospitalized to treat this event and receive intravenous therapy. This event was related with anticancer therapy. During hospitalization the patient started also with upper respiratory tract infection and other treatments were administered to treat this cconcomitant event. This event is concomitant to the hospitalization and it is not an additional SAE. He was discharged on 21.June. 2013 after the improvement of his clinical symptoms.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Febrile neutropenia
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 27 May 2013 and 01 July 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD eight days after the 2nd dose of Blinded vaccine, this 68-year-old subject developed febrile neutropenia. The subject was hospitalised. The subject was treated with loperamide hydrochloride, metoclopramide hydrochloride, metronidazole, ciprofloxacin, Tazocel and filgrastim. The event resolved on 23 July 2013. The investigator considered that there was no reasonable possibility that the febrile neutropenia may have been caused by investigational product.

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Investigator Comments :
Patient came to emergency room on 16.July. 2013 due to diarrhea and fever. Due to previous hospitaization and similar symptoms, patient was hospitalized to treat this event and receive intravenous therapy. Finally, test on stoll and blood culture performed were normal. During hospitalization the patient started also with neutropenia and filgrastim was administered to treat this concomitant event. After resolution of all the clinical symptoms, patient was discharged on 25Jul2013. FInal Diagnosis was febrile neutropenia grade 3 with abdominal focus.

Case unblinded due to end of study
Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
PPD

Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Superior vena cava occlusion, Liposarcoma
Narrative: This 47-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 16th January 2014, for prophylaxis.

Concurrent medical conditions included liposarcoma.
On PPD
224 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 superior vena cava occlusion. Serious criteria included death, hospitalization and GSK medically significant. Additional event(s) included severe - grade 3 liposarcoma on 28th August 2014 with serious criteria of death, hospitalization and GSK medically significant. The subject was treated with ceftriaxone, chlorpromazine, levetiracetam, dexamethasone, levofloxacin (Levofloxacine), morphine and pantoprazole. The outcome of superior vena cava occlusion was fatal on PPD 2014. The outcome(s) of the additional event(s) included liposarcoma (fatal on PPD 2014). The subject died on PPD PPD 2014. The reported cause of death was superior vena cava occlusion and liposarcoma. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the superior vena cava occlusion and liposarcoma may have been caused by Herpes zoster vs Placebo.

Relevant Tests: Eco doppler performed on 04sep2014, shows oscilating flow of right yugular and subclavia veins probably due to stenosis of vein superior cava vein.
Cava vein phlebography performed on 11sep2014. Shows deplacement of superior cava vein due to

## Confidential Unblinded Report - With Suspect Products and Serious Events

pleural mass.
Investigator Comments:
Patient is admitted in emergency room to to worsening of general status, loss of conciousness and weakness on 01sep2014. Eco doppler and phlebography are perfomed during hospitalization. They show deplacement of superior cava vein. On previous CT scan on 28 ago2014 there was already diminished flow of superior cava vein related to tumoral compression.
24 hours after the phlebography patient is asymptomatic and without pain, so patient is discharged. Principal diagnosis is syncope related to superior cava vein compression. This event is related to the disease under study.
Patient experiences worsening of this same symptoms, reason why comes to emergency room but no hospitalization is required. Patient is discharged from emergency room on 14oct2014. Patient was transferred to a palliative care hospital. On 23mar2015 we are aware of patient exitus occurred on PPD 2014. Exitus is due to progression disease.
Please, note that patient came to ER on 30 Aug2014 and was hospitalized. He left this hospital on $140 c t 2014$ and was admitted to an other hospital where finally patient died on PPD 2014.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding Date is 10-FEB-17
The subject developed superior vena cava occlusion and liposarcoma 224 days after receiving Herpes zoster vs Placebo and died later due to these events. The events are considered related to underlying disease or anti-cancer therapies.Causal association with vaccine is unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Seizure

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## Confidential Unblinded Report - With Suspect Products and Serious Events

The investigator considered that there was no reasonable possibility that the seizure cerebral may have been caused by Herpes zoster vs Placebo.

Relevant Tests: Brain CT Scan without contrast done on 15 Apr 2013: no metastases. Electrocardiogram on 15 apr 2013: not clinically significant Blood pressure: 140/70 (not clinically significant) on 17 apr 2013 and 184/57 on 15 april 2013 Diagnostic results (unless otherwise stated, normal values were not provided): On 15th April 2013, Blood creatine phosphokinase result was 80 IU/L (normal low: 1, normal high: 190), Blood phosphorus result was 1.2 $\mathrm{mg} / \mathrm{dL}$ (normal low: 2.5, normal high: 4.5) and Troponin I result was more than $0.01 \mathrm{mg} / \mathrm{ml}$ (normal low: 0.001, normal high: 0.05).

Investigator Comments:
Patient with lung cancer, go to the hospital for a possible syncope. The patient is admitted 15Apr2013.
26Apr2013:
The following test were performed:
Holter (18Apr2013): Not clinically significant.
Doppler SAT (19Apr2013): atheromas were found. Not clinically significant.
Brain MRI (23Apr2013): Not clinically significant
Electroencephalogram /17apr2013): Normal. Not clinically significant.
Echocardiogram (22Apr2013): LVEF 60.0\%
With these findings, diagnosis was seizures (reviewed by neurologist). The patient started taking
Levetiracetam ( $250 \mathrm{mg} / 12 \mathrm{~h} \mathrm{PO}$ ) forcontrol of news seizures. The patient was discharged on 24Apr2013. 16May2013: Actions taken with the investigational product are not appicable and medications have been updated.
29May2013, 30May2013 and 13Jun2013 more follow-up have been done to update information regarding this event.
1Jul2013 Follow-up was done to update the stop date of leviracetam.Patient with lung cancer, go to the hospital for a possible syncope. The patient is admitted 15Apr2013.
26Apr2013:
The following test were performed:
Holter (18Apr2013): Not clinically significant.
Doppler SAT (19Apr2013): atheromas were found. Not clinically significant.
Brain MRI (23Apr2013): Not clinically significant
Electroencephalogram /17apr2013): Normal. Not clinically significant.
Echocardiogram (22Apr2013): LVEF 60.0\%
With these findings, diagnosis was seizures (reviewed by neurologist). The patient started taking
Levetiracetam ( $250 \mathrm{mg} / 12 \mathrm{~h} \mathrm{PO}$ ) forcontrol of news seizures. The patient was discharged on 24Apr2013.
16May2013: Actions taken with the investigational product are not appicable and medications have been updated.
29May2013, 30May2013 and 13Jun2013 more follow-up have been done to update information regarding this event.
1Jul2013 Follow-up was done to update the stop date of leviracetam.
Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Lung neoplasm malignant
Narrative: This 72-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 29th May 2013, for prophylaxis. On 29th May 2013, the dose was administered.

Concurrent medical conditions included lung cancer.
On PPD 247 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 lung cancer. Serious criteria included death, hospitalization and GSK medically significant. The subject was treated with Antibiotic and (Corticosteroids). The outcome of lung cancer was fatal on PPD PPD 2014. The subject died on PPD 2014. The reported cause of death was lung cancer. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the lung cancer may have been caused by Herpes zoster vs Placebo.

## Relevant Tests:

Thorax X-Ray performed on 1Feb2014 showed diffuse infiltrates.
Thorax TCperformed on 1Feb2014 discarded pulmonary thromboembolism but showed progression disease with carcinomatous lymphangitis. Diagnostic results (unless otherwise stated, normal values were not provided):
On 1st February 2014, Oxygen saturation result was 94 \% (normal low: 95, normal high: 100).
Investigator Comments:
The patient came to the emergency department due to respratory insufficiency. The patient was admitted to hospital oncology on 1Feb2014 starting treatment with antibiotics, corticosteroids and oxygen. The patient progressed badly and died on PPD 2014. Respiratory insufficiency was due to the disease/tumour progression.

Additional Information:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding Date is 10-FEB-17
The subject developed malignant lung neoplasm 247 days after receiving Herpes zoster vs Placebo and died 3 days later due to the respiratory insufficiency caused by the progression of lung neoplasm. The causal association of the event with the vaccine seems unlikely.

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Febrile neutropenia
Narrative: This 73-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 1st dose of Herpes zoster vs Placebo (intramuscular) on 8th May 2013, for prophylaxis.

On PPD 6 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 febrile neutropenia. Serious criteria included hospitalization and GSK medically significant. The subject was treated with enoxaparin, filgrastim, paracetamol, ceftazidime, omeprazole (Omeprazol) and amoxicillin + clavulanic acid (Augmentine Plus). Rechallenge with Herpes zoster vs Placebo was positive. The outcome of febrile neutropenia was recovered/resolved on 26th May 2013.

The investigator considered that there was no reasonable possibility that the febrile neutropenia may have been caused by Herpes zoster vs Placebo.

Diagnostic results (unless otherwise stated, normal values were not provided): On 17th May 2013, Neutrophil count result was 16.8 \% (normal low: 40.0, normal high: 74.0). On 18th May 2013, Neutrophil count result was 32.8 \% (normal low: 40.0, normal high: 74.0). On 19th May 2013, Neutrophil count result was 67.3 \% (normal low: 40.0, normal high: 74.0).

Investigator Comments :
Patient was admitted at the hospital on 17May2013 and was discharged on 19May2013 with neuthophils between the normal ranges and without fever.

Additional Information:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Infected dermal cyst

Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 08 May 2013 and 26 June 2013 he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD 28 days after the 1st dose of Blinded vaccine, this 73-year-old subject developed scrotal sebaceous cyst infected. The subject was hospitalised. The subject was treated with Augmentin and ibuprofen. The event resolved on 13 June 2013. The investigator considered that there was no reasonable possibility that the scrotal sebaceous cyst infected may have been caused by investigational product.

Investigator Comments :
Patient comes to emergency department on 5th June with fever of 38 degrees celsius by scrotal infected sebaceous cyst. At the Department of Urology they proceed to drainageand cleaning of the cyst. There will be medical care at the health care center of the patient. The patient was discharged on the 6th of June.
12 Aug 2013: The patient completed the cure in your health center on June 13, 2013.
Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Febrile neutropenia
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 08 May 2013 and 26 June 2013 he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD 10 days after the 2nd dose of Blinded vaccine, this 73-year-old subject developed neutropenic fever. The subject was hospitalised. The subject was treated with metronidazole, meropenem, paracetamol and filgrastim. The event resolved on 09 July 2013. The investigator considered that there was no reasonable possibility that the neutropenic fever may have been caused by investigational product.

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## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Investigator Comments :
Patient was admited at the hospital on 7 Jul 2013 and discharged on 9 Jul 2013 with neutrophils between the normal ranges and without fever.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Lung infection, Neutropenia
Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 12 June 2013 and 18 July 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD five months after the 2nd dose of Blinded vaccine, this 78-year-old subject developed lung infection and neutropenia. The subject was hospitalised. The subject was treated with Amoxicillin + clavulanic acid, filgrastim, red blood cells, linezolid, fluconazole, meropenem and salbutamol sulphate. The events resolved on 19 December 2013. The investigator considered that there was no reasonable possibility that the lung infection and neutropenia may have been caused by investigational product.

Investigator Comments:
The patient goes on 4 December at the emergy room for lung infection. Analytical tests are made and given antibiotic. The patient was hospitalized on 5 December 2013.starting antibiotic treatment with empirical amoxcilina-clavulanate and oxygen with GN.
Worsening respiratory clinic with dyspnea on minimal exertion and 88-89\% saturation, requiring VMK ( Salbutamol) and expands coverage
antibiotic meropenem, linezolid and fluconazole with clinical improvement, being able remove oxygen therapy after discharge. Fill 14 days meropenem, will continue in linezolid and fluconazole discharge to complete 10 days. PET-CT is performed without observing reassessment progression disease. The patient was discharged on December 19, 2013
The patient goes on 4 December at the emergency room for neutropenia. AAnalytical tests are made and given red cell transfusion 2 packs. The patient was hospitalized on 5 December 2013. The patient was discharged on December 19, 2013

## Confidential Unblinded Report - With Suspect Products and Serious Events

Case unblinded due to end of study Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Pneumonia

Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 12 June 2013 and 18 July 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD six months after the 2nd dose of Blinded vaccine, this 78-year-old subject developed pneumonia. The subject was hospitalised. The subject was treated with antibiotics. The subject died on PP PPD 2014 due to pneumonia. An autopsy was not performed. The investigator considered that there was no reasonable possibility that the pneumonia may have been caused by investigational product.

Investigator Comments:
the patient comes to the emergency department with fever of 38.5. The patient was admitted to plant the right basal pneumonia on 21 JAN 2014. Administered antibiotics without improvement. The patient died on PPD 2014

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding date is 10 Feb 17
The subject developed pneumonia 6 months after receiving Herpes zoster vs placebo and died due to this. The event is considered related to anti-cancer treatment or underlying disease.Causal association with vaccine seems unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
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## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Serious Events: Squamous cell carcinoma of lung
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 25 July 2013 and 26 August 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE $(50 \mathrm{mcg})$ adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical condition at the time of the event included squamous cell carcinoma of lung.
On PPD five months after the 2nd dose of Blinded vaccine, this 69-year-old subject developed squamous cell carcinoma of lung. The subject died on PPD 2014 due to squamous cell carcinoma of lung. An autopsy was not performed. The investigator considered that there was no reasonable possibility that the squamous cell carcinoma of lung may have been caused by investigational product .

Investigator Comments:
The patient died on PPD due to disease progression. The family communicates the patient s death. The TC SCAN performed on 21 January 2014 showed the disease progression. Disease progression was due to the disease/tumour (lung squamous cell carcinoma).

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding date is 10 Feb 17
The subject developed progression of squamous cell carcinoma of lung 5 months after receiving Herpes zoster vs placebo and died after 3 months due to this. Event is due to progression of underlying disease.Causal association with vaccine seems unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Urinary tract infection
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 14 May 2013 and 25 June 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical condition at the time of the event included urinary retention.
On PPD 30 days after the 1st dose of Blinded vaccine, this 65-year-old subject developed urinary tract infection. The subject was hospitalised. The subject was treated with paracetamol,

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

ciprofloxacin, Co-amoxiclav, gentamicin sulphate and Augmentin. The event resolved on 01 July 2013. The investigator considered that there was no reasonable possibility that the urinary tract infection may have been caused by investigational product.

Investigator Comments:
14th June 2013 - patient reviewed in clinic, pyrexial 38.0c. Neutrophils normal, urine dip showed protein +2 and blood +4 so commenced on oral Augmentin. Patient has urethral catheter in situ.
15th June 2013 - patient developed pyrexia 38.5c so attended local hospital and was admitted to Hospital the same day.
Patient also C/O pain and tenderness in supra pubic area impression of urine track infection. UTI given as final diagnosis but not confirmed by microbiology.
Commenced on additional antibiotics as listed and monitored.
17th June apyrexial so patient discharged on oral Ciprofloxacin and Co-Amoxiclav. Chemotherapy delayed by 1 week.

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Pleural effusion
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 14 May 2013 and 25 June 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD 59 days after the 2nd dose of Blinded vaccine, this 65-year-old subject developed left pleural effusion. The subject was hospitalised. The subject was treated with Augmentin. The event resolved on August 2013 (exact date was not specified). The investigator considered that there was no reasonable possibility that the left pleural effusion may have been caused by investigational product.

Investigator Comments:
Patient admitted to Ambulatory Care Unit on 23Aug2013 presenting with shortness of breath and feeling lethargic. Chest x-ray showed small left pleural effusion. This was thought to be disease related. A therapeutic pleural aspiration removed 100 ml fluid. Patient discharged on the same day (23Aug2013) on a course or oral Augmentin. Unknown if fully resolved as patient has not had a repeat scan.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

## Confidential Unblinded Report - With Suspect Products and Serious Events

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Pleural infection

Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 14 May 2013 and 25 June 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical condition at the time of the event included pleural effusion.
On PPD 66 days after the 2nd dose of Blinded vaccine, this 65-year-old subject developed infection of pleural fluid. The subject was hospitalised. The subject was treated with ondansetron hydrochloride, Tazocin and Co-amoxiclav. The event resolved on unspecified date in September 2013. The investigator considered that there was no reasonable possibility that the infection of pleural fluid may have been caused by investigational product.

Investigator Comments :
Admitted to hospital on 30Aug2013 with chest pain and increased temperature. Feeling nauseated with some vomiting after eating. Treated as suspected infection following pleural effusion.
Treated with IV antibiotics and discharged home on 31Aug2013 on a course of oral antibiotics.
Case unblinded due to end of study
Unblinding date is 10 Feb17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD

Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Thrombosis

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 23 July 2013 and 04 September 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical conditions at the time of the event included picc line insertion.
On PPD six days after the 2nd dose of Blinded vaccine, this 65-year-old subject developed thrombosis of arm. The subject was hospitalised. The subject was treated with dalteparin sodium. The event resolved with sequelae on September 2013 (exact date unspecified). The investigator considered that there was no reasonable possibility that the thrombosis of arm may have been caused by investigational product.

Investigator Comments:
Patient phoned triage line on 17Sep2013 at 18.10 as left arm was dusky and painful since PICC insertion on 10Sep2013. The arm was not swollen and the patient did not have a temperature. Patient was advised to come into hospital as at risk orf thrombosis so was admitted that evening. Ultrasound on 18Sep2013 confirmed presence of thrombosis. Patient was discharged on 18Sep2013 on Fragmin. For long term use.

This case contains and event assessed by the investigator as related to anti cancer therapies and / or disease/ tumor.

PSUR Comment:
Case unblinded due to end of study
Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Sepsis
Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 23 July 2013 and 04 September 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical conditions at the time of the event included thrombosis.
On PPD 28 days after the 2nd dose of Blinded vaccine, this 65-year-old subject developed non-neutropenic sepsis. The subject was hospitalised. The subject was treated with Tazocin, Coamoxiclav, paracetamol, nitroglycerine and gentamicin sulphate. The event resolved on 13 October 2013. The investigator considered that there was no reasonable possibility that the non-neutropenic sepsis may

## Confidential Unblinded Report - With Suspect Products and Serious Events

have been caused by investigational product .
Investigator Comments:
Phone call placed by patient s family member to the triage line on 02Oct2013 due to high temperature of 37.6 degrees celcius. Previous cycle of chemo was given on 25Sep2013. Patient also felt generally unwell with a tightness across chest and shortness of breath. Due to high temperature patient was admitted to query neutropenic sepsis. Blood test results showed that patient was not neutropenic on admission. Temperature was managed with IV Tazocin. As tempera ture stabilised patient was discharged on 07 Oct2013 and prescribed a short course of oral anti-biotics on discharge, advised to phone triage line if becomes unwell again.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Pyrexia
Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 23 July 2013 and 04 September 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine $\mathrm{gE}(50 \mathrm{mcg})$ adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD 54 days after the 2nd dose of Blinded vaccine, this 65-year-old subject developed pyrexia. The subject was hospitalized. The subject was treated with Piperacillin + tazobactam, gentamicin sulphate, ciprofloxacin, Co-amoxiclav and paracetamol. The event resolved on 03 November 2013. The investigator considered that there was no reasonable possibility that the pyrexia may have been caused by investigational product.

Investigator Comments:
Patient phoned triage line on $280 c t 2013$ due to a high temperature of 37.6 degrees celcius. As per protocol admitted to hospital to query neutropenic sepsis. Blood tests on admittance showed not neutropenic. Also presented with some shortness of breath and fatigue. Commenced on IV antibiotics. Temperature did not rise above 37.6. Patient discharged the following day (290ct2013) on a course of oral antibiotics.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

## Confidential Unblinded Report - With Suspect Products and Serious Events

Case unblinded due to end of study Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Pyrexia
Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028).
On 23 July 2013 and 04 September 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE ( 50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD 74 days after the 2nd dose of Blinded vaccine, this 65-year-old subject developed fever. The subject was hospitalised. The subject was treated with Tazocin, paracetamol, Co-amoxiclav and ciprofloxacin. The event resolved on 24 November 2013. The investigator considered that there was no reasonable possibility that the fever may have been caused by investigational product.

Investigator Comments:
Patient was admitted to hospital on 17 Nov2013 due to a high temperature of 38 degrees celcius. Patient s previous cycle of chemotherapy had taken place on 12Nov2013.Treated with IV antibiotics. Temperature stabilised on 19 Nov2013 so discharged home on a course of oral antibiotics. No cause of infection found and although neutrophils were below normal range this was not considered significant and patient was considered not neutropenic.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo, DOXORUBICIN, CYCLOPHOSPHAMIDE
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## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Serious Events: Neutropenic sepsis

Narrative: This 65-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 1st dose of Herpes zoster vs Placebo (intramuscular) on 11th July 2013, for prophylaxis.

Co-suspect products included DOXORUBICIN and CYCLOPHOSPHAMIDE for malignant neoplasm of female breast.

On PPD 24 days after receiving Herpes zoster vs Placebo, the subject developed moderate grade 2 neutropenic sepsis. Serious criteria included hospitalization and GSK medically significant. The subject was treated with piperacillin sodium + tazobactam sodium (Tazocin) and paracetamol. Herpes zoster vs Placebo was continued with no change. The outcome of neutropenic sepsis was recovered/resolved on 8th August 2013.

The investigator considered that there was no reasonable possibility that the neutropenic sepsis may have been caused by Herpes zoster vs Placebo.
Other possible cause(s) of the neutropenic sepsis included concurrent medication.
Diagnostic results (unless otherwise stated, normal values were not provided): On 4th August 2013, Blood culture result was negative, Body temperature result was 38.9 degree C, Culture urine result was negative, Neutrophil count result was $0.27 \times 10 \mathrm{e} 9 / \mathrm{L}$ (normal low: 2.0 , normal high: 7.0 ) and White blood cell count result was $0.9 \times 10 \mathrm{e} 9 / \mathrm{L}$ (normal low: 4.0, normal high: 10.0). On 8th August 2013, Neutrophil count result was $2.4 \times 10 \mathrm{e} 9 / \mathrm{L}$ (normal low: 2.0 , normal high: 7.0 ) and White blood cell count result was 3.8 x10e9/L (normal low: 4.0, normal high: 10.0).

Investigator Comments :
Patient developed a fever so was admitted on 4th Aug to a different hospital while on holiday. On arrival the patient had a fever with a temperature of 38.9 degrees, a WBC of 0.9 and a neutrophil count of 0.27 . Patient was given IV Tazocin as per the hospital's neutropenic sepsis protocol. Patient remained afebrile for 72 hours whilst on IV antibiotics. The blood counts improved (WBC 3.8 and neutrophils 2.4 on discharge) and patient was disharged on 08Aug2013 without the need of a switch to oral antibiotics. Exact dose of Tazocin not known as patient treated in another hospital.

Additional details:
On 04 August 2013, 11 days after starting doxorubicin (non GSK, taken for breast neoplasm malignant female) and cyclophosphamide (non GSK, taken for breast neoplasm malignant female), subject experienced neutropenic sepsis.

Other possible cause of the neutropenic sepsis included concurrent medication doxorubicin and cyclophosphamide

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding Date is $10-\mathrm{FEB}-17$

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo, CYCLOPHOSPHAMIDE, DOXORUBICIN
Serious Events: Neutropenic sepsis
Narrative: This 65-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 14th August 2013, for prophylaxis.

Co-suspect products included cyclophosphamide and doxorubicin for malignant neoplasm of female breast.

Concomitant products included paracetamol, chlorhexidine gluconate (Chlorhexidine Mouthwash), potassium bicarbonate, potassium chloride (Sando-K) and benzydamine hydrochloride (Difflam Mouthwash).

On PPD 12 days after receiving Herpes zoster vs Placebo, the subject developed moderate - grade 2 neutropenic sepsis. Serious criteria included hospitalization and GSK medically significant. The subject was treated with gentamicin (Gentamycin), piperacillin sodium, tazobactam sodium (Tazocin), amoxicillin + clavulanate potassium (Co-Amoxiclav) and ciprofloxacin. The outcome of neutropenic sepsis was recovered/resolved on 4th September 2013.

The investigator considered that there was no reasonable possibility that the neutropenic sepsis may have been caused by Herpes zoster vs Placebo. Other possible cause(s) of the neutropenic sepsis included concurrent medication Cyclophosphamide.
Diagnostic results (unless otherwise stated, normal values were not provided): On 26th August 2013, Blood culture result was Negative- No growth found, Body temperature result was 38.2, Chest X-ray result was lungs clear, Culture throat result was no Streptococci isolated, Neutrophil count result was 0.26 x10e9/L (normal low: 2.0, normal high: 7.0) and White blood cell count result was 0.6 x10e9/L (normal low: 4.0, normal high: 10.0). On 27th August 2013, Microscopy result was Negative.

Investigator Comments :
The patient rang the triage line on 26Aug2013 due to a high temperature of 38.2 , feeling shivery but not unwell. Patient was advised to come into hospital and a full blood count showed them to be neutropenic (neutrophils $=0.26$ ). Patient was put on oral antibiotics for neutropenic sepsis as per hospital protocol followed by IV antibiotics on 27Aug2013. Patient also received two units (Red Cells) of blood transfusion on 28Aug2013. Throat swab, blood and urine cultures taken to query source of infection. Patient was discharged from hospital on 30Aug2013 to continue on oral antibiotics.

## Confidential Unblinded Report - With Suspect Products and Serious Events

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Additional details:
On PPD }12\mathrm{ days after starting and on same day after last dose of Cyclophosphamide (Non
GSK, taken for malignant neoplasm of female breast), and doxorubicin (Non GSK, taken for malignant
neoplasm of female breast), the subject experienced a moderate - grade 2 neutropenic sepsis.
Other possible cause of the Neutropenic Sepsis included Concurrent Medication Cyclophosphamide and
Doxorubicin
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor
Case unblinded due to end of study
Unblinding Date is 10-FEB-17
The subject developed neutropenic sepsis 12 days after recieving Herpes zoster vs placebo.After due analysis GSK accepts and agrees with the causality assessment of the Serious Adverse Event by the Principal Investigator as unrelated to participation in the study and related to concurrent medication
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Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B, Epirubicin, Cyclophosphamide, Fluorouracil
Serious Events: Neutropenic sepsis
Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 09 September 2013 and 09 October 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE ( 50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Concomitant medications included Omeprazole and Fragmin.
On PPD 19 days after the 1st dose of Blinded vaccine, 10 days after the first cycle of intravenous chemotherapy with Fluorouracil, Epirubicin and Cyclophosphamide, this 47-year-old subject developed neutropenic sepsis caused by staphylococcus haemolyticus infection. The subject was hospitalised. The subject was treated with gentamicin sulphate, Tazocin and flucloxacillin sodium. The event resolved on 06 October 2013. The investigator considered that there was no reasonable possibility that the neutropenic sepsis caused by staphylococcus haemolyticus infection may have been caused by investigational product and that the event was possibly due to the concomitant medications Fluorouracil (unknown manufacturer), Epirubicin (non-GSK) and Cyclophosphamide (non-GSK).

Investigator Comments:
Admitted to hospital on 28SEP2013 following cycle 1 chemotherapy with neutropenic sepsis. Neutrophils 0.98 on 28SEP2013, did drop to 0.65 on 29SEP2013, but did not drop any lower than this. Highest tempera
ture reading was 37.6 C , all other observations were satisfactory and no other symptoms. Given IV fluids

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

and IV antibiotics. Event related to chemotherapy; not related to trial vaccination. Patient was discharged from hospital on 03Oct2013.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B, Docetaxel
Serious Events: Lower respiratory tract infection
Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 08 October 2013 and 20 November 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE ( 50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD 27 days after the 2 nd dose of Blinded vaccine, 4 days after starting concomitant medication docetaxel this 60-year-old subject developed possible chest infection. The subject was hospitalised. The subject was treated with Tazocin, Co-amoxiclav, ciprofloxacin and doxycycline. The event resolved on January 2014. The investigator considered that there was no reasonable possibility that the possible chest infection may have been caused by investigational product and that the event was possibly due to the concomitant medication, docetaxel (Manufacturer : Sanofi - given as anti-cancer therapy).
This case contains an event assessed by the investigator as related to the anti-cancer therapy.
Investigator Comments : Admitted to hospital on 20 Dec 2013 with shortness of breath, had experienced this since 17 Dec 2013. No pain or temperature. Was not neutropenic. D Dimer raised at $1023 \mathrm{ng} / \mathrm{ml}$, but CTPA showed lungs clear and no pulmonary emboli present. Discussed with Consultant, probable chest infection due to chemotherapy. Not related to study vaccine. Was on IV antibiotics - tazocin but changed to oral antibiotics - co-amoxiclav three times per day on 23rd Dec 2013. Condition improving and for discharge home on 24th Dec 2013.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study Unblinding Date is 10-FEB-17

Study Number: 116427

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Study Center ID: PPD<br>Subject ID: PPD<br>Randomization Number:<br>Case ID: PPD<br>Suspect Products: Hz/su + AS01B

Serious Events: Metastases to liver

Narrative: This 61-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 20th November 2013, for prophylaxis.

On PPD 224 days after receiving Herpes zoster vs Placebo the subject developed severe grade 3 metastases to liver. Serious criteria included death, hospitalization and GSK medically significant. The subject was treated with CYCLIZINE HYDROCHLORIDE, DEXAMETHASONE, MACROGOL, POTASSIUM CHLORIDE, SODIUM BICARBONATE, SODIUM CHLORIDE (MOVICOL), CHLORHEXIDINE GLUCONATE, SPIRONOLACTONE, ZOPICLONE, LEVOMEPROMAZINE, MORPHINE SULFATE, MIDAZOLAM and GLYCOPYRRONIUM BROMIDE. The outcome of metastases to liver was fatal on PPD 2014. The subject died on PPD 2014. The reported cause of death was metastases to liver. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the metastases to liver may have been caused by Herpes zoster vs Placebo.

Relevant Tests: CT scan performed 24 July 2014 showed multiple hepatic metastases Diagnostic results (unless otherwise stated, normal values were not provided): On 23rd July 2014, ALKALINE PHOSPHATASE result was 434 unknown (normal low: 30, normal high: 170), Aspartate aminotransferase result was 428 unknown (normal low: 7, normal high: 35) and Blood bilirubin result was 111 unknown (normal low: 1, normal high: 21).

Investigator Comments: Admitted to hospital on 23Jul2014 with increased shortness of breath, 3 week history of abdominal pain, lethargy and generally feeling unwell. Treated with IV fluids and IV antibiotics. CT scan showed multiple liver metastases. Lungs were clear. Patient continued to decline, she became increasingly jaundiced, increasing ascites and very lethargic. Her LFTs continued to deteriorate. Was reviewed by oncologist - not for active treatment, for palliative care. Discharged to hospice on 1 August 2014. Patient passed away on PPD 2014 at the hospice.

Blood results showed raised liver function. Ct scan showed multiple hepatic metastases. For palliative care.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study

## Confidential

## Unblinded Report - With Suspect Products and Serious Events

Unblinding Date is $10-$ FEB-17
The subject developed metastasis to liver 224 days after receiving Herpes zoster vs placebo and died due to this after 1 month. The event is considered related to metastasis from underlying disease.Causal association with vaccine seems unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo, Fluorouracil
Serious Events: Rash

Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 01 October 2013 and 07 November 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE ( 50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD six days after the 2nd dose of Blinded vaccine, six days after receiving 2nd cycle of chemotherapy drug Fluorouracil, this 62-year-old subject developed a skin rash. The subject was hospitalised. The subject was treated with flucloxacillin sodium, Co-amoxiclav, Tazocin, tetanus vaccine and acyclovir. The event resolved on 23 December 2013. The investigator considered that there was no reasonable possibility that the skin rash may have been caused by investigational product. The investigator considered that there was a reasonable possibility that the skin rash may have been caused by Fluorouracil (manufacturer: Other (non-GSK), given as anti-cancer therapy).

Investigator Comments:
Patient phoned triage line on 13 November 2013 as had pricked fingers on rose thorns two days previously. Hands had become swollen and patient was concerned they may be infected. As advised attended GP who started patient on a course of oral antibiotics. Admitted to hospital on 16 November 2013 due to worsening symptoms with the development of a rash on hands and feet as well as mouth ulcers and a temperature of 37.5 degrees Celsius. Skin biopsy performed to test for viral infection. Treated with antibiotics and anti-viral therapy. As temperature stable and rash improving patient was discharged home on 22 November 2013. For GP follow-up.
Biopsy results came back negative for any viral infection. Therefore thought to be potential reaction to drugs. Reaction not thought to be due to either investigational product or antiobiotic treatment for possible infection.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

On 05 December 2013, the subject has been unblinded following the emergency unblinding process.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Sepsis

Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 01 October 2013 and 07 November 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE ( 50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD 69 days after the 2nd dose of Blinded vaccine, this 63-year-old subject developed sepsis unknown origin. The subject was hospitalised. The subject was treated with Tazocin, gentamicin sulphate and doxycycline. The event resolved on 25 January 2014. The investigator considered that there was no reasonable possibility that the sepsis unknown origin may have been caused by investigational product.

Investigator Comments :
Patient phoned trialge line on 15Jan2014 as had developed a temperature of 37.8 degrees celcius that day and was feeling cold with a headache. Advised to attend emergency department. Not neutropenic on admission. Treated with IV antibiotics until temperature stabilised. Unclear what the cause of pyrexia was. Discharged home on 19Jan2014 on a course of oral antibiotics

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo, Oxaliplatin, Fluorouracil
Serious Events: Neutropenic sepsis
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 09 July 2013 and 21 August 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE $(50 \mathrm{mcg})$ adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

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Medical conditions at the time of the event included adenocarcinoma sigmoid.
On PPD 67 days after the 2nd dose of Blinded vaccine and 96 days after received oxaliplatin and fluorouracil treatment (for sigmoid adenocarcinoma), this 69-year-old subject experienced neutropenic sepsis. The subject was hospitalised. The subject was treated with tazocin and meropenem. The event resolved on 08 November 2013. The investigator considered that there was no reasonable possibility that the neutropenic sepsis may have been caused by investigational product and that the event was possibly due to the concomitant medication, oxaliplatin and fluorouracil (both manufacturer non GSK).

Investigator comments:
Patient has been experiencing a productive cough for 7 days. He was bringing up green sputum. Also had a chest wheeze. Temperature at home was 38 degrees centigrade. No shortness of breath or chest pain. Admitted to hospital 3rd November 2013. Started on Antibiotics. Treated as Neutropenic sepsis from chest infection. Remains an InPatient at present. Trials team aware of admission to hospital.
Patient discharged home from hospital 08/11/13.
Neutropenic sepsis has been related to anti-cancer treatment, which drug has not been specified in patient medical note.
Principal investigator has reviewed the event and he has confirmed that neutropenic sepsis is assocciated to either oxaliplatin or Fluorouracil.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Colorectal cancer metastatic

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## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

On PPD
264 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 metastatic colorectal cancer. Serious criteria included hospitalization and GSK medically significant. The outcome of metastatic colorectal cancer was recovered/resolved on 28th July 2014.

The investigator considered that there was no reasonable possibility that the metastatic colorectal cancer may have been caused by Herpes zoster vs Placebo.

Relevant Tests: Histology from surgery confirmed bilateral ovarian masses - metastatic colorectal cancer.
Investigator Comments : Annotation in hospital notes from 7/7/14 states that Abdo pain for last week. See by GP with constipation, given Abdominal pain Abdominal pain was caused by disease/tumour. Pt admitted to hospital on 21st July 2014 with lower abdominal pain. 21/7/14 Abdominal Ultrasound, 23/7/14 CT abdomen and pelvis (appearances slightly suspicipous of secondary mass arising from left side), 24/7/14 Pelvis ultrasound. Surgery performed on 25/7/14. Histology confirmed bilateral ovarian masses metastatic colorectal cancer.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B, Oxaliplatin
Serious Events: Diabetic ketoacidosis, Nausea
Narrative: This 69-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 1st dose of Herpes zoster vs Placebo (intramuscular) on 27th January 2014, for prophylaxis.

Co-suspect products included oxaliplatin unknown for cancer.
Concurrent medical conditions included diabetes mellitus. Concomitant products included fluorouracil.
On PPD 33 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 nausea. Serious criteria included hospitalization. Additional event(s) included severe - grade 3 diabetic ketoacidosis on 8th March 2014 with serious criteria of hospitalization and GSK medically significant. The subject was treated with nystatin, trimethoprim, insulin glulisine (Apidra), insulin glargine

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## Unblinded Report - With Suspect Products and Serious Events

(Lantus), calcium carbonate, sodium alginate, sodium bicarbonate (Peptac) and insulin nos (Insulin). The outcome of nausea was recovered/resolved on 12th March 2014. The outcome(s) of the additional event(s) included diabetic ketoacidosis (recovered/resolved on 12th March 2014).

The investigator considered that there was no reasonable possibility that the nausea and diabetic ketoacidosis may have been caused by Herpes zoster vs Placebo. Other possible cause(s) of the nausea included concurrent medication, medical condition and Oxaliplatin. Other possible cause(s) of the diabetic ketoacidosis included medical condition.

Relevant Tests: positive nitrites, lymphocytes (urinary tract infection)
Positive on urine dipstick. Diagnostic results (unless otherwise stated, normal values were not provided): On 8th March 2014, Blood glucose result was 28.4 mmol/L (normal low: 3.6, normal high: 6.0) and Blood pH result was 7.27 (normal low: 7.34, normal high: 7.44).

Investigator Comments:
Patient was admitted on 8/03/2014 following one week reduced oral intake and nausea post chemotherapy. On admission he was found to be in diabetic ketoacidosis with raised blood glucose (hyperglycemia) and acidosis. Also presented with urinary tract infection (positive nitrites, lymphocytes). Commenced on oral antibiotics for this. Commenced on sliding scale IV insulin, late changing to insulin for control of diabetes. Event is related to diabetes.
Urinary tract infection is a concomitant event. Results positive on urine dipstick
Peptac did not cause diabetic ketoacidosis - given for dyspepsia
Nausea not a sign / symptom of diabetic ketoacidosis
Discharge date 12/03/2014
Only nausea is caused by chemotherapy

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding date is 10 Feb17Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Pneumonia

Narrative: This 58-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly

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## Unblinded Report - With Suspect Products and Serious Events

on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 24th October 2013, for prophylaxis.

On PPD 168 days after receiving Herpes zoster vs Placebo, the subject developed moderate grade 2 pneumonia. Serious criteria included hospitalization and GSK medically significant. The subject was treated with amoxicillin trihydrate, clavulanate potassium (Augmentin), clarithromycin, tramadol and paracetamol. The outcome of pneumonia was recovered/resolved on 21st April 2014.

The investigator considered that there was no reasonable possibility that the pneumonia may have been caused by Herpes zoster vs Placebo.

Relevant Tests: Physical examination: crackles at both lung bases, $L>R$. Chest x-ray: consolidation at left base. CTPA: no pulmonary embolism, bilateral mild pleural effusion, some collapse of left lower lobe. Diagnostic results (unless otherwise stated, normal values were not provided): On 11th April 2014, C-reactive protein result was $146 \mathrm{mg} / \mathrm{L}$ (normal low: 0, normal high: 5).

Investigator Comments: Presenting on 11.04 .14 to the emergency department with new onset of pleuritic chest pain. Inspiratory crackles noted on examination and abnormal CXR as well as raised CRP. Normal observations, aterial blood gases, white cell count, ECG and echocardiogram. Pulmonary embolism excluded on CTPA. Treated for pneumonia with intravenous, then oral antibiotics.

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Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo, PACLITAXEL
Serious Events: Urosepsis

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## Unblinded Report - With Suspect Products and Serious Events

applicable urosepsis. Serious criteria included hospitalization and GSK medically significant. The subject was treated with gentamicin, piperacillin sodium, tazobactam sodium (Tazocin), trimethoprim and paracetamol. The outcome of urosepsis was recovered/resolved on 10th October 2013.

The investigator considered that there was no reasonable possibility that the urosepsis may have been caused by Herpes zoster vs Placebo. Other possible cause(s) of the urosepsis included concurrent medication.

Relevant Tests: Mid stream urine specimen 08OCT2013 inconclusive result Blood culture 08OCT2013 no growth recorded Full blood count shows neutropenia 1.3 (10e9/L) range 1.8-7.5 Diagnostic results (unless otherwise stated, normal values were not provided): On 8th October 2013, White blood cell count result was $2.2 \times 10 \mathrm{e} 9 / \mathrm{L}$ (normal low: 3.6, normal high: 11.0).

Investigator Comments : 09/10/2013 Patient admitted to hospital with 3 day history of feeling generally unwell, urinary frequency and pain between legs. Diagnosed with urinary sepsis and treated with intravenous fluids and antibiotics. Assessment and treatment ongoing, patient is 8 days post vaccination 2 in zoster study and post cycle 2 chemotherapy, no obvious connection to investigational vaccine. Admitted to hospital 08/10/2013, discharged $10 / 10 / 2013$. This SAE of urinary sepsis was attributable to anti-cancer therapy of paclitaxel for this subject.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo, Capecitabine
Serious Events: Constipation
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 26 March 2013 and 03 May 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical conditions at the time of the event included rectosigmoid carcinoma. Concomitant medications included Oxaliplatin.

On PPD 4 months after the concomittant Capecitabine, 110 days after the 2 nd dose of Blinded vaccine, this 76-year-old subject developed constipation. The event was disabling, clinically significant (or

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## Unblinded Report - With Suspect Products and Serious Events

requiring intervention). The subject was treated with Movicol, cyclizine, morphine and hyoscine butylbromide. The event resolved on 04 September 2013. The investigator considered that there was no reasonable possibility that the constipation may have been caused by investigational product and that the event was possibly due to the concomitant medication, capecitabine (Roche, given in chemotherapy).

Investigator comments:
This participant contacted the Oncology dept today with a 1 day history of colicky generalised abdominal pain, grade 2, in combination with increased belching and fatigue. The participant reports no nausea or vomiting. The participant was advised to attend the hospital for assessment. The participant is currently undergoing palliative oxaliplatin and capecitabine chemotherapy for locally advanced recto-sigmoid adenocarcinoma. The current cycle (cycle 7) of their chemotherapy commenced on 16Aug2013. They had a CT scan performed on 25Jun2013 which showed a good partial response to the chemotherapy.

Blood tests were performed for full blood count, urea and electrolytes, liver function tests and CRP and reviewed by the Doctor - all of which were satisfactory. Bowel sounds present. Observations performed which were all satisfactory. Abdominal x-ray performed and reviewed by the Doctors. It shows ? constipation ? bowel obstruction. Upon discussion with the Doctor it was felt that this event required reporting as an SAE because it was resulting in significant disruption and pain to the patient which caused them a degree of incapacity, and because the Doctor felt it was medically signficant and something which, if left untreated, would result in hospitalisation.
The capecitabine for this cycle has been suspended today and the participant has been commenced on buscopan; movicol; cyclizine and oromorph prn for the pain. After review it was felt that the participant did not require admitting to hospital at present; however, if the pain worsened then they should contact the hospital to be admitted. Formal report for the abdominal x-ray awaited.
This report has been agreed with reporting Doctor.
04 Sep 2013 - This participant was seen again in clinic by the Doctor. Following the events noted above they had taken the medication as prescribed until the 22Aug2013. This had a good effect with the participant having their bowels open and the abdominal pain resolving. The SAE discussed with the Doctor who feels it has now completely resolved. The participant did not restart their capecitabine chemotherapy following it being witheld on the 21Aug2013; however, the Doctor feels they are fit enough to go ahead with their final cycle this week, pending blood tests. This report has been agreed with the reporting Doctor.
04Jun2014 - Discussed the above with the PI for the trial. The constipation is related to his anticancer therapies.

24 june 2014: discussed the above with the PI for the trial, who advises that the capecitabine was supected to have been a causal factor in this SAE.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

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Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD

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Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B, Bevacizumab
Serious Events: Pulmonary embolism
Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 05 September 2013 and 16 October 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE ( 50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical conditions at the time of the event included colon cancer with metastases.
On PPD six days after the 2nd dose of Blinded vaccine, 35 days after the concomitant treatment Bevacizumab, this 69-year-old subject developed pulmonary embolism. The event was clinically significant (or requiring intervention). The subject was treated with paracetamol, morphine and enoxaparin. The event resolved on 04 December 2013. The investigator considered that there was no reasonable possibility that the pulmonary embolism may have been caused by investigational product and that the event was possibly due to the concomitant medication, bevacizumab (taken for colon cancer, Roche).

Investigator Comments:
Medically significant event: On 22OCT2013 around 20:00 patient had a sudden pain - pleuritic pain on right side, under right breast. The pain made it hard to breathe normally - shallow breathing according to patient (the patient has no previous history of DVT and no known history of DVT in the family). Patient consulted in ER at 22:10 the same day. Tylenol and Morphine were given for the pain. Blood tests and a pulmonary scintigraphy were done. D-Dimer came back clinically significant. The pulmonary scintigraphy confirmed the diagnosis of multiple pulmonary embolism. The patient was treated with Lovenox S/C and was sent home on 23OCT2013 at 13:41 after all symptoms were resolved (pain and difficulty breathing). The pulmonary embolism will be treated with Lovenox S/C once daily for a minimum of 6 months but probably for the rest of the patient s life. In the opinion of the Investigator, the event is related to the anticancer therapy and/or disease tumour (related to neoplasia with Avastin as a possible contributing factor). This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: P
PPD
Randomization Number:
Case ID: PPD

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Suspect Products: Vaccine placebo

Serious Events: Lumbar vertebral fracture

Narrative: This 63-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 2nd April 2014, for prophylaxis.

Concurrent medical conditions included lung cancer, osteoporosis and lung cancer metastatic.
On PPD 59 days after receiving Herpes zoster vs Placebo, the subject developed moderate grade 2 lumbar vertebral fracture 14 . Serious criteria included hospitalization and GSK medically significant. The subject was treated with naproxen (Naprosyn), hydromorphone hydrochloride (Dilaudid), morphine and paracetamol (Tylenol). The outcome of lumbar vertebral fracture 14 was not recovered/not resolved.

The investigator considered that there was no reasonable possibility that the lumbar vertebral fracture 14 may have been caused by Herpes zoster vs Placebo.

## Investigator Comments:

We learned today (04June2014) that the patient is hospitalised in our institution since 02June2014.
Patient came to the ER on 02June2014 with severe lumbar pain that was radiating to his right thigh. This pain had started 2 days before (31May2014). Patient was given analgesics for his pain and a scan was done on June 2nd - revealing the appearence of wedging of L4 secondary to osteopenia/osteoporosis. There is no evidence of progressive bone disease. Patient received his 5th cycle of chemotherapy on May 16th, 2014 (Carboplatin IV and Alimta IV). This SAE is not related to the patient's vaccinations, procedures nor to progression of disease. Bone scan done on 11 June 2014 revealed a compression fracture of the L4 vertebra. Fracture still present on most recent scan done on 06 February 2015 so fracture considered to be ongoing at the end of the patient's participation in the study.

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Malignant melanoma
Narrative: This 69-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised,

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observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 11th June 2013, for prophylaxis.

On PPD 1 year and 7 days after receiving Herpes zoster vs Placebo, the subject developed moderate - grade 2 malignant melanoma. Serious criteria included GSK medically significant and clinically significant/intervention required. The outcome of malignant melanoma was resolved with sequelae on 29th May 2015.

The investigator considered that there was no reasonable possibility that the malignant melanoma may have been caused by Herpes zoster vs Placebo.

Relevant Tests: biopsy of skin lesion.
Investigator comments:
when pt inh for final visit Aug 62014 notified us he had a biopsy left shoulder back.
Unable to track down results not available from dermatologist
Patient in for appt 28 oct 2014 and notified us that it was malignant melanoma
booked for wide excision and sentinel sampling Oct 292014 at outside facility
Will get results and follow.
new entry Pathology shows residual 18 mm level V melanoma-- ulcerated DESMOLASTIC in subtype Margins clear No lymph vascular invasion considering INTERFERON treatment.
Patient opted not to take interferon.
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Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Non-small cell lung cancer
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 29 October 2013 and 03 December 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine $\mathrm{gE}(50 \mathrm{mcg})$ adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical condition at the time of the event included non small cell lung cancer.
On PPD six months after the 2nd dose of Blinded vaccine, this 70-year-old subject developed progression of non small cell lung cancer. The subject was hospitalised. The subject died on PPD

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2014 due to progression of non small cell lung cancer. An autopsy was not performed. The investigator considered that there was no reasonable possibility that the progression of non small cell lung cancer may have been caused by investigational product.

Investigator Comments:
Patient admitted to hospital 14 Jun 2014 with functional decline due to progression of his lung cancer. confirmed with CT 17 Jun 2014
Transferred to palliative care 19 Jun 2014
Late entry: Patient felt unwell week before coming to hospital Unable to verify to what degree or if relevant to progressive disease.
Patient expired PPD 2014 due to disease progression.
As per GSK request, start date of SAE changed to 07JUN2014 when patient complained of being unwell; Difficult to ascertain start date of progression or decline.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding date is 10 Feb 17
The subject developed progression of non-small cell lung cancer 6 months after recieving Herpes zoster vs placebo and died due to this.As the event is due to progression of underlying disease.Causal association with vaccine is unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID: P PPD

Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Arthralgia


#### Abstract

Narrative: This 54-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 21st October 2013, for prophylaxis.

On PPD 205 days after receiving Herpes zoster vs Placebo, the subject developed moderate grade 2 arthralgia. Serious criteria included hospitalization. The outcome of arthralgia was recovered/resolved on 5th August 2014.

The investigator considered that there was no reasonable possibility that the arthralgia may have been caused by Herpes zoster vs Placebo.


## Confidential Unblinded Report - With Suspect Products and Serious Events

Investigator Comments:
She felt knee pain and knee swelling from 14May2014. So, she hospitalized local hospital from 15July2014 to 05Aug2014. This event is first time. It just by her age and life style. But she does not have any medication during hospitalization. Because she said to doctor that she has target medication for cancer. So, She had just relax and physical therapy in hospital. And Itt s not rheumatois arthralgia, just arthralgia pain.
PI recognized this event during EMR reviwe on 08Aug2014 at 17:00.
lab work up been performed such as RF, ANA, CRP, anti-CCP, ESR, viral serology, test for bacterial infections has not performed.
And imaging not taken by patient.
Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B, Fluorouracil, CYCLOPHOSPHAMIDE, Doxorubicin
Serious Events: Febrile neutropenia
Narrative: This 58-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 1st dose of Herpes zoster vs Placebo (intramuscular) on 13th November 2013, for prophylaxis. On 23rd December 2013, the second dose was administered.

Co-suspect products included fluorouracil solution for injection for chemotherapy, cyclophosphamide for chemotherapy and doxorubicin unknown for chemotherapy.

The subject's past medical history included quadrantectomy. Concurrent medical conditions included breast cancer. Concomitant products included palonosetron, dexamethasone, aprepitant, metoclopramide and famotidine.

On PPD 13 days after receiving Herpes zoster vs Placebo,13 days after receiving cosuspect Fluorouracil (GSK) the subject developed severe - grade 3 febrile neutropenia. Serious criteria included hospitalization and GSK medically significant. The subject was treated with chlorhexidine gluconate, nystatin, piperacillin, tobramycin, paracetamol (Acetaminophen), propacetamol hydrochloride, tramadol, potassium chloride, cefpodoxime, paracetamol (Tacenol Er) and filgrastim. Herpes zoster vs Placebo was continued with no change. The outcome of febrile neutropenia was recovered/resolved on 3rd December 2013.

## Confidential Unblinded Report - With Suspect Products and Serious Events

The investigator considered that there was no reasonable possibility that the febrile neutropenia may have been caused by Herpes zoster vs Placebo. Other possible cause(s) of the febrile neutropenia included concurrent medication Fluorouracil. Diagnostic results (unless otherwise stated, normal values were not provided): On 26th November 2013, Body temperature result was 38.7 unknown (normal low: NA, normal high: NA), Neutrophil count result was 4 \% (normal low: 50, normal high: 75) and White blood cell count result was 0.40 unknown (normal low: 4.0, normal high: 10). On 29th November 2013, Body temperature result was 36 unknown (normal low: NA, normal high: NA), Neutrophil count result was 70 \% (normal low: 50, normal high: 75) and White blood cell count result was 3.8 unknown (normal low: 4.0, normal high: 10). On 3rd December 2013, Neutrophil count result was 51 \% (normal low: 50, normal high: 75) and White blood cell count result was 3.52 unknown (normal low: 4.0, normal high: 10).

## Investigator Comments :

05 Dec2013
This subject had breast cancer. And she enrolled our trial and was randomized onchemo arm.
She took first adjuvant chemotherapy(FAC) and 1st investigational product on 13Nov2013.
she visited ER due to febrile sense on 26Nov2013.
Body temperature was checked 38.7 degree Celcius
So she was hopitalized and took antibiotics and filgrastim.
Investigator awareness date was 28Nov2013 17:30.
There was no relationship to study drug.
This AE was related chemotherapy(FAC).
She recovered fever and dischargedon 30NOV2013.
Investigator thouht SAE was recovered on 03DEC2013. She take 2nd chemotherapy on 03DEC2013.
29Nov2013: inital report narration part
This is initial SAE report in 6 .narration part. Initial SAE report was deleted on 04DEC2013 due to system error. This subject enrolled Zoster-028 study and was randomized onchemo arm. She took investigator product with Chemotherapy on 13Nov2013. And then she experienced mild general weakness. She experienced febrile sense on 26 nov2013. She visited ER. Body temperature was checked 38.7 c (tympanic) on 26Nov2013. She took filgrastim and antibiotics. And she was hospitalizsed . Date of Investigator awareness was 28Nov2013 17:30. Febrile neutropenia caused by chemotherapy. There was not related IP. Body temperature is checked 36.0c (tympanic) on 29 Nov2013.
As per eCRF system error, initial SAE report was deleted on 04Dec2013
This is follow up SAE report
Cyclophosmamide is non comparator GSK
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding date is $10-\mathrm{Feb}-17$

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Case ID: PPD<br>Suspect Products: Hz/su + AS01B, Fluorouracil, Doxorubicin, CYCLOPHOSPHAMIDE

Serious Events: Febrile neutropenia


#### Abstract

Narrative: This 59-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 23rd December 2013, for prophylaxis.


Co-suspect products included fluorouracil solution for injection for chemotherapy, doxorubicin unknown for chemotherapy and CYCLOPHOSPHAMIDE for chemotherapy.

The subject's past medical history included quadrantectomy. Concurrent medical conditions included breast cancer. Concomitant products included palonosetron, dexamethasone, aprepitant, famotidine and metoclopramide.

On PPD 33 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 febrile neutropenia. Serious criteria included hospitalization and GSK medically significant. The subject was treated with chlorhexidine gluconate, filgrastim, amoxicillin, piperacillin and nystatin. Herpes zoster vs Placebo was continued with no change. The outcome of febrile neutropenia was recovered/resolved on 28th January 2014.

The investigator considered that there was no reasonable possibility that the febrile neutropenia may have been caused by Herpes zoster vs Placebo. Other possible cause(s) of the febrile neutropenia included concurrent medication Fluorouracil.
Diagnostic results (unless otherwise stated, normal values were not provided): On 25th January 2014, Neutrophil count result was 12 \% (normal low: 50, normal high: 75) and White blood cell count result was $0.37 \times 10 \mathrm{e} 3 / \mathrm{mm} 3$ (normal low: 4.0, normal high: 10). On 26th January 2014, Neutrophil count result was 43 \% (normal low: 50, normal high: 75) and White blood cell count result was $1.01 \times 10 \mathrm{e} 3 / \mathrm{mm} 3$ (normal low: 4.0, normal high: 10). On 27th January 2014, Body temperature result was 38.4 degree $C$ (normal low: NA, normal high: NA), Neutrophil count result was 72 \% (normal low: 50, normal high: 75) and White blood cell count result was $2.29 \times 10 \mathrm{e} 3 / \mathrm{mm} 3$ (normal low: 4.0, normal high: 10). On 28th January 2014, Neutrophil count result was 78 \% (normal low: 50, normal high: 75) and White blood cell count result was $5.41 \times 10 \mathrm{e} 3 / \mathrm{mm} 3$ (normal low: 4.0, normal high: 10).

Investigator Comments : <05FEB2014>
This subject had breast cancer and she enrolled our trial and was randomized onchemo arm. She visited ER due to febrile sense on 25Jan2014. So she was hopitalized and took antibiotics and filgrastim. Investigator awareness date was 05Feb2014 16:30. There was no relationship to study drug. This AE was related chemotherapy (FAC). She discharged on 28Jan2014. She took chemotherapy (FAC) and 2st investigational product on 23Dec201.

Additional information :
On 25 January 2014, 12 days after starting the concomitant medication Doxorubicin, the subject developped febrile neutropenia. Other possible causes of the febrile neutropenia included the concomitant medication Doxorubicin (not GSK, taken for chemotherapy).

## Confidential

## Unblinded Report - With Suspect Products and Serious Events

On 25 January 2014, 12 days after starting the concomitant medication Cyclophosphamide, the subject developped febrile neutropenia. Other possible causes of the febrile neutropenia included the concomitant medication Cyclophosphamide (not GSK, taken for chemotherapy).
On 25 January 2014, 53 days after starting the concomitant medication Fluorouracil, the subject developped febrile neutropenia. Other possible causes of the febrile neutropenia included the concomitant medication Fluorouracil (possibly GSK, taken for chemotherapy).

This case contains an event assessed by the investigator as related to the anti-cancer therapies.
Case unblinded due to end of study
Unblinding date is $10-\mathrm{Feb}-17$

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B, DOXORUBICIN, FLUOROURACIL, CYCLOPHOSPHAMIDE
Serious Events: Febrile neutropenia
Narrative: This 59-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 23rd December 2013, for prophylaxis.

Co-suspect products included doxorubicin for chemotherapy, fluorouracil for chemotherapy and cyclophosphamide for chemotherapy.

The subject's past medical history included quadrantectomy. Concurrent medical conditions included breast cancer. Concomitant products included famotidine (Gaster (Famotidin)), palonosetron, aprepitant, metoclopramide, famotidine and dexamethasone.

On PPD 80 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 febrile neutropenia. Serious criteria included hospitalization and GSK medically significant. The subject was treated with anticough (nos) (Anticough), arginine hydrochloride, ibuprofen (Carol-F), ciprofloxacin (Citopcin), ciprofloxacin, amoxicillin + clavulanate, nystatin, filgrastim (Grasin), ketorolac trometamol (Ketocin), piperacillin (Peracillin) and glucose + sodium chloride (Dextrose In Normal Saline). The outcome of febrile neutropenia was recovered/resolved on 17th March 2014.

The investigator considered that there was no reasonable possibility that the febrile neutropenia may have been caused by Herpes zoster vs Placebo. Other possible cause(s) of the febrile neutropenia included concurrent medication.

## Confidential Unblinded Report - With Suspect Products and Serious Events

Diagnostic results (unless otherwise stated, normal values were not provided):
On 13th March 2014, Neutrophil percentage result was 43 \% (normal low: 50, normal high: 75) and White blood cell count result was $0.60 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4.0, normal high: 10).
On 14th March 2014, Body temperature result was 38.5 degree C (normal low: NA, normal high: NA), Neutrophil percentage result was 78 \% (normal low: 50, normal high: 75) and White blood cell count result was $3.42 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4.0 , normal high: 10).
On 15th March 2014, Neutrophil percentage result was 86 \% (normal low: 50, normal high: 75) and White blood cell count result was $2.60 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4.0, normal high: 10).
On 16th March 2014, Body temperature result was 37.6 degree C (normal low: NA, normal high: NA), Neutrophil percentage result was 72 \% (normal low: 50, normal high: 75) and White blood cell count result was $1.96 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4.0, normal high: 10).
On 17th March 2014, Neutrophil percentage result was 90.1 \% (normal low: 50, normal high: 75) and White blood cell count result was $13.65 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4.0, normal high: 10).

Investigator Comments :
17MAR2014 :
This subject had breast cancer. And she enrolled our trial and was randomized on chemo arm. she visited PPD ER due to febrile sense on 13MAR2014.
So she was hopitalized on 14MAR2014 and took antibiotics and filgrastim.
Investigator awareness date was 17MAR2014 10:45.
There was no relationship to study drug.
This AE was related chemotherapy(FAC).
And then she was discharged on 17MAR2014.
Additional information:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Additional information :
On 13MAR2014, 36 days after being given a single course of concomitant chemotherapy drugs Cyclophosphamid, Fluorouracil and Doxorubicin, the subject developed febrile neutropenia. Other possible causes of febrile neutropenia included Cyclophosphamid, Fluorouracil and Doxorubicin (all nonGSK drugs, given as chemotherapy).

Case unblinded due to end of study
Unblinding date is $10-\mathrm{Feb}-17$

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Upper respiratory tract infection

## Confidential

## Unblinded Report - With Suspect Products and Serious Events

Narrative: This 50-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 17th December 2013, for prophylaxis.

Concomitant products included glucose, potassium nos, sodium chloride (Dextrose + Sodium + Potassium) and glucose (Dextrose).

On PPD 241 days after receiving Herpes zoster vs Placebo the subject developed severe grade 3 upper respiratory tract infection. Serious criteria included hospitalization. The subject was treated with propacetamol, filgrastim, piperacillin, tazobactam (Piperacillin + Tazobactam), codeine, ciprofloxacin and amoxicillin. The outcome of upper respiratory tract infection was recovered/resolved on 20th August 2014.

The investigator considered that there was no reasonable possibility that the upper respiratory tract infection may have been caused by Herpes zoster vs Placebo. Diagnostic results (unless otherwise stated, normal values were not provided): On 18th August 2014, Neutrophil count result was 8 \% (normal low: 50, normal high: 75) and White blood cell count result was 0.89 unknown (normal low: 4.0, normal high: 10.0). On 19th August 2014, Neutrophil count result was 80 ml (normal low: 1800, normal high: 7000), Neutrophil count result was 685 ml (normal low: 1800, normal high: 7000), Neutrophil count result was 35 \% (normal low: 50, normal high: 75) and White blood cell count result was 1.67 unknown (normal low: 4.0, normal high: 10.0). On 20th August 2014, Neutrophil count result was 52 \% (normal low: 50, normal high: 75), Neutrophil count result was 3185 ml (normal low: 1800, normal high: 7000) and White blood cell count result was 5.79 unknown (normal low: 4.0, normal high: 10.0).

Investigator Comments:
The patient had chemotherapy during 2013.11.26.-2014.8.7.(Docetaxel/Cisplatin)
And she denied chemotherapy because it is so hard.
So, she relax in Nursing home. Suddenly, she had cough, sputum, rhinorrhea from 15Aug2014. And then added fever on 17Aug2014. Nursing home suggest to go to university hospital. So, the patient came hospital on 18Aug2014. Result of blood sample is Neutropenic fever due to R/O upper respiratory infection. Then, she hospitalization during 19Aug2014 to 20Aug2014. So, the patient take empirical antibiotic, G-CSF support. Finally, she recovered on 20Aug2014.

Commonly, We reporting SAE when SAE relevant with study drug or anticancer therapy. But this case is not relevant with study drug or anticancer therapy but following the protocol SAE should be reported to sponsor 24 hours from PI awareness regardless of relationship. PI recognized this event during EMR reviwe on 08oct2014 at 17:00 and it is intial and Final report.

Case unblinded due to end of study
Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo, Trastuzumab
Serious Events: Cardiac failure congestive
Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 05 July 2013 and 27 August 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE $(50 \mathrm{mcg})$ adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical conditions at the time of the event included right breast cancer.
On PPD 114 days after the 2nd dose of Blinded vaccine, 72 days after the first intake and 9 days after last intake of Trastuzumab, this 49-year-old subject developed congestive heart failure. The event was clinically significant (or requiring intervention). The subject was treated with digoxin, perindopril erbumine, isosorbide dinitrate, frusemide and carvedilol. The event resolved on 19 February 2014. The investigator considered that there was no reasonable possibility that the congestive heart failure may have been caused by investigational product and and that the event was possibly due to Trastuzumab (taken as chemotherapy for right breast cancer, ROCHE).

Investigator Comments : This subjectPPD was diagnosed as breast cancer on 13MAY2013 and had breast conserving operation on 24JUN2013.
The subject signed ICF for participating in Zoster 028 study on 05JUL2013 and randomized on Pre-chemo Arm.
She had started study vaccine/placebo, had completed second dose of studyvaccine/placebo.

- First dose: 05JUL2013
- Second dose: 27AUG2013

The chemotherapy was started on 16JUL2013.

- doxorubicin hcl 60 mg/m2 IV (q 3weeks): 16JUL2013

17SEP2013

- Cyclophosphamide 600 mg/m2 IV (q 3weeks): 16JUL2013 17SEP2013
- trastuzumab 8mg/kg IV(q 3weeks): 08OCT2013 ongoing

On 10DEC2013 she received 4th cycle with trastuzumab.
Dyspnea(MRC Gr3) occurred on 19DEC2013.
On 23DEC2013, orthopnea occurred, and the subject was admitted to ER for evaluation.
Vital sign: BP 156/113mmHg, PR 106/min, RR 18/min, BT 36.5
SpO2: 96\%
The investigator assessed the event as possibly related to trastuzumab. The investigator was consulted the cardiology, and ordered drug.

Her condition was improved, so she was discharged from the hospital on 25DEC2013.
On 28JAN2014, the investigator reported SAE that find this event after EMR review.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or

## Confidential Unblinded Report - With Suspect Products and Serious Events

disease/tumor

Case unblinded due to end of study Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Nasopharyngitis
Narrative: This 40-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 22nd August 2013, for prophylaxis.

On PPD 21 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 acute nasopharyngitis. Serious criteria included hospitalization. The subject was treated with cefepime, CHLORPHENAMINE (CHLORPHENIRAMINE) and SODIUM CHLORIDE. The outcome of acute nasopharyngitis was recovered/resolved on 17th September 2013.

The investigator considered that there was no reasonable possibility that the acute nasopharyngitis may have been caused by Herpes zoster vs Placebo.

Investigator Comments:
This subject(PPD was diagnosed as breast cancer on 27 MAY2013 and had breast conserving operation on 01JUL2013.
The subject signed ICF for participating in Zoster 028 study on 16 JUL2013 and randomized on $P$ re-chemo Arm.
She had started study vaccine/placebo, had completed second dose of study vaccine/placebo.

- First dose: 16JUL2013
- Second dose: 22AUG2013

The cycle 1 chemotherapy was started on 31JUL2013.
And the cycle 3 chemotherapy was scheduled to
be admit on 13SEP2013.
On 12SEP2013, she was visited to the ER because she had persisted fever, chilling sense and sore throat, sputum.
When she arrived at the ER, the body temporature was 38.3 degrees centigrade.

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

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(V/S: BP 115/76mmHg, PR 115/min, RR 20/
min, BT 38.3, SpO2 99%)
CBC showed Hb 11.8 g/dl, WBC 8.8 x10/uL, Platelet 250 x10/uL, E-ANC 5890/uL, CRP(quant) 0.40
mg/dL.
Sputum culture and Chest X-ray were performed.
She was hospitalized, and has received antibiotics(Cepefime 2000mg TID IV).
On
14SEP2013, she had a rash due to antibiotics(Cepefime) side effect.
She was improving sore throat, the body temporature was 36.5 degrees centigrade.
So she had to stop taking antibiotics(Cepefime), but she had persisted sputum, cough.
On 15SEP2013, sor
e throat and sputum were resolved.
On 16SEP2013, all symptums(sore throat, sputum, cough) resolved.
(2013/09/16 Hb 12.0 g/dl, E-ANC 2470 /uL, CRP(quant) 0.92 mg/dL)
So the cycle 3 chemotherapy was started on 16SEP2013.
On 17SEP2013, she was discharged
with improved condition.
The principal investigator considered that there could be causally as not related to study drug.
Case unblinded due to end of study
Unblinding Date is 10-FEB-17
```

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Breast cancer recurrent

Narrative: This 40-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 22nd August 2013.

Concurrent medical conditions included breast cancer.
On PPD 109 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 breast cancer recurrent. Serious criteria included GSK medically significant and clinically significant/intervention required. The action taken with Herpes zoster vs Placebo was no action taken. The outcome of breast cancer recurrent was resolved on 31st December 2013.

The investigator considered that there was no reasonable possibility that the breast cancer recurrent may

## Confidential Unblinded Report - With Suspect Products and Serious Events

have been caused by Herpes zoster vs Placebo.
Relevant Tests: Lab Tests: [2013/12/09 - US, Breast

1. Newly appeared indeterminate mass in adjacent op. site in right breast.
2. Postop. change in 12 o clock direction of right breast.
3. Postop. change in UOQ of left breast.
4. Benign cyst in left breast. [2013/12/09-Breast, ( right, 11:30), core needle biopsy - INVASIVE DUCTAL CARCINOMA, NUCLEAR GRADE 3/3,
HISTOLOGIC GRADE 2/3.- No microcalcification.
Investigator Comments:
This subject(PPD was diagnosed as breast cancer on 27 MAY2013 and had a breast conserving operation on 01JUL2013.
The subject signed ICF for participating in Zoster 028 study on 16JUL2013 and randomized on Pre-chemo Arm.
She had started study vaccine/placebo, had completed second dose of study vaccine/placebo.

- First dose: 16JUL2013
- Second dose: 22AUG2013

The cycle 1 chemotherapy was started on 31JUL2013.

- Last cycle chemotherapy: 04DEC2013

On 04DEC2013, she find a mass in her right breast.
So she was performed the breast US and biopsy on 09DEC2013.
2013/12/09 - US, Breast

1. Newly appeared indeterminate mass in adjacent op. site in right breast.
2. Postop. change in 12 o'clock direction of right breast.
3. Postop. change in UOQ of left breast.
4. Benign cyst in left breast.

2013/12/09 - Breast, ( right), core needle biopsy

- INVASIVE DUCTAL CARCINOMA, NUCLEAR GRADE 3/3, HISTOLOGIC GRADE $2 / 3$.
- No microcalcification.

On 17DEC2013, she was visited the doctor of breast surgery, and the doctor planning surgery for her.(OP date: 26DEC2013)

On 18DEC2013, PI reported SAE that find this event after EMR review.
Additional report
The subject was admitted to the hospital on 25DEC2013 at the afternoon, and she underwent right breast USG-widw excision on 26DEC2013.
No postoperative complications.
The subject was recovered and discharged on 31DEC2013.
The principal investigator considered that there could be causally as not related to study drug.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

## Confidential Unblinded Report - With Suspect Products and Serious Events

Case unblinded due to end of study
Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Breast cancer recurrent
Narrative: This 40-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. On 22nd August 2013, the subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) for prophylaxis.

Concurrent medical conditions included breast cancer.
On PPD 295 days after receiving Herpes zoster vs Placebo the subject developed severe grade 3 right breast tumor recurrence. Serious criteria included GSK medically significant and clinically significant/intervention required. Herpes zoster vs Placebo was continued with no change. The outcome of right breast tumor recurrence was recovered/resolved on 30th October 2014.

The investigator considered that there was no reasonable possibility that the right breast tumor recurrence may have been caused by Herpes zoster vs Placebo.

Relevant Tests: 2014/04/28 - Breast with Cell Block, FNAB
Breast, ( right ), fine needle aspiration biopsy:
Blood only. (See note )
NOTE: Biopsy is recommended if malignancy is suspected clinically.
2014/05/08 - US, Guided Breast Biopsy

1. III-defined hypoechoic lesion in superficial layer of right breast.
-- US-guided core needle biopsy was done without complication.
2. Postop. change in both breasts.
3. A cyst in left breast.

2014/05/08 - Needle Biopsy (Breast)
Breast, ( right, 12 oclock ), core needle biopsy:

- Fat necrosis with foreign body reaction.
- No microcalcification.


## Confidential Unblinded Report - With Suspect Products and Serious Events

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2014/06/13 - Incisional Biopsy (1)
Skin, ( right breast ), punch biopsy:
    - METASTATIC CARCINOMA, BREAST ORIGIN
    ( s/p wide excision and breast conserving operation for
                invasive ductal carcinoma of right breast; 13S-118516
                13S-58665 ).
```

2014/06/20 Fusion Whole Body PET (F18 FDG)

1) Biopsy proven recurrent skin lesions in 12 and 30 clock direction of right breast
2) Probable metastatic lymphadenopathy in right axillary level I to II and right interlobar areas
3) Multiple mild hypermetabolic nodule like consolidation in lung RML anterior subpleural area; Post RT change

2014/08/11-CT, Chest with Enhance

1. No change of focal skin thickening with soft tissue change and suture meterials in Rt. breast.
--- R/O breast cancer or inflammatory lesion.
2. Several enhancing lymph nodes in Rt. axillar and Rt. interlobar areas.
--- R/O LN metastasis.
3. Focal fibrotic change in anterior area of Rt. lung.
--- R/O RTx. change.

I cannot entry, please refer to the narration.
Diagnostic results (unless otherwise stated, normal values were not provided): On an unknown date, .
Investigator Comments : This subject(PPDwas diagnosed as breast cancer on 27MAY2013 and had a breast conserving operation on 01JUL2013.
The subject signed ICF for participating in Zoster 028 study on 16JUL2013 and randomized on Pre-chemo Arm.
She had started study vaccine/placebo, had completed second dose of study vaccine/placebo.

- First dose: 16JUL2013
- Second dose: 22AUG2013
- Adujuvant chemotherapy: 31JUL2013 to 04DEC2013
- Right breast USG-widw excision(Cancer recurrence): 26DEC2013
- RT: 28JAN2014 to 12MAR2014

On 28APR2014, she found a mass in right breast.
So she was performed needle aspiration biopsy and US guided breast biopsy.
2014/04/28 - Breast with Cell Block, FNAB
Breast, ( right), fine needle aspiration biopsy:
Blood only. (See note )
NOTE: Biopsy is recommended if malignancy is suspected clinically.
2014/05/08 - US, Guided Breast Biopsy

1. III-defined hypoechoic lesion in superficial layer of right breast.
-- US-guided core needle biopsy was done without complication.
2. Postop. change in both breasts.
3. A cyst in left breast.

## Confidential Unblinded Report - With Suspect Products and Serious Events

2014/05/08 - Needle Biopsy (Breast)
Breast, ( right, 12 o clock ), core needle biopsy:

- Fat necrosis with foreign body reaction.
- No microcalcification.

But the right breast mass is oozing, so she had a biopsy done again.
2014/06/13 Incisional Biopsy (1)
Skin, ( right breast ), punch biopsy:
METASTATIC CARCINOMA, BREAST ORIGIN
( $s / p$ wide excision and breast conserving operation for invasive ductal carcinoma of right breast; 13S-118516 13S-58665 ).

2014/06/20 Fusion Whole Body PET (F18 FDG) 2013.12 PET hilar LN uptake

1) Biopsy proven recurrent skin lesions in 12 and $3 O$ clock direction of right breast
2) Probable metastatic lymphadenopathy in right axillary level I to II and right interlobar areas
3) Multiple mild hypermetabolic nodule like consolidation in lung RML anterior subpleural area;

- Post RT change

The subject is planning the operation(mastectomy) after chemotherapy.
The principal investigator considered that there could be causally as not related to study drug.
The additional report will be followed.
The additional report
The subject was started chemotherapy on 25JUN2014.

- Paclitaxel, Carboplatin: 25JUN2014 to ongoing

After 2nd cycle, chest CT was performed on 11AUG2014.
2014/08/11-CT, Chest with Enhance

1. No change of focal skin thickening with soft tissue change and suture meterials in Rt. breast.
--- R/O breast cancer or inflammatory lesion.
2. Several enhancing lymph nodes in Rt. axillar and Rt. interlobar areas.
--- R/O LN metastasis.
3. Focal fibrotic change in anterior area of Rt. lung.
--- R/O RTx. change.
Evaluation of subject response is SD(stable disease) according to RECIST 1.1.
She will be continue chemotherapy.
The principal investigator considered that there could be causally as not related to study drug.
The additional report will be followed.
<The additional report
After 3nd cycle, chest CT was performed on 11SEP2014.
Evaluation of subject response is PD(Progression disease) according to RECIST 1.1.
The patient had a operation on 06OCT2014.

- operation name: Right completion mastectomy ALND(axillary lymph node dissection) c skin graft.

No post-operative complications.
The subject was recovered and discharged on 190CT2014.
She visited outpatient clinic on 300CT2014.

## Confidential Unblinded Report - With Suspect Products and Serious Events

She seemed to be improvement of general condition.
On 300CT2014, the principal investigator assessed that Right breast tumor recurrence
was stable and the SAE(Right breast tumor recurrence) resolved.
The principal investigator considered that there could be causally as not related to study drug.
2014/09/11-CT, Chest with Enhance

1. Irregular mass around rigth breast areolar area and skin thickening.

Right interlobar LN enlargement (3 to 37).
--- slightly increased extent since last CT. r/o minimal interval aggravation of right breast cancer with LN metastasis.
2. Minimal focal fibrosis with irregular patchy opacities in anterolateral subpleural portion of RML.
--- grossly no significant interval change since last CT. r/o RT-induced lung fibrosis.
3. Otherwise, no definite evidence of newly-appeared active lesion such as non-calcified nodule or patchy consolidation in both lungs.
Patent trachea and major central airway without focal wall thickening or obstructive lesion.
No significant effusion or irregular pleural thickening in both hemithorax.

```
2014/10/08 Breast (Rt)
DIAGNOSIS
Breast, ( right ), completion mastectomy
    INVASIVE DUCTAL CARCINOMA, NUCLEAR GRADE 3 of 3,
        HISTOLOGIC GRADE 3 of 3,
        OUTER UPPER QUADRANT TO SUBAREOLAR AREA,
        (wide excision and breast conserving operation of
        breast for invasive ductal carcinoma)
    ( chemoradiation therapy ),
        with 1) intraductal component: EIC (negative),
                nuclear grade 3 of 3, without necrosis.
            2) LYMPHOVASCULAR INVASION: PRESENT.
            3) lymphocytic infiltration: no or minimal.
            4) INVOLVEMENT OF SKIN
                ( UP TO EPIDERMIS WITH ULCER).
            5) no involvement of resection margins
            6) METASTASIS IN 2 OF 10 LYMPH NODE ( 2 of 10)
                ( axillary LN level 3,1 of 1;
                axillary LN, 1 of 9)
                ( metastatic tumor size 9 mm,
                without extranodal extension ).
    Microcalcification present.
```

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding date is 10 Feb 17

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Colon cancer

Narrative: This 54-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 20th December 2013, for prophylaxis.

Concurrent medical conditions included hydronephrosis and malignant neoplasm of sigmoid colon.
On PPD 145 days after receiving Herpes zoster vs Placebo, the subject developed moderate grade 2 colon cancer. Serious criteria included hospitalization and GSK medically significant. The outcome of colon cancer was not recovered/not resolved.

The investigator considered that there was no reasonable possibility that the colon cancer may have been caused by Herpes zoster vs Placebo. Diagnostic results (unless otherwise stated, normal values were not provided): On 14th May 2014, Blood albumin result was $2.5 \mathrm{~g} / \mathrm{dL}$ (normal low: 3.5, normal high: 5.2) and Haemoglobin result was $10.4 \mathrm{~g} / \mathrm{dL}$ (normal low: 13.1, normal high: 17.2).

Investigator Comments :
This subject PPD was diagnosed as colon cancer on 30Oct2013.
The subject signed ICF for participating in Zoster 028 study on 13Nov2013 and randomized on Pre-chemo Arm.
He has started study vaccine/placebo, has completed second dose of study vaccine/placebo.

- First dose: 13Nov2013
- Second dose: 20Dec2013

The cycle 1 chemotherapy was started on 23 Nov2013 and he was hospitalized on 14May2014 for chemotherapy according to protocol.
On 14May2014, He had complained of general weakness.
Furthermore, He was judged increasing mass size of cancer on 15May2014 by CT test.

- Result of Abdomen and pelvis CT :

1. Newly seen enhancing mass like lesion at right adrenal gland ; R/O metastasis.
2. Newly seen small soft tissue lesion at upper abdominal cavity; R/O seeding nodule.
3. Increased in size of mass lesion in left adrenal gland and urinary bladder; R/O aggravated metastasis.
4. No definitely primary tumor delineation in sigmoid colon.
5. Extensive lymphadenopathy at retroperitoneum, mesentery and left inguinal area : grossly no interval change.

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

6. No significant interval change of diffuse wall thickening of both pelvocalyceal system and ureters. ; R/O periureteral metastasis.
Therefore, he had to postponed chemotherapy for a long time. In addition, he has hydronephrosis and general weakness since Oct2013.
He had received treatment about it including supportive care when he was hospitalized instead of chemotherapy.
On 23Jun2014, he was discharged with resolved serious general weakness. He was decided to stop taking no more chemotherapy due to the progress of disease and condition.
Lastly, the principal investigator has judged that there could be causally as not related to study drug. On 24Sep2014, PI aware of the SAE that meet the protocol definition of a SAE event during EMR review at 5 pm .
On 24Sep2014, we had realized that why he was hospitalized for a long time and reported this event as Initial and final SAE report.
on 20nov2014.
Final event term was changed.
because, the principal investigator has judged that the final diagnosis was colon cancer progress disease.
The SAE is not required fllow-up no longer.
On 23Jun2014, he was discharged, And then be does not come to the hospital anymore. The phone visit also did not receive.So, we have failed to follow up

Additional details:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B, DOCETAXEL, ADRIAMYCIN, CYCLOPHOSPHAMIDE
Serious Events: Neutropenia
Narrative: This 48-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 27th May 2013, for prophylaxis.

Co-suspect products included docetaxel for breast cancer, doxorubicin hydrochloride (Adriamycin) for breast cancer and cyclophosphamide for breast cancer.

## Confidential

## Unblinded Report - With Suspect Products and Serious Events

On PPD
75 days after receiving Herpes zoster vs Placebo, the subject developed moderate

- grade 2 neutropenia. Serious criteria included hospitalization and GSK medically significant. The subject was treated with ciprofloxacin (Ciprofloxacine), amoxicillin, clavulanate potassium (Augmentin) and red blood cells (Red Cell Transfusion). Herpes zoster vs Placebo was continued with no change. The outcome of neutropenia was recovered/resolved on 13th August 2013.

The investigator considered that there was no reasonable possibility that the neutropenia may have been caused by Herpes zoster vs Placebo. Other possible cause(s) of the neutropenia included concurrent medication.

## Relevant Tests:

On 11Aug2013, Neutrophils result was $0.2 \times 10 \mathrm{e} 9 / \mathrm{mL}$ ( Low normal 1.7 - High normal 7.5 )
On 11Aug2013, Platelet count result was $73 \times 10 \mathrm{e} 9 / \mathrm{mL}$ ( Low normal 140 - High normal 420 )
On 11Aug2013, White Blood Cell Count result was $0.84 \times 10 \mathrm{e} 9 / \mathrm{mL}$ ( Low normal 4.0 - High normal 10.5 )
On 11Aug2013, Lymphocytes result was $0.3 \times 10 e 9 / \mathrm{mL}$ ( Low normal 1 - High normal 4 )
On 13Aug2013, Neutrophils result was $2.2 \times 10 \mathrm{e} 9 / \mathrm{mL}$ ( Low normal 1.7 - High normal 7.5 )
On 13Aug2013, Platelet count result was $139 \times 10 \mathrm{e} 9 / \mathrm{mL}$ ( Low normal 140 - High normal 420 )
On 13Aug2013, White Blood Cell Count result was $3.6 \times 10 \mathrm{e} 9 / \mathrm{mL}$ ( Low normal 4.0 - High normal 10.5 )
On 13Aug2013, Lymphocytes result was $0.8 \times 10 \mathrm{e} 9 / \mathrm{mL}$ ( Low normal 1 - High normal 4 )
Diagnostic results (unless otherwise stated, normal values were not provided): On 11th August 2013, Haemoglobin result was 9.1 G/DL (normal low: 12, normal high: 16), Lymphocyte count result was 0.3 X10E9/ML (normal low: 1, normal high: 4), Neutrophil count result was 0.2 X10E9/ML (normal low: 1.7, normal high: 7.5), Platelet count result was $73 \times 10 E 9 / \mathrm{ML}$ (normal low: 140, normal high: 420) and White blood cell count result was 0.84 X10E9/ML (normal low: 4.0, normal high: 10.5). On 13th August 2013, Haemoglobin result was 9.5 G/DL (normal low: 12, normal high: 16), Lymphocyte count result was 0.8 X10E9/ML (normal low: 1, normal high: 4), Neutrophil count result was 2.2 X10E9/ML (normal low: 1.7, normal high: 7.5), Platelet count result was 139 X10E9/ML (normal low: 140, normal high: 420) and White blood cell count result was 3.6 X10E9/ML (normal low: 4, normal high: 10.5).

Investigator Comments : Patient PPD was admitted on 10/aug/2013 due to chemotherapy
toxicity:docetaxel, adriamicine and ciclophosphamide (not related to study vaccine administration)
Diagnosis: afebrile neutropenia and anemia
Treatments: red cell transfusion
Patient improved and was discharged on 13/aug/2013
knowledged patient admision on 20/08/2013.
Additional information:
On 10th August 2013, 11 days after receiving docetaxel for breast cancer, doxorubicin hydrochloride (Adriamycin) for breast cancer and cyclophosphamide for breast cancer, the subject developed moderate - grade 2 neutropenia.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Study Center ID: PPD<br>Subject ID: PPD<br>Randomization Number:<br>Case ID: PPD<br>Suspect Products: Hz/su + AS01B, DOCETAXEL, ADRIAMYCINE, CYCLOPHOSPHAMIDE<br>Serious Events: Pancytopenia

Narrative: This 48-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 27th May 2013, for prophylaxis.

Co-suspect products included docetaxel for breast cancer, DOXORUBICIN (ADRIAMYCINE) for breast cancer and cyclophosphamide for breast cancer.

On PPD 93 days after receiving Herpes zoster vs Placebo, the subject developed moderate - grade 2 pancytopenia. Serious criteria included hospitalization and GSK medically significant. The subject was treated with levofloxacin and red blood cells, concentrated (Red Cell Concentrate). Herpes zoster vs Placebo was continued with no change. The outcome of pancytopenia was recovered/resolved on 3rd September 2013.

The investigator considered that there was no reasonable possibility that the pancytopenia may have been caused by Herpes zoster vs Placebo. Other possible cause(s) of the pancytopenia included concurrent medication. Diagnostic results (unless otherwise stated, normal values were not provided): On 28th August 2013, Haemoglobin result was $8.1 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 16), Lymphocyte count result was 0.3 unknown (normal low: 1, normal high: 4), Neutrophil count result was 0.3 unknown (normal low: 1.7, normal high: 7.5), Platelet count result was 56 unknown (normal low: 140, normal high: 420) and White blood cell count result was 0.63 unknown (normal low: 4, normal high: 10.5). On 2nd September 2013, Haemoglobin result was 10.6 g/dL (normal low: 12, normal high: 16), Lymphocyte count result was 0.9 unknown (normal low: 1, normal high: 4), Neutrophil count result was 3.1 unknown (normal low: 1.7, normal high: 7.5), Platelet count result was 99 unknown (normal low: 140, normal high: 420) and White blood cell count result was 4.53 unknown (normal low: 4, normal high: 10.5).

Investigator Comments : patient PPD was admittend due to chemotherapy toxicity (not related with the study vaccine administration)
diagnosis: pancytopenia afebrile
discharged on 03/sep/2013
knowledged patient admision on 29/08/2013.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Additional information:

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On 28 August 2013, 8 days after receiving docetaxel for breast cancer, doxorubicin hydrochloride (Adriamycin) for breast cancer and cyclophosphamide for breast cancer, the subject developed moderate - grade 2 pancytopenia.

Case unblinded due to end of study Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Ovarian cancer

Narrative: This 57-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 11th November 2013, for prophylaxis.

Concurrent medical conditions included ovarian cancer. Concomitant products included dexamethasone and prednisone.

On PPD 338 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 ovarian cancer. Serious criteria included death, hospitalization and GSK medically significant. The subject was treated with amoxicillin, clavulanate potassium (Augmentin), hyoscine butylbromide (Butylscopolamine), dexketoprofen trometamol (Enantyum), metamizole sodium (Metamizol), piperacillin (Piperacilline), tazobactam, red blood cells, concentrated (Red Cell Concentrates-Leukocytes Reduced) and midazolam. The outcome of ovarian cancer was fatal on PPD 2015. The subject died on PPD PPD 2015. The reported cause of death was ovarian cancer. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the ovarian cancer may have been caused by Herpes zoster vs Placebo.

Investigator comments:
Patient began with fever in the context of probable gastrointestinal origin (infiltrating tumor implants colon).
Antibiotic therapy and total parenteral nutrition starts on 22/dec2014. During admission, abdominal CT objective disease progression. Due tothe poor clinical situation and lack of effective treatment options, it was decided to perform only symptomatic treatment with acceptable control of symptoms. The last days progressive deterioration and abdominal pain was worsening and requiring sedation palliative. The patient died on PPD 2015.
the symptoms/signs the patient had on 15-OCT-2014. ADMISSION ON 19/DEC/2014

## Confidential Unblinded Report - With Suspect Products and Serious Events

## NO DISCHARGE DUE TO DEATH ON PPD 2015

SAE is related to disease progression (ovarian cancer progression).
Additional Details:
The subject was withdrawn from the study due to SAE intestinal perforation.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding Date is 10-FEB-17
The subject developed progression of ovarian cancer 338 days after receiving Herpes zoster vs Placebo and died later due to this. The event is considered related to the underlying disease progression.Causal association with vaccine is unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Clostridium bacteraemia

Narrative: This 57-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 11th November 2013, for prophylaxis.

Concomitant products included prednisone.
On PPD 1 year and 14 days after receiving Herpes zoster vs Placebo, the subject developed moderate - grade 2 clostridium bacteremia. Serious criteria included hospitalization and GSK medically significant. The subject was treated with red blood cells, concentrated (Red Cell Concentrate), imipenem, amoxicillin, clavulanate potassium (Augmentine) and dexamethasone. The outcome of clostridium bacteremia was recovered/resolved on 3rd December 2014.

The investigator considered that there was no reasonable possibility that the clostridium bacteremia may have been caused by Herpes zoster vs Placebo.

Relevant Tests: CULTURE TEST ON 26NOV2014: CLOSTRIDIUM POSITIVE CULTURE TEST ON 03dec2014: CLOSTRIDIUM negaTIVE Diagnostic results (unless otherwise stated, normal values were not provided): On 26th November 2014, Haemoglobin result was $7.8 \mathrm{~g} / \mathrm{dL}$ (normal low: 12, normal high: 16). On 5th December 2014, Haemoglobin result was $10.5 \mathrm{~g} / \mathrm{dL}$ (normal low: 12,

## Confidential Unblinded Report - With Suspect Products and Serious Events

normal high: 16).
Investigator Comments :
Patient admitted (27nov2014) for febrile syndrome secondary to Clostridium spp bacteremia. The most likely origin is abdominal due to tumor infiltration

Infection reservoir is discarded. The clinical course is favorable with antibiotics.
After transfusion Hb remains at $10 \mathrm{~g} / \mathrm{dL}$, has deposicones of normal aspect, the patient is stable, and the number of stools is reduced.

Before we proceed improvement at hospital discharge on 05dec2014, CULTURE TEST ON 03dec2014: CLOSTRIDIUM negaTIVE

WE confirm SAE IS related to disease tumour
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Gastrostomy failure
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 17 July 2013 and 04 September 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine $\mathrm{gE}(50 \mathrm{mcg})$ adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical condition at the time of the event included oral mucosal tumor.
On PPD 28 days after the 1st dose of Blinded vaccine, this 48-year-old subject developed gastrostomy failure. The subject was hospitalised. The event resolved on 22 August 2013. The investigator considered that there was no reasonable possibility that the gastrostomy failure may have been caused by investigational product.

Investigator Comments:
Subject has a stomach probe due to his cancer. He has difficulty to eat by mouth.
Patient hospitalized on 14 auf 2013 because of Leakage of the stomach probe.

## Confidential Unblinded Report - With Suspect Products and Serious Events

Gastroenterologists have pumped up balloon and position the probe.
An other doctor changed the cannula and patient the patient was able to return to this home on 22 Aug. 2013.

Case unblinded due to end of study Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Tumour haemorrhage
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 17 July 2013 and 04 September 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical condition at the time of the event included oral mucosal tumor.
On PPD 48 days after the 2nd dose of Blinded vaccine, this 49-year-old subject developed bleeding from his primary tumor. The subject was hospitalised. The subject died on PPD 2013 due to bleeding from his primary tumor. An autopsy was not performed. The investigator considered that there was no reasonable possibility that the bleeding from his primary tumor may have been caused by investigational product.

Investigator Comments :
Patient hospitalized on 22 Oct 2013 due to Bleeding from his primary tumour.
Patient died on PPD 2013.
Because of the severity of the bleeding no particular procedure was performed except to stop bleeding.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding Date is 10-FEB-17
The subject developed bleeding from primary pre-existing tumour 48 days after receiving 2nd dose of Herpes zoster vs placebo and died after 2 days due to this. The event is related to primary tumour. Hence,causal association with vaccine is unlikely. Based on unblnding information,the vaccine received by subject was Herpes zoster vaccine.

Study Number: 116427

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Study Center ID: PPD

Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Tongue neoplasm malignant stage unspecified
Narrative: This 73-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults equal to 18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 8th January 2014, for prophylaxis.

Concurrent medical conditions included carcinoma of tongue.
On PPD 2014, 159 days after receiving Herpes zoster vs Placebo, the subject developed not applicable carcinoma of tongue. Serious criteria included death and GSK medically significant. The outcome of carcinoma of tongue was fatal on PPD 2014. The subject died on PPD 2014. The reported cause of death was carcinoma of tongue. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the carcinoma of tongue may have been caused by Herpes zoster vs Placebo.

Investigator comment:
Patient died at home on PPD 2014 due to disease progression.
This event is linked to disease/tumor and no anti-cancer therapies
Additonal Details:
The subject was withdrawn from the study due to SAE progressive disease of tong cancer.
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study
Unblinding Date is $10-F E B-17$
The subject developed carcinoma of tongue progression 159 days after receiving Herpes zoster vs Placebo and died due to this malignancy. The event is related to progression of underlying medical condition.Causal association with vaccine seems unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Prostate cancer
Narrative: This 83-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 8th January 2014, for prophylaxis.

Concurrent medical conditions included prostate cancer. Concomitant products included influenza vaccine.

In PPD 274 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 progression of prostate cancer. Serious criteria included death and GSK medically significant. The outcome of progression of prostate cancer was fatal on PPD 2014. The subject died on PPD PPD 2014. The reported cause of death was progression of prostate cancer. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the progression of prostate cancer may have been caused by Herpes zoster vs Placebo.

Investigator Comments:
Patient died on PPD 2014 due to prostate cancer. SAE related to disease/ tumor and no anti-cancer therapies.

Additional Information:
This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.
Subject withdrawn from study due to event of progression of prostate cancer.
Case unblinded due to end of study
Unblinding Date is $10-F E B-17$
The subject developed progression of prostate cancer 274 days after receiving Herpes zoster vs Placebo and died due to this. The event is considered related to the use of anti-cancer therapies or the underlying disease progression. Causal association with vaccine seems unlikely.

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD
Randomization Number:
Case ID: PPD

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Suspect Products: Vaccine placebo

Serious Events: Sepsis
Narrative: This 60-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 16th December 2013, for prophylaxis.

On PPD 173 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 sepsis. Serious criteria included hospitalization and GSK medically significant. The subject was treated with cilastatin, imipenem (Tienam) and cefotaxime. The outcome of sepsis was recovered/resolved on 10th July 2014.

The investigator considered that there was no reasonable possibility that the sepsis may have been caused by Herpes zoster vs Placebo.

Investigator Comments:
Patient hospitalized from 4 july 2014 to 10 july 2014. First symptoms on 1 jul 2014 : fever with 41 degrees, shivers, hypotension anemia with $8 \mathrm{~g} / \mathrm{dL}$.

After antibiotherapy with TIENAM, patient discharged from the hospital.
No more information

Case unblinded due to end of study
Unblinding Date is 10-FEB-17
The 60 year old female subject developed sepsis 173 days after receiving Herpes zoster vs Placebo and recovered from this. After due analysis GSK accepts and agrees with the causality assessment of the Serious Adverse Event by the Principal Investigator as unrelated to participation in the study.

Study Number: 116427
Study Center ID: PPD
Subject ID:
PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Uterine leiomyosarcoma
Narrative: This 61-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 16th December 2013, for prophylaxis.

On PPD 2014, 344 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 uterine leiomyosarcoma. Serious criteria included death and GSK medically significant. The outcome of uterine leiomyosarcoma was fatal on PPD 2014. The subject died on PPD PPD 2014. The reported cause of death was uterine leiomyosarcoma. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the uterine leiomyosarcoma may have been caused by Herpes zoster vs Placebo.

Investigator Comments: Patient died due to her disease the PPD 2014. No more information available.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding Date is 10-FEB-17
The subject developed uterine leiomyosarcoma 344 days after receiving Herpes zoster vs Placebo and died due to this. The event is considered related to anti-cancer therapy or underlying disease.Causal association with vaccine is unlikley.

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Bladder cancer

Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 28 October 2013 and 10 December 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE ( 50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical conditions at the time of the event included prostate disorder.
On PPD 99 days after the 2nd dose of Blinded vaccine, this 45-year-old subject developed noninvasive bladder tumor (carcinoma). The subject was hospitalised. The subject was treated with ceftriaxone, cefuroxime, Dipyrone + hyoscine butylbromide, paracetamol, ciprofloxacin hydrochloride, lorazepam, dalteparin sodium, ondansetron hydrochloride, pantoprazole and ketoprofen. The event resolved on 15 May 2014. The investigator considered that there was no reasonable possibility that the

## Confidential Unblinded Report - With Suspect Products and Serious Events

noninvasive bladder tumor (carcinoma) may have been caused by investigational product .
Investigator Comments:
Patient male on chemotherapy treatment.Admission date: 20MAR2014 ONLY MILD HEMATURIA. NO FEVER, NO PAIN. After hydratation with saline solution and treatment with ceftriaxone, hematuria was resolved spontaneusly on 20th March 2014.Discharge date: 20MAR2014 New admission date: 06MAY2014 Patient diagnosed of NON INVASIVE BLADDER CANCER, removed by surgery on April.ONLY MILD HEMATURIA. NO FEVER, NO PAIN. Discharge date: 15 May 2014

Case unblinded due to end of study
Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Abdominal hernia repair
Narrative: This 60-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. On 15th January 2014, the subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) for prophylaxis.

Concurrent medical conditions included abdominal operation.
On PPD 265 days after receiving Herpes zoster vs Placebo the subject developed mild grade 1 abdominal hernia repair. Serious criteria included hospitalization and GSK medically significant. The outcome of abdominal hernia repair was recovered/resolved on 7th October 2014.

The investigator considered that there was no reasonable possibility that the abdominal hernia repair may have been caused by Herpes zoster vs Placebo.

Investigator Comments : Patient admitted 7th October 2014 to proceed surgical correction of abdominal hernia secondary to former surgery (right hemicolectomy). Surgical procedure without complications.Discharged today 8th October 2014.

Case unblinded due to end of study
Unblinding date is 10 Feb 17

Study Number: 116427

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Study Center ID: PPD

Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Pleural effusion

Narrative: This 52-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 17th March 2014, for prophylaxis.

Concomitant products included omeprazole (Omeprazol).
On PPD 348 days after receiving Herpes zoster vs Placebo, the subject developed mild grade 1 pleural effusion. Serious criteria included hospitalization. The subject was treated with ceftriaxone, paracetamol (Acetaminophen), ibuprofen, dalteparin (Dalteparine), metamizole, clindamycin, meropenem and linezolid. The outcome of pleural effusion was recovered/resolved on 14th April 2015.

The investigator considered that there was no reasonable possibility that the pleural effusion may have been caused by Herpes zoster vs Placebo.

Relevant Tests: PLAIN X RAYS (02/MAR/2015): MILD LEFT PLEURAL EFFFUSSION THORACIC CT (03MAR2015): MILD LEFTPLEURAL EFFUSSION AND PNEUMONIA. Diagnostic results (unless otherwise stated, normal values were not provided): On 2nd March 2015, White blood cell count result was $11.25 \times 10 \mathrm{e} 3 / \mathrm{mcL}$ (normal low: 4, normal high: 11).

Investigator Comments:
Patient admitted on 2nd March 2015 due to thoracic pain.
Pleural effussion and pneumonia was discovered in plain RX (2nd March 2015) an thoracic CT (3rd and 4th March 2015).
Ceftriaxone was started on 3thMarch 2015 and Clindamicine was added from 3rt to 9th March 2015 but, due to fever persistance, they werw changed to Meropenem (from 4th to 20th March) and Linezolid (from 6th to 21st MArch 2015).
Positive evolution was demonstrated on plain RX (18th March 2015).
Once antibiotic therapy was conmpleted, patient was discharged on 23rd March 2015.
On 14thAPril 2015 the pleural effussion has disappeared in CT control.
Case unblinded due to end of study
Unblinding Date is $10-$ FEB-17

Study Number: 116427
Study Center ID: PPD

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo, Taxotere, CYCLOPHOSPHAMIDE
Serious Events: Neutropenia, Anaemia


#### Abstract

Narrative: This 58-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 1st dose of Herpes zoster vs Placebo (intramuscular) on 26th April 2013, for prophylaxis.

Co-suspect products included docetaxel (Taxotere) unknown for solid tumor and cyclophosphamide for solid tumor.

Concomitant products included amoxicillin, omeprazole, metoclopramide (Primperan) and lorazepam. On PPD 21 days after receiving Herpes zoster vs Placebo, the subject developed moderate grade 2 neutropenia. Serious criteria included hospitalization and GSK medically significant. Additional event(s) included moderate - grade 2 anemia on 17th May 2013 with serious criteria of hospitalization. The subject was treated with filgrastim (Neupogen), paracetamol (Perfalgan), metoclopramide (Primperan) and meropenem. Herpes zoster vs Placebo was discontinued (Dechallenge was positive). The outcome of neutropenia was recovered/resolved on 23rd May 2013. The outcome(s) of the additional event(s) included anemia (recovered/resolved on 23rd May 2013).

The investigator considered that there was no reasonable possibility that the neutropenia and anemia may have been caused by Herpes zoster vs Placebo. Other possible cause(s) of the neutropenia included concurrent medication (Cyclophosphamide) and Docetaxel. Other possible cause(s) of the anemia included concurrent medication (Cyclophosphamide) and Docetaxel. Diagnostic results (unless otherwise stated, normal values were not provided): On 19th May 2013, Neutrophil count result was $0.2 \times 10 \mathrm{e} 3 / \mathrm{mm} 3$ (normal low: 1.5, normal high: 7.5).

Investigator Comments : Patient requieres inpatien hopitalitation on 19MAY2013 for neutropenia due to chemotherapy(not study investigational product).Patient was released on 23MAY2013. SAE is resolvedThe anemia is due to cytotoxic chemotherapy,

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study Unblinding Date is $10-$ FEB-17


Study Number: 116427
Study Center ID: PPD

## Confidential <br> Unblinded Report - With Suspect Products and Serious Events

Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B, Cisplatin
Serious Events: Pancytopenia, Mucosal inflammation, Candida infection, Neutropenia
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 07 May 2013 and 10 June 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE (50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Concomitant medications included Seguril, Protonix, Primperan, Omeprazole, Morphine, Meropenem, Matrifen, Imipenem, influenza vaccine, fentanyl, Durogesic and Dexketoprofen.

On PPD 21days after the 1st dose of Blinded vaccine and 21days after last dose of Cisplatin, this 51-year-old subject developed mucositis. On PPD 39 days after the 2nd dose of blinded vaccine and 73 days after last dose of Ciplastin, he developed candidiasis, toxic pancytopenia and neutropenia. The subject was hospitalised. The subject was treated with Augmentin, nystatin, fluconazole, paracetamol, filgrastim, lignocaine hydrochloride and red blood cells. The events resolved on 25 July 2013. The investigator considered that there was no reasonable possibility that the toxic pancytopenia, mucositis, candidiasis and neutropenia may have been caused by investigational product and that the events were possibly due to Ciplastin (Other manufacturer) taken for cancer treatment.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Investigator Comments :
Patients required hospitalization on 19Jul2013 for Toxic Pancytopnia due to las chemotherapy cycle received on 09Jul2013 (Not study investigational product), patient also presented mucositis, neutropenia and candidiais. Patient was released on 25Jul2013. SAE is resolved.

Case unblinded due to end of study
Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo
Serious Events: Rectal cancer metastatic

## Confidential

## Unblinded Report - With Suspect Products and Serious Events

Narrative: This 68-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults =18 years of age with solid tumours receiving chemotherapy. On 26th August 2013, the subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) for prophylaxis.

The subject's past medical history included abdominal operation and abdominal operation. Concurrent medical conditions included rectal cancer.

On PPD 213 days after receiving Herpes zoster vs Placebo the subject developed moderate - grade 2 rectal cancer metastatic. Serious criteria included death, hospitalization and GSK medically significant. The subject was treated with metoclopramide, ENOXAPARIN, omeprazole, paracetamol, nystatin (Micostatin), cefazolin sodium (Cefazoline), metamizole, acetylcysteine, furosemide and pantoprazole (Pantoprazol). The outcome of rectal cancer metastatic was fatal on PPD 2014. The subject died on PPD 2014. The reported cause of death was rectal cancer metastatic. An autopsy was not performed.

The investigator considered that there was no reasonable possibility that the rectal cancer metastatic may have been caused by Herpes zoster vs Placebo.

Investigator Comments : Patient that requieres inpatient hospitalization on 31mar2014 due to bowel obstruction as a complication after an scheduled abdominal surgery for rectal tumor that was performed on on 05mar2014.
Patient is still hospitalized but is recovering from SAE.
SAE is not related to investigational product.
SAE symptoms started on 27mar2014.
On 8apr2014 patient is still hospitalized.
Patient was released on 22apr2014. During the hospitalization patient required adhesiolysis surgery and bypass due to the bowel obstruction, surgery was performed on 11apr2014. Computed Tomography was performed on 11apr2014 where bowel obstruction and liver metastic lession were observed so disease progession was diagnosed.

SAE status is resolved with secuelae. SAE is not related to investigational product.
On 28aug2014 while we were scheduling the next visit 5 of the patient, family have informed us that patient died on PPD of 2014 due to disease progression.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor

Case unblinded due to end of study Unblinding date is 10 Feb 17
The subject developed metastatis of rectal carcinoma 213 days after receiving Herpes zoster vs placebo and died later due to this. The event is due to progression of the underlying rectal cancer.Hence,causal association with vaccine seems unlikely.

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B
Serious Events: Diverticulitis
Narrative: This 60-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 16th September 2013, for prophylaxis.

Concurrent medical conditions included anemia hypoplastic. Concomitant products included amiloride hydrochloride, hydrochlorothiazide (Ameride), candesartan cilexetil (Parapres) and letrozole.

On PPD 361 days after receiving Herpes zoster vs Placebo the subject developed moderate - grade 2 diverticulitis. Serious criteria included hospitalization and GSK medically significant. The subject was treated with omeprazole, paracetamol, metamizole, heparin sodium (Heparin Sodium Salt), meropenem, dexketoprofen trometamol (Enantyum), metronidazole, gentamicin (Gentamicine), piperacillin, tazobactam (Piperacilina + Tazobactam), dexchlorpheniramine maleate (Polaramine), tigecycline, amikacin and rifaximin. The outcome of diverticulitis was recovered/resolved on 29th September 2014.

The investigator considered that there was no reasonable possibility that the diverticulitis may have been caused by Herpes zoster vs Placebo.

Relevant Tests: ABDOMEN TC Diagnostic results (unless otherwise stated, normal values were not provided): On 14th September 2014, Haemoglobin result was 8,3 g/dL, Monocyte count result was 20900 IU/L and White blood cell count result was 27100 IU/L.

Investigator Comments:
Patient begins with symptoms of abdominal pain, vomiting and constipation.
He takes prubas diagnosed, abdomino-pelvic tac where the large intestine inflated support diverticulitis looks, leading to his admission to the hospital.
The admission date was the 13/09/2014.
The patient was discharged from the hospital on 29/09/2014 for good evolution, intestinal transit restored. Afebrile and asymptomatic.
continued with their usual treatment.
Case unblinded due to end of study
Unblinding date is 10 Feb 17

# Confidential <br> Unblinded Report - With Suspect Products and Serious Events 

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Hz/su + AS01B, 5-Fluorouracil, Cyclophosphamide, 4-epirubicin
Serious Events: Diabetic ketoacidosis

Narrative: This female subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 22 October 2013 and 10 December 2013, she received the 1st and 2nd dose of Varicella Zoster vaccine gE ( 50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

Medical conditions at the time of the event included depressive syndrome, hypertension and diabetes mellitus type II. Concomitant medications included Paracetamol, Mycostatin and Antibiotic.

On PPD 71 days after the 2nd dose of Blinded vaccine, five days after starting the concomitant chemotherapy medication 5-Fluorouracil, five days after starting the concomitant chemotherapy medication Cyclophosphamide, and five days after starting the concomitant chemotherapy medication 4-epirubicin, this 62-year-old subject developed diabetic ketoacidosis. The subject was hospitalised and the event was life-threatening. The event resolved on 12 March 2014. The investigator considered that there was no reasonable possibility that the diabetic ketoacidosis may have been caused by investigational product and that the event was possibly due to the concomitant chemotherapy medications : 5-Fluorouracil (taken for breast cancer, unknown manufacturer), Cyclophosphamide (taken for breast cancer, non-GSK) and 4-epirubicin (taken for breast cancer, non-GSK).

Investigator Comments:
Patient that requires inpatient hospitalization on 22 feb2014 for vomiting since $19 f e b 2014$ and constipation since 20feb2014. Patient presents a decreased level of consciousness, dysnea and disorientation at the time of examination on 22 feb2014.
Brain acute disease is discarded by CAT on 22 feb2014.
Analytical findings on 22 feb2014 were: hyperglycidemia, renal failure. Attending the severity of the event the patient requires intensive care.
On 25feb2014 analytical values are: glycidemia $119 \mathrm{mg} / \mathrm{dl}$ and creatinine $0.56 \mathrm{mg} / \mathrm{dl}$.
There is a possible relationship between anticancer therapy and vomiting. These vomiting may cause the hyperglycidemia. SAE is not related to investigational product. Patient has not been released yet. On 05mar2014 patient is stable but still hospitalized.
On 12mar2014 patient has been released with final diagnosis diabetic ketoacidosis, SAE is considered resolved. Chemotherapy treatment has been definitely interrupted.
SAE start date was $19 F e b 2014$ when symptoms started. During hospitalization patient suffered a febrile syndrome from 03 Mar 2014 that disappeared when the intravenous catheter was removed. Patient received antibiotherapy (principle active unknown) for this syndrome. The febrile syndrome was a nonserious concurrent event, not an SAE.
The subject did not experience a previous viral or bacterial infection. blood culture was performed with negative result and catheter culture was negative as well.

## Confidential Unblinded Report - With Suspect Products and Serious Events

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study Unblinding date is 10 Feb 17

Study Number: 116427
Study Center ID: PPD
Subject ID: PPD
Randomization Number:
Case ID: PPD
Suspect Products: Vaccine placebo, Erbitux
Serious Events: Drug hypersensitivity
Narrative: This male subject was enrolled in the prophylactic observer-blind study 116427 (Zoster-028). On 14 August 2013 and 13 September 2013, he received the 1st and 2nd dose of Varicella Zoster vaccine gE ( 50 mcg ) adjuvanted with AS01B or lyophilized sucrose reconstituted with saline as placebo.

On PPD four days after the 2nd dose of Blinded vaccine and same day of receiving Erbitux, this 39 -year-old subject developed Erbitux drug allergy. The subject was hospitalised. The subject was treated with dipyrone, metoclopramide hydrochloride, omeprazole, Dexamed and sodium chloride. The event resolved on 18 September 2013. The investigator considered that there was no reasonable possibility that the Erbitux drug allergy may have been caused by investigational product and that the event was possibly due to the concomitant medication, cetuximab (Erbitux, chemotherapy) given for colon carcinoma.

Investigator Comments :
Patient was hospitalized on 17 sep 2013 for allergic reaction on chemotherapy (Erbitux). Planned dose was 1000 mg , there was reaction after 10 minutes of application, dose was discontinued (application of aprox. 80 mg ). Symptoms: nausea, tremor and hypotension.Patient released on 18 sep 2013 in good health condition.

This case contains an event assessed by the investigator as related to the anti-cancer therapies and/or disease/tumor.

Case unblinded due to end of study
Unblinding Date is 10-FEB-17

## 13. POST-TEXT TABLES AND FIGURES

## Table 6.1 Number of subjects by center (Total Vaccinated Cohort)

|  | HZ/su | Placebo |  | tal |
| :---: | :---: | :---: | :---: | :---: |
| Center <br> PPD | n | n | n | \% |
|  | 2 | 0 | 2 | 0.9 |
|  | 5 | 6 | 11 | 4.7 |
|  | 8 | 8 | 16 | 6.9 |
|  | 2 | 4 | 6 | 2.6 |
|  | 15 | 13 | 28 | 12.1 |
|  | 9 | 8 | 17 | 7.3 |
|  | 3 | 3 | 6 | 2.6 |
|  | 2 | 1 | 3 | 1.3 |
|  | 5 | 5 | 10 | 4.3 |
|  | 1 | 0 | 1 | 0.4 |
|  | 6 | 4 | 10 | 4.3 |
|  | 3 | 2 | 5 | 2.2 |
|  | 2 | 0 | 2 | 0.9 |
|  | 2 | 3 | 5 | 2.2 |
|  | 1 | 2 | 3 | 1.3 |
|  | 2 | 2 | 4 | 1.7 |
|  | 1 | 2 | 3 | 1.3 |
|  | 0 | 2 | 2 | 0.9 |
|  | 2 | 3 | 5 | 2.2 |
|  | 8 | 9 | 17 | 7.3 |
|  | 1 |  | 5 | 2.2 |
|  | 3 | 1 | 4 | 1.7 |
|  | 2 | 1 | 3 | 1.3 |
|  | 6 | 5 | 11 | 4.7 |
|  | 0 | 1 | 1 | 0.4 |
|  | 5 | 5 | 10 | 4.3 |
|  | 18 | 17 | 35 | 15.1 |
|  | 2 | 3 | 5 | 2.2 |
|  | 1 | 1 | 2 | 0.9 |
| All | 117 | 115 | 232 |  |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{n}=$ number of subjects included in each group or in total for a given center or for all centers
All = sum of all subjects in each group or in total (sum of all groups)
\% = n/All x 100
Center $=$ GSK Biologicals assigned center number

Table 6.2 Number of subjects by center by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  | PreChemo |  | OnChemo |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HZ/su | Placebo | HZ/su | Placebo |  | Z/su | Plac | cebo |
| Center | n | n | n | n | n | \% | n | \% |
| PPD | 1 | 0 | 1 | 0 | 2 | 1.7 | 0 | 0.0 |
|  | 4 | 5 | 1 | 1 | 5 | 4.3 | 6 | 5.2 |
|  | 6 | 7 | 2 | 1 | 8 | 6.8 | 8 | 7.0 |
|  | 2 | 3 | 0 | 1 | 2 | 1.7 | 4 | 3.5 |
|  | 11 | 9 | 4 | 4 | 15 | 12.8 | 13 | 11.3 |
|  | 7 | 6 | 2 | 2 | 9 | 7.7 | 8 | 7.0 |
|  | 3 | 2 | 0 | 1 | 3 | 2.6 | 3 | 2.6 |
|  | 1 | 1 | 1 | 0 | 2 | 1.7 | 1 | 0.9 |
|  | 4 | 4 | 1 | 1 | 5 | 4.3 | 5 | 4.3 |
|  | 0 | 0 | 1 | 0 | 1 | 0.9 | 0 | 0.0 |
|  | 4 | 3 | 2 | 1 | 6 | 5.1 | 4 | 3.5 |
|  | 3 | 2 | 0 | 0 | 3 | 2.6 | 2 | 1.7 |
|  | 2 | 0 | 0 | 0 | 2 | 1.7 | 0 | 0.0 |
|  | 1 | 1 | 1 | 2 | 2 | 1.7 | 3 | 2.6 |
|  | 1 | 2 | 0 | 0 | 1 | 0.9 | 2 | 1.7 |
|  | 1 | 2 | 1 | 0 | 2 | 1.7 | 2 | 1.7 |
|  | 1 | 1 | 0 | 1 | 1 | 0.9 | 2 | 1.7 |
|  | 0 | 2 | 0 | 0 | 0 | 0.0 | 2 | 1.7 |
|  | 1 | 2 | 1 | 1 | 2 | 1.7 | 3 | 2.6 |
|  | 7 | 8 | 1 | 1 | 8 | 6.8 | 9 | 7.8 |
|  | 1 | 3 | 0 | 1 | 1 | 0.9 | 4 | 3.5 |
|  | 2 | 1 | 1 | 0 | 3 | 2.6 | 1 | 0.9 |
|  | 1 | 1 | 1 | 0 | 2 | 1.7 | 1 | 0.9 |
|  | 5 | 4 | 1 | 1 | 6 | 5.1 | 5 | 4.3 |
|  | 0 | 0 | 0 | 1 | 0 | 0.0 | 1 | 0.9 |
|  | 3 | 4 | 2 | 1 | 5 | 4.3 | 5 | 4.3 |
|  | 15 | 14 | 3 | 3 | 18 | 15.4 | 17 | 14.8 |
|  | 2 | 3 | 0 | 0 | 2 | 1.7 | 3 | 2.6 |
|  | 1 | 1 | 0 | 0 | 1 | 0.9 | 1 | 0.9 |
| All | 90 | 91 | 27 | 24 | 117 | 7100 | 115 | 100 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{n}=$ number of subjects included in each group or in total for a given center or for all centers
All = sum of all subjects in each group or in total (sum of all groups)
$\%=n /$ All $\times 100$
Center $=$ GSK Biologicals assigned center number

Table 6.3 Number of subjects by center by age strata (Total Vaccinated Cohort)

|  | 18-49ys |  | $\geq 50 y s$ |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HZ/su | Placebo | HZ/su | Placebo |  | HZ/su |  | acebo |
| Center | n | n | n | n | n | \% | n | \% |
| PPD | 0 | 0 | 2 | 0 | 2 | 1.7 | 0 | 0.0 |
|  | 0 | 1 | 5 | 5 | 5 | 4.3 | 6 | 5.2 |
|  | 1 | 2 | 7 | 6 | 8 | 6.8 | 8 | 7.0 |
|  | 1 | 3 | 1 | 1 | 2 | 1.7 | 4 | 3.5 |
|  | 6 | 5 | 9 | 8 | 15 | 12.8 | 813 | 11.3 |
|  | 2 | 0 | 7 | 8 | 9 | 7.7 | 8 | 7.0 |
|  | 0 | 0 | 3 | 3 | 3 | 2.6 | 3 | 2.6 |
|  | 0 | 1 | 2 | 0 | 2 | 1.7 | 1 | 0.9 |
|  | 1 | 0 | 4 | 5 | 5 | 4.3 | 5 | 4.3 |
|  | 0 | 0 | 1 | 0 | 1 | 0.9 | 0 | 0.0 |
|  | 2 | 2 | 4 | 2 | 6 | 5.1 | 4 | 3.5 |
|  | 0 | 0 | 3 | 2 | 3 | 2.6 | 2 | 1.7 |
|  | 1 | 0 | 1 | 0 | 2 | 1.7 | 0 | 0.0 |
|  | 1 | 0 | 1 | 3 | 2 | 1.7 | 3 | 2.6 |
|  | 1 | 1 | 0 | 1 | 1 | 0.9 | 2 | 1.7 |
|  | 2 | 0 | 0 | 2 | 2 | 1.7 | 2 | 1.7 |
|  | 0 | 1 | 1 | 1 | 1 | 0.9 | 2 | 1.7 |
|  | 0 | 0 | 0 | 2 | 0 | 0.0 | 2 | 1.7 |
|  | 0 | 2 | 2 | 1 | 2 | 1.7 | 3 | 2.6 |
|  | 5 | 4 | 3 | 5 | 8 | 6.8 | 9 | 7.8 |
|  | 0 | 0 | 1 | 4 | 1 | 0.9 | 4 | 3.5 |
|  | 2 | 0 | 1 | 1 | 3 | 2.6 | 1 | 0.9 |
|  | 1 | 0 | 1 | 1 | 2 | 1.7 | 1 | 0.9 |
|  | 1 | 1 | 5 | 4 | 6 | 5.1 | 5 | 4.3 |
|  | 0 | 0 | 0 | 1 | 0 | 0.0 | 1 | 0.9 |
|  | 1 | 0 | , | 5 | 5 | 4.3 | 5 | 4.3 |
|  | 2 | 5 | 16 | 12 | 18 | 15.4 | 417 | 14.8 |
|  | 1 | 2 | 1 | 1 | 2 | 1.7 | 3 | 2.6 |
|  | 0 | 0 | 1 | 1 | 1 | 0.9 | 1 | 0.9 |
| All | 31 | 30 | 86 | 85 | 117 | 17100 | 115 |  |

18-49ys $=$ Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{n}=$ number of subjects included in each group or in total for a given center or for all centers
All = sum of all subjects in each group or in total (sum of all groups)
\% = n/All x 100
Center $=$ GSK Biologicals assigned center number

Table 6.4 Number of subjects vaccinated, completed up to visit 3 and withdrawn with reason for withdrawal (Total Vaccinated Cohort)

|  | HZ/su | Placebo | Total |
| :--- | :--- | :--- | :--- |
| Number of subjects vaccinated | 117 | 115 | 232 |
| Number of subjects completed Visit 3 | 102 | 107 | 209 |
| Number of subjects withdrawn | 15 | 8 | 23 |
| Reasons for withdrawal : |  |  |  |
| Serious Adverse Event | 3 | 2 | 5 |
| Non-Serious Adverse Event | 0 | 0 | 0 |
| Protocol violation | 0 | 0 | 0 |
| Consent withdrawal (not due to an adverse event) | 11 | 5 | 16 |
| Migrated/moved from study area | 0 | 0 | 0 |
| Lost to follow-up (subjects with incomplete vaccination course) | 0 | 0 | 0 |
| Lost to follow-up (subjects with complete vaccination course) | 0 | 0 | 0 |
| Suspected HZ Episode | 0 | 0 | 0 |
| Sponsor study termination | 0 | 0 | 0 |
| Others | 1 | 1 | 2 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed study visit 3
Withdrawn = number of subjects who did not come back for the visit 3

Table 6.5 Number of subjects vaccinated, completed up to visit 3 and withdrawn with reason for withdrawal by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  | PreChemo |  | OnChemo |  | Total |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |
| Number of subjects vaccinated | 90 | 91 | 27 | 24 | 117 | 115 |
| Number of subjects completed Visit 3 | 77 | 84 | 25 | 23 | 102 | 107 |
| Number of subjects withdrawn | 13 | 7 | 2 | 1 | 15 | 8 |
| Reasons for withdrawal : |  |  |  |  |  |  |
| Serious Adverse Event | 3 | 2 | 0 | 0 | 3 | 2 |
| Non-Serious Adverse Event | 0 | 0 | 0 | 0 | 0 | 0 |
| Protocol violation | 0 | 0 | 0 | 0 | 0 | 0 |
| Consent withdrawal (not due to an adverse event) | 9 | 4 | 2 | 1 | 11 | 5 |
| Migrated/moved from study area | 0 | 0 | 0 | 0 | 0 | 0 |
| Lost to follow-up (subjects with incomplete vaccination course) | 0 | 0 | 0 | 0 | 0 | 0 |
| Lost to follow-up (subjects with complete vaccination course) | 0 | 0 | 0 | 0 | 0 | 0 |
| Suspected HZ Episode | 0 | 0 | 0 | 0 | 0 | 0 |
| Sponsor study termination | 0 | 0 | 0 | 0 | 0 | 0 |
| Others | 1 | 1 | 0 | 0 | 1 | 1 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group
Vaccinated = number of subjects who were vaccinated in the study
Completed $=$ number of subjects who completed study visit 3
Withdrawn = number of subjects who did not come back for the visit 3

Table 6.6 Number of subjects vaccinated, completed up to visit 3 and withdrawn with reason for withdrawal by age strata (Total Vaccinated Cohort)

|  | 18-49ys |  | $\geq$ 50ys |  | Total |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |
| Number of subjects vaccinated | 31 | 30 | 86 | 85 | 117 | 115 |
| Number of subjects completed Visit 3 | 31 | 30 | 71 | 77 | 102 | 107 |
| Number of subjects withdrawn | 0 | 0 | 15 | 8 | 15 | 8 |
| Reasons for withdrawal : |  |  |  |  |  |  |
| Serious Adverse Event | 0 | 0 | 3 | 2 | 3 | 2 |
| Non-Serious Adverse Event | 0 | 0 | 0 | 0 | 0 | 0 |
| Protocol violation | 0 | 0 | 0 | 0 | 0 | 0 |
| Consent withdrawal (not due to an adverse event) | 0 | 0 | 11 | 5 | 11 | 5 |
| Migrated/moved from study area | 0 | 0 | 0 | 0 | 0 | 0 |
| Lost to follow-up (subjects with incomplete vaccination course) | 0 | 0 | 0 | 0 | 0 | 0 |
| Lost to follow-up (subjects with complete vaccination course) | 0 | 0 | 0 | 0 | 0 | 0 |
| Suspected HZ Episode | 0 | 0 | 0 | 0 | 0 | 0 |
| Sponsor study termination | 0 | 0 | 0 | 0 | 0 | 0 |
| Others | 0 | 0 | 1 | 1 | 1 | 1 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed study visit 3
Withdrawn = number of subjects who did not come back for the visit 3
Table 6.7 Number of subjects vaccinated, completed up to the study end and withdrawn with reason for withdrawal by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  | PreChemo |  | OnChemo |  | Total |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |
| Number of subjects vaccinated | 90 | 91 | 27 | 24 | 117 | 115 |
| Number of subjects completed | 68 | 72 | 22 | 18 | 90 | 90 |
| Number of subjects withdrawn | 22 | 19 | 5 | 6 | 27 | 25 |
| Reasons for withdrawal : |  |  |  |  |  |  |
| Serious Adverse Event | 10 | 11 | 3 | 1 | 13 | 12 |
| Non-Serious Adverse Event | 0 | 0 | 0 | 0 | 0 | 0 |
| Protocol violation | 0 | 0 | 0 | 0 | 0 | 0 |
| Consent withdrawal (not due to an adverse event) | 10 | 5 | 2 | 4 | 12 | 9 |
| Migrated/moved from study area | 1 | 1 | 0 | 0 | 1 | 1 |
| Lost to follow-up (subjects with incomplete vaccination course) | 0 | 0 | 0 | 0 | 0 | 0 |
| Lost to follow-up (subjects with complete vaccination course) | 1 | 1 | 0 | 0 | 1 | 1 |
| Suspected HZ Episode | 0 | 0 | 0 | 0 | 0 | 0 |
| Sponsor study termination | 0 | 0 | 0 | 0 | 0 | 0 |
| Others | 0 | 1 | 0 | 1 | 0 | 2 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed last study visit
Withdrawn = number of subjects who did not come back for the last visit

Table 6.8 Number of subjects vaccinated, completed up to the study end and withdrawn with reason for withdrawal by age strata (Total Vaccinated Cohort)

|  | 18-49ys |  | $\geq 50 y s$ |  | Total |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |
| Number of subjects vaccinated | 31 | 30 | 86 | 85 | 117 | 115 |
| Number of subjects completed | 30 | 26 | 60 | 64 | 90 | 90 |
| Number of subjects withdrawn | 1 | 4 | 26 | 21 | 27 | 25 |
| Reasons for withdrawal : |  |  |  |  |  |  |
| Serious Adverse Event | 1 | 2 | 12 | 10 | 13 | 12 |
| Non-Serious Adverse Event | 0 | 0 | 0 | 0 | 0 | 0 |
| Protocol violation | 0 | 0 | 0 | 0 | 0 | 0 |
| Consent withdrawal (not due to an adverse event) | 0 | 1 | 12 | 8 | 12 | 9 |
| Migrated/moved from study area | 0 | 1 | 1 | 0 | 1 | 1 |
| Lost to follow-up (subjects with incomplete vaccination course) | 0 | 0 | 0 | 0 | 0 | 0 |
| Lost to follow-up (subjects with complete vaccination course) | 0 | 0 | 1 | 1 | 1 | 1 |
| Suspected HZ Episode | 0 | 0 | 0 | 0 | 0 | 0 |
| Sponsor study termination | 0 | 0 | 0 | 0 | 0 | 0 |
| Others | 0 | 0 | 0 |  | 0 | 2 |
| $\begin{aligned} & \text { 18-49ys = Subjects aged between } 18 \text { and } 49 \text { years } \\ & \geq 50 y s=\text { Subjects aged } 50 \text { years and older } \\ & \text { HZ/su }=\text { Herpes Zoster sub-unit vaccine group } \\ & \text { Placebo = Placebo group } \end{aligned}$ |  |  |  |  |  |  |
| Vaccinated = number of subjects who were vaccinated in the stud Completed = number of subjects who completed last study visit Withdrawn = number of subjects who did not come back for the | ludy |  |  |  |  |  |

Table 6.9 Number of subjects at each visit and list of withdrawn subjects (Total Vaccinated Cohort)

| Group | VISIT | N Withdrawn <br> Subject <br> numbers | Reason for withdrawal |
| :---: | :---: | :---: | :---: |
| HZ/su | VISIT 1 - M0 | 117 |  |
|  |  | PPD | Consent withdrawal, not due to an adverse event |
|  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  | Consent withdrawal, not due to an adverse event |
|  | VISIT 2 - M1 | 105 |  |
|  |  |  | VISIT 3 DIDNT PERFORM BY ERROR*Serious Adverse Event and/or pIMD |
|  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  | Consent withdrawal, not due to an adverse event |
|  | VISIT 3 - M2 | 102 |  |
|  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  | THE PATIENT FINALIZED THE FIRST CHEMOTHEPARY COURSE IN LESS THAN TWO MONTHS AFTER V3*Serious Adverse Event and/or pIMD |
|  | $\begin{aligned} & \text { VISIT4-M4 to } 13 \\ & \hline \text { PHONE CONT } \\ & \text { M5 } \end{aligned}$ | 100 |  |
|  |  | 100 |  |
|  |  |  | Migrated / moved from the study area |
|  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  | Serious Adverse Event and/or pIMD |


| Group | VISIT | N | Withdrawn Subject numbers | Reason for withdrawal |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | PHONE CONT M9 | 94 |  |  |  |
|  |  |  | PPD | Consent withdrawal, not due to an adverse event |  |
|  |  |  |  | Lost to follow-up |  |
|  |  |  |  | Serious Adverse Event and/or pIMD |  |
|  |  |  |  | Serious Adverse Event and/or pIMD |  |
|  | VISIT 5 - M13 | 90 |  |  |  |
| Placebo | VISIT 1 - M0 | 115 |  |  |  |
|  |  |  |  | Consent withdrawal, not due to an adverse event |  |
|  |  |  |  | Consent withdrawal, not due to an adverse event |  |
|  |  |  |  | Serious Adverse Event and/or pIMD |  |
|  |  |  |  | Consent withdrawal, not due to an adverse event |  |
|  |  |  |  | Consent withdrawal, not due to an adverse event |  |
|  | VISIT 2 - M1 | 110 |  |  |  |
|  |  |  |  | PATIENT DETERIORATION , FOR PALLIATIVE CARE, REMOVAL OF PICC LINE |  |
|  |  |  |  | Serious Adverse Event and/or pIMD |  |
|  |  |  |  | Consent withdrawal, not due to an adverse event |  |
|  | VISIT 3-M2 | 107 |  |  |  |
|  |  |  |  | Consent withdrawal, not due to an adverse event |  |
|  |  |  |  | Serious Adverse Event and/or pIMD |  |
|  |  |  |  | Serious Adverse Event and/or pIMD |  |
|  |  |  |  | Serious Adverse Event and/or pIMD |  |
|  |  |  |  | NOT APPLICABLE BY PROTOCOL*MEDICAL DECISION |  |
|  | VISIT4-M4 to 13 | 102 |  |  |  |
|  | PHONE CONT M5 | 102 |  |  |  |
|  |  |  |  | Lost to follow-up |  |
|  |  |  |  | Serious Adverse Event and/or pIMD |  |
|  |  |  |  | Serious Adverse Event and/or pIMD |  |
|  |  |  |  | Serious Adverse Event and/or pIMD |  |
|  |  |  |  | Serious Adverse Event and/or pIMD |  |
|  | PHONE CONT M9 | 97 |  |  |  |


| Group | VISIT | N | Withdrawn Subject numbers | Reason for withdrawal |
| :---: | :---: | :---: | :---: | :---: |
| VISIT 5 M13 |  |  | PPD | Consent withdrawal, not due to an adverse event |
|  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  | Migrated / moved from the study area |
|  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  | 90 |  |  |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ Number of subjects who are still in the study up to the visit
Withdrawn = Subject who did not return after the visit

Table 6.10 Number of subjects at each visit and list of withdrawn subjects by PreChemo/OnChemo groups (Total Vaccinated Cohort)

| Subgroup | Group | VISIT | N | Withdrawn Subject numbers | Reason for withdrawal |
| :---: | :---: | :---: | :---: | :---: | :---: |
| PreChemo | HZ/su | VISIT 1 - M0 | 90 |  |  |
|  |  |  |  | PPD | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  | VISIT 2 - M1 | 80 |  |  |
|  |  |  |  |  | VISIT 3 DIDNT PERFORM BY ERROR*Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  | VISIT 3 - M2 | 77 |  |  |
|  |  |  |  |  | THE PATIENT FINALIZED THE FIRST CHEMOTHEPARY COURSE IN LESS THAN TWO MONTHS AFTER V3*Serious Adverse Event and/or pIMD |
|  |  | VISIT4-M4 to 13 PHONE CONT M5 |  |  |  |
|  |  |  | 76 |  |  |
|  |  |  |  |  | Migrated / moved from the study area |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  | PHONE CONT M9 | 72 |  |  |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Lost to follow-up |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |


| Subgroup | Group | VISIT | N Withdrawn Subject numbers | Reason for withdrawal |
| :---: | :---: | :---: | :---: | :---: |
|  |  |  | PPD | Serious Adverse Event and/or pIMD |
|  |  | VISIT 5 - M13 | 68 |  |
|  | Placebo | VISIT 1 - M0 | 91 |  |
|  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  | VISIT 2 - M1 | 87 |  |
|  |  |  |  | PATIENT DETERIORATION, FOR PALLIATIVE CARE, REMOVAL OF PICC LINE |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  | VISIT 3 - M2 | 84 |  |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  | VISIT4-M4 to 13 | 81 |  |
|  |  | PHONE CONT M5 | 81 |  |
|  |  |  |  | Lost to follow-up |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  | PHONE CONT M9 | 76 |  |
|  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  | Migrated / moved from the study area |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  | VISIT 5 - M13 | 72 |  |
| OnChemo | HZ/su | VISIT 1 - M0 | 27 |  |
|  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  | Consent withdrawal, not due to an adverse event |



PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ Number of subjects who are still in the study up to the visit
Withdrawn = Subject who did not return after the visit

Table 6.11 Number of subjects at each visit and list of withdrawn subjects by age strata (Total Vaccinated Cohort)

| Subgroup | Group | VISIT | $\begin{array}{l\|l} \mathrm{N} & \mathrm{~W} \\ \mathrm{~S} \\ \mathrm{n} \end{array}$ | Withdrawn Subject numbers | Reason for withdrawal |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 18-49ys | HZ/su | VISIT 1 - M0 | 31 |  |  |
|  |  | VISIT 2 - M1 | 31 |  |  |
|  |  | VISIT 3-M2 | 31 |  |  |
|  |  |  | PPD |  | Serious Adverse Event and/or pIMD |
|  |  | VISIT4-M4 to 13 |  |  |  |
|  |  | PHONE CONT M5 |  |  |  |
|  |  | $\begin{aligned} & \text { PHONE CONT } \\ & \text { M9 } \end{aligned}$ |  |  |  |
|  |  | VISIT 5 - M13 | 30 |  |  |
|  | Placebo | VISIT 1 - M0 | 30 |  |  |
|  |  | VISIT 2 - M1 | 30 |  |  |
|  |  | VISIT 3 - M2 | 30 |  |  |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  | VISIT4-M4 to 13 | 29 |  |  |
|  |  | PHONE CONT M5 | 29 |  |  |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  | PHONE CONT M9 | 28 |  |  |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Migrated / moved from the study area |
|  |  | VISIT 5 - M13 | 26 |  |  |
| $\geq 50 y s$ | HZ/su | VISIT 1 - M0 | 86 |  |  |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |


| Subgroup | Group | VISIT | N | Withdrawn Subject numbers | Reason for withdrawal |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | Placebo |  |  | PPD | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  | VISIT 2 - M1 | 74 |  |  |
|  |  |  |  |  | VISIT 3 DIDNT PERFORM BY ERROR*Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  | VISIT 3 - M2 | 71 |  |  |
|  |  |  |  |  | THE PATIENT FINALIZED THE FIRST CHEMOTHEPARY COURSE IN LESS THAN TWO MONTHS AFTER V3*Serious Adverse Event and/or pIMD |
|  |  | $\begin{array}{\|l\|} \hline \text { VISIT4-M4 to } 13 \\ \hline \text { PHONE CONT } \\ \hline \text { M5 } \end{array}$ |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  | Migrated / moved from the study area |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  | PHONE CONT M9 | 64 |  |  |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Lost to follow-up |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  | VISIT 5-M13 | 60 |  |  |
|  |  | VISIT 1 - M0 | 85 |  |  |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |
|  |  |  |  |  | Serious Adverse Event and/or pIMD |
|  |  |  |  |  | Consent withdrawal, not due to an adverse event |



18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ Number of subjects who are still in the study up to the visit
Withdrawn = Subject who did not return after the visit

## Table 6.12 Number of subjects enrolled into the study as well as the number excluded from ATP safety analyses up to 30 days post last vaccination with reasons for exclusion

|  | Total |  |  | HZ/su |  | Placebo |  | NOGRP |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Title | n | s | \% | n | s | n | S | n | s |
| Total Enrolled Cohort | 266 |  |  | 130 |  | 132 |  | 4 |  |
| Study vaccine dose not administered but subject number allocated ( code 1030 ) | 34 | 34 |  | 13 | 13 | 17 | 17 | 4 | 4 |
| Total Vaccinated Cohort | 232 |  | 100 | 117 |  | 115 |  | 0 |  |
| Administration of vaccine(s) forbidden in the protocol up to 30 days post last dose ( code 1041 ) | 1 | 1 |  | 0 | 0 | 1 | 1 | 0 | 0 |
| Randomisation code broken at the investigator site ( code 1060) | 0 | 1 |  | 0 | 0 | 0 | 1 | 0 | 0 |
| Protocol violation linked to the inclusion/exclusion criteria including age ( code 1600) | 6 | 6 |  | 4 | 4 | 2 | 2 | 0 | 0 |
| ATP Cohort for Safety up to 30 days post last vaccination | 225 |  | 97.0 | 113 |  | 112 |  | 0 |  |

NOGRP = No assigned group
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Note: Subjects may have more than one elimination code assigned
$\mathrm{n}=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower
elimination code number
$s=$ number of subjects with the elimination code assigned
$\%=$ percentage of subjects in the considered ATP cohort relative to the Total Vaccinated Cohort

Table 6.13 Number of subjects enrolled into the study as well as the number excluded from ATP analyses for Humoral immunogenicity with reasons for exclusion

|  | Total |  |  | HZ/su |  | Placebo |  | NOGRP |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Title | n | s | \% | n | S | n | s | n | s |
| Total Enrolled Cohort | 266 |  |  | 130 |  | 132 |  | 4 |  |
| Study vaccine dose not administered but subject number allocated ( code 1030 ) | 34 | 34 |  | 13 | 13 | 17 | 17 | 4 | 4 |
| Total Vaccinated Cohort | 232 |  | 100 | 117 |  | 115 |  | 0 |  |
| Administration of vaccine(s) forbidden in the protocol up to PII (Month 2) ( code 1040) | 1 | 1 |  | 0 | 0 | 1 | 1 | 0 | 0 |
| Administration of vaccine(s) forbidden in the protocol up to 30 days post last dose ( code 1041 ) | 0 | 1 |  | 0 | 0 | 0 | 1 | 0 | 0 |
| Randomisation code broken at the investigator site ( code 1060 ) | 0 | 1 |  | 0 | 0 | 0 | 1 | 0 | 0 |
| Protocol violation linked to the inclusion/exclusion criteria including age ( code 1600 ) | 6 | 6 |  | 4 | 4 | 2 | 2 | 0 | 0 |
| Administration of any medication forbidden by the protocol ( code 2040 ) | 2 | 2 |  | 1 | 1 | 1 | 1 | 0 | 0 |
| Concomitant infection related to the vaccine which may influence immune response ( code 2060 ) | 1 | 1 |  | 1 | 1 | 0 | 0 | 0 | 0 |
| Non compliance with blood sampling schedule (including wrong and unknown dates ) ( code 2090 ) | 6 | 6 |  | 3 | 3 | 3 | 3 | 0 | 0 |
| Essential serological data missing ( code 2100 ) | 28 | 29 |  | 18 |  | 10 | 11 | 0 | 0 |
| Subjects who did not complete the full vaccination course (2 doses) ( code 2500) | 3 | 22 |  | 3 |  | 0 | 5 | 0 | 0 |
| ATP cohort for Humoral immunogenicity | 185 |  |  | 87 |  | 98 |  | 0 |  |

NOGRP = No assigned group
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Note: Subjects may have more than one elimination code assigned
$\mathrm{n}=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
$s=$ number of subjects with the elimination code assigned
$\%=$ percentage of subjects in the considered ATP cohort relative to the Total Vaccinated Cohort

## Table 6.14 Number of subjects enrolled into the study as well as the number excluded from TVC analyses for CMI immunogenicity with reasons for exclusion

|  | Total |  |  | HZ/su |  | Placebo |  | NOGRP |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Title | n | S | \% | n | S | n | S | n | S |
| Total Enrolled Cohort | 266 |  |  | 130 |  | 132 |  | 4 |  |
| Study vaccine dose not administered but subject number allocated ( code 1030) | 34 | 34 |  | 13 | 13 | 17 | 17 | 4 | 4 |
| Total Vaccinated Cohort | 232 |  | 100 | 117 |  | 115 |  | 0 |  |
| Subjects not belonging to CMI sub-cohort ( code 4130 ) | 156 | 156 |  | 78 | 78 | 78 | 78 | 0 | 0 |
| Total Vaccinated Cohort for CMI immunogenicity | 76 |  | 32.8 | 39 |  | 37 |  | 0 |  |

## NOGRP = No assigned group

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Note: Subjects may have more than one elimination code assigned
$n=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
$s=$ number of subjects with the elimination code assigned
\% = percentage of subjects in the considered Total Vaccinated Cohort for CMI immunogenicity relative to the Total Vaccinated Cohort

Table 6.15 Number of subjects vaccinated in the CMI sub-cohort into the study as well as the number excluded from ATP analyses for CMI immunogenicity with reasons for exclusion

|  | Total |  |  | HZ/su |  | Placebo |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Title | n | S | \% | n | S | n | s |
| Total Vaccinated Cohort for CMI immunogenicity | 76 |  | 100 | 39 |  | 37 |  |
| Protocol violation linked to the inclusion/exclusion criteria including age ( code 1600 ) | 4 | 4 |  | 2 | 2 | 2 | 2 |
| Concomitant infection related to the vaccine which may influence immune response ( code 2060) | 1 | 1 |  | 1 | 1 | 0 | 0 |
| Non compliance with blood sampling schedule ( including wrong and unknown dates ) ( code 2090 ) | 2 | 2 |  | 1 | 1 | 1 | 1 |
| Essential serological data missing ( code 2100 ) | 10 | 10 |  | 7 | 7 | 3 | 3 |
| Subjects who did not complete the full vaccination course (2 doses) ( code 2500 ) | 1 | 8 |  | 1 | 8 | 0 | 0 |
| ATP cohort for CMI immunogenicity | 58 |  | 76.3 | 27 |  | 31 |  |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Note: Subjects may have more than one elimination code assigned
$\mathrm{n}=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
$s=$ number of subjects with the elimination code assigned
\% = percentage of subjects in the considered ATP cohort for CMI relative to the Total Vaccinated Cohort for CMI immunogenicity

Table 6.16 Number of subjects enrolled into the study as well as the number excluded from ATP analyses for Humoral immunogenicity with reasons for exclusion by PreChemo/OnChemo groups

|  | Total |  |  |  |  |  |  |  |  |  | PreChemo |  |  |  |  |  | OnChemo |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | NOGRP |  |  | HZ/su |  |  | Placebo |  |  |  | NOGRP |  | HZ/su |  | Placebo |  | HZ/su |  | Placebo |  |
| Title | n | s | \% | n | s | \% | n | s |  | \% | n | s | n | s | n | s | n | s | n | s |
| Total Enrolled Cohort | 4 |  |  | 130 |  |  | 132 |  |  |  | 4 |  | 103 |  | 108 |  | 27 |  | 24 |  |
| Study vaccine dose not administered but subject number allocated ( code 1030) | 4 | 4 |  | 13 | 13 |  | 17 | 17 |  |  | 4 | 4 | 13 | 13 | 17 | 17 | 0 | 0 | 0 | 0 |
| Total Vaccinated Cohort | 0 |  | - | 117 |  | 100 | 115 |  |  | 100 | 0 |  | 90 |  | 91 |  | 27 |  | 24 |  |
| Administration of vaccine(s) forbidden in the protocol up to PII (Month 2) ( code 1040) | 0 | 0 |  | 0 | 0 |  | 1 | 1 |  |  | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 |
| Administration of vaccine(s) forbidden in the protocol up to 30 days post last dose ( code 1041) | 0 | 0 |  | 0 | 0 |  | 0 | 1 |  |  | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Randomisation code broken at the investigator site ( code 1060 ) | 0 | 0 |  | 0 | 0 |  | 0 | 1 |  |  | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Protocol violation linked to the inclusion/exclusion criteria including age ( code 1600) | 0 | 0 |  | 4 | 4 |  | 2 | 2 |  |  | 0 | 0 | 4 | 4 | 2 | 2 | 0 | 0 | 0 | 0 |
| Administration of any medication forbidden by the protocol ( code 2040 ) | 0 | 0 |  | 1 | 1 |  | 1 | 1 |  |  | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 |
| Concomitant infection related to the vaccine which may influence immune response ( code 2060) | 0 | 0 |  | 1 | 1 |  | 0 | 0 |  |  | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Non compliance with blood sampling schedule ( including wrong and unknown dates ) ( code 2090 ) | 0 | , |  | 3 | 3 |  | 3 | 3 |  |  | 0 |  | 2 |  | 2 | 2 | 1 | 1 | 1 | 1 |
| Essential serological data missing ( code 2100 ) | 0 | 0 |  | 18 | 18 |  | 10 | 1 |  |  |  | 0 | 15 | 15 | 8 | 9 | 3 | 3 | 2 | 2 |
| Subjects who did not complete the full vaccination course (2 doses) ( code 2500 ) | 0 | 0 |  | 3 | 17 |  | 0 | 5 |  |  | 0 | 0 | 2 | 14 | 0 |  | 1 | 3 | 0 | 1 |
| ATP cohort for Humoral immunogenicity | 0 |  | - | 87 |  | 74.4 | 98 |  |  | 85.2 |  |  | 65 |  | 78 |  | 22 |  | 20 |  |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
NOGRP = No assigned group
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Note: Subjects may have more than one elimination code assigned
$n=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
$s=$ number of subjects with the elimination code assigned
$\%=$ percentage of subjects in the considered ATP cohort relative to the Total Vaccinated Cohort

Table 6.17 Number of subjects enrolled into the study as well as the number excluded from ATP analyses for Humoral immunogenicity with reasons for exclusion by age strata

|  | Total |  |  |  |  |  |  |  |  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Missing |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | NOGRP |  |  | HZ/su |  |  | Placebo |  |  |  | HZ/su |  | Placebo |  | HZ/su |  | Placebo |  | NOGRP |  | HZ/su |  | Placebo |  |
| Title | n | s | \% | n | s | \% | n | s | \% | \% | n | s | n | s | n | s | n | s | n | s | n | s | n | s |
| Total Enrolled Cohort | 4 |  |  | 130 |  |  | 132 |  |  |  | 31 |  | 30 |  | 86 |  | 85 |  | 4 |  | 13 |  | 17 |  |
| Study vaccine dose not administered but subject number allocated ( code 1030) | 4 | 4 |  | 13 | 13 |  | 17 | 17 |  |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 4 | 13 | 13 | 17 | 17 |
| Total Vaccinated Cohort | 0 |  | - | 117 |  | 100 | 115 |  |  | 100 | 31 |  | 30 |  | 86 |  | 85 |  | 0 |  | 0 |  | 0 |  |
| Administration of vaccine(s) forbidden in the protocol up to PII (Month 2) ( code 1040) | 0 | 0 |  | 0 | 0 |  | 1 | 1 |  |  | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Administration of vaccine(s) forbidden in the protocol up to 30 days post last dose ( code 1041) | 0 | 0 |  | 0 | 0 |  | 0 | 1 |  |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Randomisation code broken at the investigator site ( code 1060 ) | 0 | 0 |  | 0 | 0 |  | 0 | 1 |  |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Protocol violation linked to the inclusion/exclusion criteria including age ( code 1600) | 0 | 0 |  | 4 | 4 |  | 2 | 2 |  |  | 2 | 2 | 0 | 0 | 2 | 2 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Administration of any medication forbidden by the protocol ( code 2040 ) | 0 | 0 |  | 1 | 1 |  | 1 | 1 |  |  | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Concomitant infection related to the vaccine which may influence immune response ( code 2060 ) | 0 | 0 |  | 1 | 1 |  | 0 | 0 |  |  | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Non compliance with blood sampling schedule (including wrong and unknown dates ) ( code 2090 ) | 0 | 0 |  | 3 | 3 |  | 3 | 3 |  |  | 0 | 0 | 1 | 1 | 3 | 3 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Essential serological data missing ( code 2100 ) | 0 | - |  | 18 | 18 |  | 10 | 1 |  |  | 0 | 0 | 0 | 0 | 18 | 18 | 10 | 11 | 0 | 0 | 0 | 0 | 0 | 0 |
| Subjects who did not complete the full vaccination course (2 doses) ( code 2500 ) |  | 0 |  | 3 | 17 |  | 0 | 5 |  |  | 2 | 2 | 0 | 0 | 1 | 15 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | 0 |
| ATP cohort for Humoral immunogenicity | 0 |  | - | 87 |  | 74.4 | 98 |  |  | 85.2 | 27 |  | 29 |  | 60 |  | 69 |  | 0 |  | 0 |  | 0 |  |

ATP cohort for Humoral immunogenicity
18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
Missing = Subjects did not receive the first vaccine dose at Month 0
NOGRP = No assigned group
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Note: Subjects may have more than one elimination code assigned
$n=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number $s=$ number of subjects with the elimination code assigned
$\%=$ percentage of subjects in the considered ATP cohort relative to the Total Vaccinated Cohort

Table 6.18 Number of subjects enrolled into the study as well as the number excluded from TVC analyses for CMI immunogenicity with reasons for exclusion by age strata

|  | Total |  |  |  |  |  |  |  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Missing |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | NOGRP |  |  | HZ/su |  |  | Placebo |  |  | HZ/su |  | Placebo |  | HZ/su |  | Placebo |  | NOGRP |  | HZ/su |  | Placebo |  |
| Title | $n$ | s | \% | n | s | \% | n | s | \% | n | s | n | s | n | s | n | s | n | s | n | s | n | s |
| Total Enrolled Cohort | 4 |  |  | 130 |  |  | 132 |  |  | 31 |  | 30 |  | 86 |  | 85 |  | 4 |  | 13 |  | 17 |  |
| Study vaccine dose not administered but subject number allocated ( code 1030) | 4 | 4 |  | 13 | 13 |  | 17 | 17 |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 4 | 13 | 13 | 17 | 17 |
| Total Vaccinated Cohort | 0 |  | - | 117 |  | 100 | 115 |  | 100 | 31 |  | 30 |  | 86 |  | 85 |  | 0 |  | 0 |  | 0 |  |
| Subjects not belonging to CMI sub-cohort ( code 4130 ) | 0 | 0 |  | 78 | 78 |  | 78 | 78 |  | 20 | 20 | 21 | 21 | 58 | 58 | 57 | 57 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total Vaccinated Cohort for CMI immunogenicity | 0 |  | - | 39 |  | 33.3 | 37 |  | 32.2 | 11 |  | 9 |  | 28 |  | 28 |  | 0 |  | 0 |  | 0 |  |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
Missing = Subjects did not receive the first vaccine dose at Month 0
NOGRP = No assigned group
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Note: Subjects may have more than one elimination code assigned
$n=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
$s=$ number of subjects with the elimination code assigned
\% = percentage of subjects in the considered Total Vaccinated Cohort for CMI immunogenicity relative to the Total Vaccinated Cohort

Table 6.19 Number of subjects vaccinated in the CMI sub-cohort into the study as well as the number excluded from ATP analyses for CMI immunogenicity with reasons for exclusion by age strata

|  | Total |  |  |  |  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HZ/su |  |  | Placebo |  |  | HZ/su |  | Placebo |  | HZ/su |  | Placebo |  |
| Title | $n$ |  | \% | n | s | \% | n | s | n | s | n | s | n | s |
| Total Vaccinated Cohort for CMI immunogenicity | 39 |  | 100 | 37 |  | 100 | 11 |  | 9 |  | 28 |  | 28 |  |
| Protocol violation linked to the inclusion/exclusion criteria including age ( code 1600) | 2 | 2 |  | 2 | 2 |  | 1 | 1 | 0 | 0 | 1 | 1 | 2 | 2 |
| Concomitant infection related to the vaccine which may influence immune response ( code 2060) | 1 | 1 |  | 0 | 0 |  | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| Non compliance with blood sampling schedule ( including wrong and unknown dates ) ( code 2090 ) | 1 | 1 |  | 1 | 1 |  | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| Essential serological data missing ( code 2100) | 7 | 7 |  | 3 | 3 |  | 0 | 0 | 0 | 0 | 7 | 7 | 3 | 3 |
| Subjects who did not complete the full vaccination course (2 doses) ( code 2500 ) | 1 | 8 |  | 0 | 0 |  | 1 | 1 | 0 | 0 | 0 | 7 | 0 | 0 |
| ATP cohort for CMI immunogenicity | 27 |  | 69.2 | 31 |  | 83.8 | 9 |  | 9 |  | 18 |  | 22 |  |

ATP cohort for CMI immunogenicity
$27 \quad 69.231 \quad 83.89$
18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Note: Subjects may have more than one elimination code assigned
$\mathrm{n}=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
$s=$ number of subjects with the elimination code assigned
\% = percentage of subjects in the considered ATP cohort for CMI relative to the Total Vaccinated Cohort for CMI immunogenicity

Table 6.20 Number of subjects enrolled into the study as well as the number excluded from ATP safety analyses up to study end with reasons for exclusion

|  | Total |  |  | HZ/su |  | Placebo |  | NOGRP |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Title | n | s | \% | n | s | n | S | n | S |
| Total Enrolled Cohort | 266 |  |  | 130 |  | 132 |  | 4 |  |
| Study vaccine dose not administered but subject number allocated ( code 1030 ) | 34 | 34 |  | 13 | 13 | 17 | 17 | 4 | 4 |
| Total Vaccinated Cohort | 232 |  | 100 | 117 |  | 115 |  | 0 |  |
| Administration of vaccine(s) forbidden in the protocol up to study end ( code 1040) | 1 | 1 |  | 0 | 0 | 1 | 1 | 0 | 0 |
| Randomisation code broken at the investigator site ( code 1060) | 0 | 1 |  | 0 | 0 | 0 | 1 | 0 | 0 |
| Protocol violation linked to the inclusion/exclusion criteria including age ( code 1600) | 6 | 6 |  | 4 | 4 | 2 | 2 | 0 | 0 |
| ATP Cohort for Safety - up to the study end | 225 |  | 97.0 | 113 |  | 112 |  | 0 |  |

NOGRP = No assigned group
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Note: Subjects may have more than one elimination code assigned
$\mathrm{n}=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower
elimination code number
$s=$ number of subjects with the elimination code assigned
$\%=$ percentage of subjects in the considered ATP cohort relative to the Total Vaccinated Cohort

Table 6.21 Number of subjects enrolled into the study as well as the number excluded from ATP analyses for Humoral persistence with reasons for exclusion

|  | Total |  |  | HZ/su |  | Placebo |  | NOGRP |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Title | n | s | \% | n | s | n | s | n | S |
| Total Enrolled Cohort | 266 |  |  | 130 |  | 132 |  | 4 |  |
| Study vaccine dose not administered but subject number allocated ( code 1030 ) | 34 | 34 |  | 13 | 13 | 17 | 17 | 4 | 4 |
| Total Vaccinated Cohort | 232 |  | 100 | 117 |  | 115 |  | 0 |  |
| Administration of vaccine(s) forbidden in the protocol up to study end ( code 1040) | 1 | 1 |  | 0 | 0 | 1 | 1 | 0 | 0 |
| Randomisation code broken at the investigator site ( code 1060 ) | 0 | 1 |  | 0 | 0 | 0 | 1 | 0 | 0 |
| Protocol violation linked to the inclusion/exclusion criteria including age ( code 1600) | 6 | 6 |  | 4 | 4 | 2 | 2 | 0 | 0 |
| Administration of any medication forbidden by the protocol ( code 2040 ) | 4 | 4 |  | 2 | 2 | 2 | 2 | 0 | 0 |
| Concomitant infection related to the vaccine which may influence immune response ( code 2060 ) | 3 | 3 |  | 1 | 1 | 2 | 2 | 0 | 0 |
| Non compliance with blood sampling schedule ( including wrong and unknown dates ) ( code 2090) | 11 | 11 |  | 6 | 6 | 5 | 5 | 0 | 0 |
| Essential serological data missing ( code 2100 ) | 67 | 68 |  | 34 | 35 | 533 | 33 | 0 | 0 |
| Subjects who did not complete the full vaccination course (2 doses) ( code 2500) | 2 | 22 |  | 2 | 17 | 0 | 5 | 0 | 0 |
| ATP cohort for Humoral persistence | 138 |  | 59.5 | 68 |  | 70 |  | 0 |  |
| NOGRP = No assigned group |  |  |  |  |  |  |  |  |  |
| $\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group |  |  |  |  |  |  |  |  |  |
| Placebo = Placebo group |  |  |  |  |  |  |  |  |  |
| $\mathrm{n}=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number |  |  |  |  |  |  |  |  |  |
| $\mathrm{s}=$ number of subjects with the elimination code assigned |  |  |  |  |  |  |  |  |  |

Table 6.22 Number of subjects vaccinated in the CMI sub-cohort into the study as well as the number excluded from ATP analyses for CMI persistence with reasons for exclusion

|  | Total |  |  | HZ/su |  | Placebo |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Title | n | s | \% | n | S | n | s |
| Total Vaccinated Cohort for CMI immunogenicity | 76 |  | 100 | 39 |  | 37 |  |
| Protocol violation linked to the inclusion/exclusion criteria including age ( code 1600 ) | 4 | 4 |  | 2 | 2 | 2 | 2 |
| Administration of any medication forbidden by the protocol ( code 2040 ) | 2 | 2 |  | 1 | 1 | 1 | 1 |
| Concomitant infection related to the vaccine which may influence immune response ( code 2060) | 2 | 2 |  | 1 | 1 | 1 | 1 |
| Non compliance with blood sampling schedule ( including wrong and unknown dates ) ( code 2090 ) | 3 | 3 |  | 1 | 1 | 2 | 2 |
| Essential serological data missing ( code 2100 ) | 25 | 25 |  | 14 | 14 | 11 | 11 |
| Subjects who did not complete the full vaccination course (2 doses) ( code 2500 ) | 0 | 8 |  | 0 | 8 | 0 | 0 |
| Obvious incoherence, abnormal serology evolution or error in data for cmi results ( code 4140) | 0 | 1 |  | 0 | 1 | 0 | 0 |
| ATP cohort for CMI persistence | 40 |  |  | 20 |  | 20 |  |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Note: Subjects may have more than one elimination code assigned
$\mathrm{n}=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
$s=$ number of subjects with the elimination code assigned
\% = percentage of subjects in the considered ATP cohort for CMI relative to the Total Vaccinated Cohort for CMI immunogenicity

Table 6.23 Number of subjects enrolled into the study as well as the number excluded from ATP analyses for Humoral persistence with reasons for exclusion by PreChemo/OnChemo groups

|  | Total |  |  |  |  |  |  |  |  | PreChemo |  |  |  |  |  |  | OnChemo |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | NOGRP |  |  | HZ/su |  |  | Placebo |  |  | NOGRP |  |  | HZ/su |  | Placebo |  | HZ/su |  | Placebo |  |
| Title | n | s | \% | n | s | \% | n | s | \% | n |  | s | n | s | n | s | n | s | n | s |
| Total Enrolled Cohort | 4 |  |  | 130 |  |  | 132 |  |  | 4 |  |  | 103 |  | 108 |  | 27 |  | 24 |  |
| Study vaccine dose not administered but subject number allocated ( code 1030) | 4 | 4 |  | 13 | 13 |  | 17 | 17 |  | 4 |  | 4 | 13 | 13 | 17 | 17 | 0 | 0 | 0 | 0 |
| Total Vaccinated Cohort | 0 |  | - | 117 |  | 100 | 115 |  | 10 | 0 |  |  | 90 |  | 91 |  | 27 |  | 24 |  |
| Administration of vaccine(s) forbidden in the protocol up to study end ( code 1040) | 0 | 0 |  | 0 | 0 |  | 1 | 1 |  | 0 |  | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 |
| Randomisation code broken at the investigator site ( code 1060) | 0 | 0 |  | 0 | 0 |  | 0 | 1 |  | 0 |  | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Protocol violation linked to the inclusion/exclusion criteria including age ( code 1600) | 0 | 0 |  | 4 | 4 |  | 2 | 2 |  | 0 |  | 0 | 4 | 4 | 2 | 2 | 0 | 0 | 0 | 0 |
| Administration of any medication forbidden by the protocol ( code 2040 ) | 0 | 0 |  | 2 | 2 |  | 2 | 2 |  | 0 |  | 0 | 2 | 2 | 1 | 1 | 0 | 0 | 1 | 1 |
| Concomitant infection related to the vaccine which may influence immune response ( code 2060 ) | 0 | 0 |  | 1 | 1 |  | 2 | 2 |  | 0 |  | 0 | 1 | 1 | 2 | 2 | 0 | 0 | O | 0 |
| Non compliance with blood sampling schedule (including wrong and unknown dates ) ( code 2090 ) | 0 | 0 |  | 6 | 6 |  | 5 | 5 |  | 0 |  | 0 | 4 | 4 | 4 | 4 | 2 | 2 | 1 | 1 |
| Essential serological data missing ( code 2100 ) | 0 |  |  | 34 | 35 |  | 33 | 33 |  | 0 |  | 0 | 27 | 28 | 25 | 25 | 7 | 7 | 8 | 8 |
| Subjects who did not complete the full vaccination course (2 doses) ( code 2500 ) | 0 |  |  | 2 | 17 |  | 0 | 5 |  | 0 |  | 0 | 1 | 14 | 0 | 4 | 1 | 3 | 0 | 1 |
| ATP cohort for Humoral persistence | 0 |  | - | 68 |  | 58.1 | 70 |  | 60 | 0 |  |  | 51 |  | 56 |  | 17 |  | 14 |  |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
NOGRP = No assigned group
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Note: Subjects may have more than one elimination code assigned
$\mathrm{n}=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
$s=$ number of subjects with the elimination code assigned
$\%=$ percentage of subjects in the considered ATP cohort relative to the Total Vaccinated Cohort

Table 6.24 Number of subjects enrolled into the study as well as the number excluded from ATP analyses for Humoral persistence with reasons for exclusion by age strata

|  | Total |  |  |  |  |  |  |  |  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Missing |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | NOGRP |  |  | HZ/su |  |  | Placebo |  |  |  | HZ/su |  | Placebo |  | HZ/su |  | Placebo |  | NOGRP |  | HZ/su |  | Placebo |  |
| Title | n | s | \% | n | s | \% | n | s | \% |  | n | S | n | s | n | s | n | s | n | s | n | s | n | s |
| Total Enrolled Cohort | 4 |  |  | 130 |  |  | 132 |  |  |  | 31 |  | 30 |  | 86 |  | 85 |  | 4 |  | 13 |  | 17 |  |
| Study vaccine dose not administered but subject number allocated ( code 1030) | 4 | 4 |  | 13 | 13 |  | 17 | 17 |  |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 4 | 13 | 13 | 17 | 17 |
| Total Vaccinated Cohort | 0 |  | - | 117 |  | 100 | 115 |  |  | 00 | 31 |  | 30 |  | 86 |  | 85 |  | 0 |  | 0 |  | 0 |  |
| Administration of vaccine(s) forbidden in the protocol up to study end ( code 1040) | 0 | 0 |  | 0 | 0 |  | 1 | 1 |  |  | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Randomisation code broken at the investigator site ( code 1060 ) | 0 | 0 |  | 0 | 0 |  | 0 | 1 |  |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Protocol violation linked to the inclusion/exclusion criteria including age ( code 1600) | 0 | 0 |  | 4 | 4 |  | 2 | 2 |  |  | 2 | 2 | 0 | 0 | 2 | 2 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Administration of any medication forbidden by the protocol ( code 2040 ) | 0 | 0 |  | 2 | 2 |  | 2 | 2 |  |  | 1 | 1 | 0 | 0 | 1 | 1 | 2 | 2 | 0 | 0 | 0 | 0 | - | 0 |
| Concomitant infection related to the vaccine which may influence immune response ( code 2060 ) | 0 | 0 |  | 1 | 1 |  | 2 | 2 |  |  | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Non compliance with blood sampling schedule ( including wrong and unknown dates ) ( code 2090 ) | 0 | 0 |  | 6 | 6 |  | 5 | 5 |  |  | 2 | 2 | 2 | 2 | 4 | 4 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 |
| Essential serological data missing ( code 2100 ) | 0 | 0 |  | 34 | 35 |  | 33 | 33 |  |  | 3 | 3 | 6 | 6 | 31 | 32 | 27 | 27 | 0 | 0 | 0 | 0 | 0 | 0 |
| Subjects who did not complete the full vaccination course (2 doses) ( code 2500) | 0 | 0 |  | 2 | 17 |  | 0 | 5 |  |  | 1 | 2 | 0 | 0 | 1 | 15 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | 0 |
| ATP cohort for Humoral persistence | 0 |  | - | 68 |  | 58.1 | 70 |  |  | 0.9 | 22 |  | 22 |  | 46 |  | 48 |  | 0 |  | 0 |  | 0 |  |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
Missing = Subjects did not receive the first vaccine dose at Month 0
NOGRP = No assigned group
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Note: Subjects may have more than one elimination code assigned
$\mathrm{n}=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
$s=$ number of subjects with the elimination code assigned
$\%=$ percentage of subjects in the considered ATP cohort relative to the Total Vaccinated Cohort

Table 6.25 Number of subjects vaccinated in the CMI sub-cohort into the study as well as the number excluded from ATP analyses for CMI persistence with reasons for exclusion by age strata

|  | Total |  |  |  |  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HZ/su |  |  | Placebo |  |  | HZ/su |  | Placebo |  | HZ/su |  | Placebo |  |
| Title | n | s | \% | n | s | \% | n | s | n | s | n | s | n | s |
| Total Vaccinated Cohort for CMI immunogenicity | 39 |  | 100 | 37 |  | 100 | 11 |  | 9 |  | 28 |  | 28 |  |
| Protocol violation linked to the inclusion/exclusion criteria including age ( code 1600) | 2 | 2 |  | 2 | 2 |  | 1 | 1 | 0 | 0 | 1 | 1 | 2 | 2 |
| Administration of any medication forbidden by the protocol ( code 2040 ) | 1 | 1 |  | 1 | 1 |  | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 |
| Concomitant infection related to the vaccine which may influence immune response ( code 2060) | 1 | 1 |  | 1 | 1 |  | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| Non compliance with blood sampling schedule ( including wrong and unknown dates ) ( code 2090 ) | 1 | 1 |  | 2 | 2 |  | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 |
| Essential serological data missing ( code 2100) | 14 | 14 |  | 11 | 11 |  | 1 |  | 3 | 3 | 13 | 13 | 8 | 8 |
| Subjects who did not complete the full vaccination course (2 doses) ( code 2500 ) | 0 | 8 |  | 0 | 0 |  | 0 |  | 0 | 0 | 0 | 7 | 0 | 0 |
| Obvious incoherence, abnormal serology evolution or error in data for cmi results ( code 4140 ) | 0 | 1 |  | 0 | 0 |  | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| ATP cohort for CMI persistence | 20 |  | 51.3 | 20 |  | 54.1 | 7 |  | 5 |  | 13 |  | 15 |  |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Note: Subjects may have more than one elimination code assigned
$n=$ number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
$\mathrm{s}=$ number of subjects with the elimination code assigned
$\%$ = percentage of subjects in the considered ATP cohort for CMI relative to the Total Vaccinated Cohort for CMI immunogenicity

Table 6.26 Deviations from specifications for age and intervals between study visits (Total Vaccinated Cohort)

|  |  | Age | Dose:1-Dose:2 |  | Dose:2-PII(M2) |  | Dose:2-PII(M13) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Group |  | Protocol | Protocol | Adapted | Protocol | Adapted | Protocol |
|  |  | At least 18 years | $\begin{aligned} & \text { from } 30 \text { to } 60 \\ & \text { days } \end{aligned}$ | $\begin{aligned} & \text { from } 30 \text { to } 84 \\ & \text { days } \end{aligned}$ | $\begin{aligned} & \text { from } 30 \text { to } 48 \\ & \text { days } \end{aligned}$ | $\begin{aligned} & \text { from } 21 \text { to } 63 \\ & \text { days } \end{aligned}$ | $\begin{aligned} & \text { from } 335 \text { to } 425 \\ & \text { days } \end{aligned}$ |
| HZ/su | N | 117 | 100 | 100 | 96 | 96 | 80 |
|  | n | 0 | 6 | 0 | 14 | 3 | 6 |
|  | \% | 0.0 | 6.0 | 0.0 | 14.6 | 3.1 | 7.5 |
|  | range | 35 to 85 | 30 to 74 | 30 to 74 | 23 to 98 | 23 to 98 | 324 to 478 |
| Placebo | N | 115 | 110 | 110 | 105 | 105 | 83 |
|  | n | 0 | 2 | 0 | 12 | 3 | 5 |
|  | \% | 0.0 | 1.8 | 0.0 | 11.4 | 2.9 | 6.0 |
|  | range | 31 to 87 | 30 to 68 | 30 to 68 | 21 to 80 | 21 to 80 | 327 to 495 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Adapted = interval used for defining the ATP cohorts for immunogenicity
$\mathrm{N}=$ total number of subjects with available results
$\mathrm{n} / \%=$ number / percentage of subjects with results outside of the interval range $=$ minimum-maximum for age and intervals
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 6.27 Deviation from specifications for age and intervals between study visits by PreChemo/OnChemo groups (Total Vaccinated Cohort)


PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Adapted = interval used for defining the ATP cohorts for immunogenicity
$\mathrm{N}=$ total number of subjects with available results
$\mathrm{n} / \%=$ number / percentage of subjects with results outside of the interval
range $=$ minimum-maximum for age and intervals
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 6.28 Deviation from specifications for age and intervals between study visits by age strata (Total Vaccinated Cohort)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Adapted = interval used for defining the ATP cohorts for immunogenicity
$\mathrm{N}=$ total number of subjects with available results
$\mathrm{n} / \%=$ number $/$ percentage of subjects with results outside of the interval
range $=$ minimum-maximum for age and intervals
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 6.29 Summary of demographic characteristics (ATP cohort for safety - up to 30 days post last vaccination)

|  |  | $\begin{gathered} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=113 \end{gathered}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=112 \end{aligned}$ |  | Total$N=225$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Characteristics | Parameters or Categories | Value or n | \% | Value or $n$ | \% | Value or n | \% |
| Age[years] at vaccination dose:1 | Mean | 57.1 | - | 58.2 |  | 57.7 | - |
|  | SD | 10.9 | - | 11.7 | - | 11.3 | - |
|  | Median | 57.0 | - | 59.0 | - | 58.0 | - |
|  | Minimum | 35.0 | - | 31.0 | - | 31.0 | - |
|  | Maximum | 85.0 | - | 87.0 | - | 87.0 | - |
|  | Missing | 0 | - | 0 | - | 0 | - |
| Gender | Male | 46 | 40.7 | 45 | 40.2 | 91 | 40.4 |
|  | Female | 67 | 59.3 | 67 | 59.8 | 134 | 59.6 |
| Ethnicity | American Hispanic or Latino | 5 | 4.8 | 6 | 5.7 | 11 | 5.3 |
|  | Not American Hispanic or Latino | 99 | 95.2 | 99 | 94.3 | 198 | 94.7 |
|  | Missing | 9 | - | 7 | - | 16 | - |
| Geographic Ancestry | African Heritage / African American | 2 | 1.9 | 2 | 1.9 | 4 | 1.9 |
|  | American Indian or Alaskan Native | 2 | 1.9 | 0 | 0.0 | 2 | 1.0 |
|  | Asian - East Asian Heritage | 11 | 10.6 | 14 | 13.3 | 25 | 12.0 |
|  | Asian - South East Asian Heritage | 0 | 0.0 | 2 | 1.9 | 2 | 1.0 |
|  | White - Arabic / North African Heritage | 1 | 1.0 | 0 | 0.0 | 1 | 0.5 |
|  | White - Caucasian / European Heritage | 88 | 84.6 | 86 | 81.9 | 174 | 83.3 |
|  | Other | 0 | 0.0 | 1 | 1.0 | 1 | 0.5 |
|  | Missing | 9 | - | 7 | - | 16 | - |
| Solid Tumor diagnosis | Bladder | 1 | 0.9 | 4 | 3.6 | 5 | 2.2 |
|  | Breast | 50 | 44.2 | 51 | 45.5 | 101 | 44.9 |
|  | Colorectal | 24 | 21.2 | 22 | 19.6 | 46 | 20.4 |
|  | Lung | 8 | 7.1 | 11 | 9.8 | 19 | 8.4 |
|  | Melanoma | 1 | 0.9 | 0 | 0.0 | 1 | 0.4 |
|  | Pancreas | 1 | 0.9 | 1 | 0.9 | 2 | 0.9 |
|  | Prostate | 5 | 4.4 | 4 | 3.6 | 9 | 4.0 |
|  | Other^ | 23 | 20.4 | 19 | 17.0 | 42 | 18.7 |
| Performance Status (ECOG) | Fully active* | 91 | 82.7 | 85 | 75.9 | 176 | 79.3 |
|  | Restricted in physically strenuous activity** | 18 | 16.4 | 26 | 23.2 | 44 | 19.8 |
|  | Ambulatory and capable of all selfcare*** | 1 | 0.9 | 1 | 0.9 | 2 | 0.9 |
|  | Missing | 3 | - | 0 | - | 3 | - |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** $=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature,
e.g., light house work, office work
${ }^{* * *}=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.30 Summary of demographic characteristics (ATP cohort for Humoral immunogenicity)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=87 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=98 \end{gathered}$ |  | Total N = 185 |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Characteristics | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% |
| Age[years] at vaccination dose:1 | Mean | 55.5 | - | 57.0 |  | 56.3 | - |
|  | SD | 11.0 | - | 11.1 | - | 11.1 | - |
|  | Median | 56.0 | - | 57.0 |  | 56.0 | - |
|  | Minimum | 35.0 | - | 31.0 | - | 31.0 | - |
|  | Maximum | 85.0 | - | 78.0 | - | 85.0 | - |
|  | Missing | 0 | - | 0 | - | 0 | - |
| Gender | Male | 30 | 34.5 | 38 | 38.8 | 68 | 36.8 |
|  | Female | 57 | 65.5 | 60 | 61.2 | 117 | 63.2 |
| Ethnicity | American Hispanic or Latino | 4 | 5.1 | 6 | 6.6 | 10 | 5.9 |
|  | Not American Hispanic or Latino | 75 | 94.9 | 85 | 93.4 | 160 | 94.1 |
|  | Missing | 8 | - | 7 | - | 15 | - |
| Geographic Ancestry | African Heritage / African American | 2 | 2.5 | 2 | 2.2 | 4 | 2.4 |
|  | American Indian or Alaskan Native | 2 | 2.5 | 0 | 0.0 | 2 | 1.2 |
|  | Asian - East Asian Heritage | 8 | 10.1 | 13 | 14.3 | 21 | 12.4 |
|  | Asian - South East Asian Heritage | 0 | 0.0 | 2 | 2.2 | 2 | 1.2 |
|  | White - Arabic / North African Heritage | 1 | 1.3 | 0 | 0.0 | 1 | 0.6 |
|  | White - Caucasian / European Heritage | 66 | 83.5 | 73 | 80.2 | 139 | 81.8 |
|  | Other | 0 | 0.0 | 1 | 1.1 | 1 | 0.6 |
|  | Missing | 8 | - | 7 | - | 15 | - |
| Solid Tumor diagnosis | Bladder | 1 | 1.1 | 1 | 1.0 | 2 | 1.1 |
|  | Breast | 47 | 54.0 | 48 | 49.0 | 95 | 51.4 |
|  | Colorectal | 17 | 19.5 | 22 | 22.4 | 39 | 21.1 |
|  | Lung | 4 | 4.6 | 10 | 10.2 | 14 | 7.6 |
|  | Melanoma | 1 | 1.1 | 0 | 0.0 | 1 | 0.5 |
|  | Pancreas | 1 | 1.1 | 1 | 1.0 | 2 | 1.1 |
|  | Prostate | 2 | 2.3 | 2 | 2.0 | 4 | 2.2 |
|  | Other ${ }^{\wedge}$ | 14 | 16.1 | 14 | 14.3 | 28 | 15.1 |
| Performance Status (ECOG) | Fully active* | 74 | 88.1 | 77 | 78.6 | 151 | 83.0 |
|  | Restricted in physically strenuous activity** | 10 | 11.9 | 20 | 20.4 | 30 | 16.5 |
|  | Ambulatory and capable of all selfcare*** | 0 | 0.0 | 1 | 1.0 | 1 | 0.5 |
|  | Missing | 3 | - | 0 | - | 3 | - |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** $=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature,
e.g., light house work, office work
${ }^{* * *}=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.31 Summary of demographic characteristics (Total Vaccinated Cohort for CMI immunogenicity)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=39 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=37 \end{aligned}$ |  | $\begin{aligned} & \text { Total } \\ & \mathrm{N}=76 \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Characteristics | Parameters or Categories | Value or n | \% | Value or $n$ | \% | Value or $n$ | \% |
| Age[years] at vaccination dose:1 | Mean | 58.4 | - | 60.2 | - | 59.3 | - |
|  | SD | 11.5 | - | 12.7 | - | 12.1 | - |
|  | Median | 60.0 | - | 62.0 | - | 60.0 | - |
|  | Minimum | 41.0 | - | 36.0 | - | 36.0 | - |
|  | Maximum | 85.0 | - | 87.0 | - | 87.0 | - |
|  | Missing | 0 | - | 0 | - | 0 | - |
| Gender | Male | 18 | 46.2 | 18 | 48.6 | 36 | 47.4 |
|  | Female | 21 | 53.8 | 19 | 51.4 | 40 | 52.6 |
| Ethnicity | American Hispanic or Latino | 2 | 5.9 | 1 | 3.0 | 3 | 4.5 |
|  | Not American Hispanic or Latino | 32 | 94.1 | 32 | 97.0 | 64 | 95.5 |
|  | Missing | 5 | - | 4 | - | 9 | - |
| Geographic Ancestry | African Heritage / African American | 1 | 2.9 | 1 | 3.0 | 2 | 3.0 |
|  | American Indian or Alaskan Native | 1 | 2.9 | 0 | 0.0 | 1 | 1.5 |
|  | White - Caucasian / European Heritage | 32 | 94.1 | 32 | 97.0 | 64 | 95.5 |
|  | Missing | 5 | - | 4 | - | 9 | - |
| Solid Tumor diagnosis | Breast | 12 | 30.8 | 15 | 40.5 | 27 | 35.5 |
|  | Colorectal | 8 | 20.5 | 5 | 13.5 | 13 | 17.1 |
|  | Lung | 5 | 12.8 | 7 | 18.9 | 12 | 15.8 |
|  | Melanoma | 1 | 2.6 | 0 | 0.0 | 1 | 1.3 |
|  | Prostate | 3 | 7.7 | 3 | 8.1 | 6 | 7.9 |
|  | Other^ | 10 | 25.6 | 7 | 18.9 | 17 | 22.4 |
| Performance Status (ECOG) | Fully active* | 28 | 71.8 | 24 | 64.9 | 52 | 68.4 |
|  | Restricted in physically strenuous activity** | 11 | 28.2 | 12 | 32.4 | 23 | 30.3 |
|  | Ambulatory and capable of all selfcare*** | 0 | 0.0 | 1 | 2.7 | 1 | 1.3 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** $=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
${ }^{* * *}=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.32 Summary of demographic characteristics (ATP cohort for safety - up to the study end)

|  |  | $\begin{gathered} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=113 \end{gathered}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=112 \end{aligned}$ |  | Total$N=225$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Characteristics | Parameters or Categories | Value or n | \% | Value or $n$ | \% | Value or n | \% |
| Age[years] at vaccination dose:1 | Mean | 57.1 | - | 58.2 | - | 57.7 | - |
|  | SD | 10.9 | - | 11.7 | - | 11.3 | - |
|  | Median | 57.0 | - | 59.0 | - | 58.0 | - |
|  | Minimum | 35.0 | - | 31.0 | - | 31.0 | - |
|  | Maximum | 85.0 | - | 87.0 | - | 87.0 | - |
|  | Missing | 0 | - | 0 | - | 0 | - |
| Gender | Male | 46 | 40.7 | 45 | 40.2 | 91 | 40.4 |
|  | Female | 67 | 59.3 | 67 | 59.8 | 134 | 59.6 |
| Ethnicity | American Hispanic or Latino | 5 | 4.8 | 6 | 5.7 | 11 | 5.3 |
|  | Not American Hispanic or Latino | 99 | 95.2 | 99 | 94.3 | 198 | 94.7 |
|  | Missing | 9 | - | 7 | - | 16 | - |
| Geographic Ancestry | African Heritage / African American | 2 | 1.9 | 2 | 1.9 | 4 | 1.9 |
|  | American Indian or Alaskan Native | 2 | 1.9 | 0 | 0.0 | 2 | 1.0 |
|  | Asian - East Asian Heritage | 11 | 10.6 | 14 | 13.3 | 25 | 12.0 |
|  | Asian - South East Asian Heritage | 0 | 0.0 | 2 | 1.9 | 2 | 1.0 |
|  | White - Arabic / North African Heritage | 1 | 1.0 | 0 | 0.0 | 1 | 0.5 |
|  | White - Caucasian / European Heritage | 88 | 84.6 | 86 | 81.9 | 174 | 83.3 |
|  | Other | 0 | 0.0 | 1 | 1.0 | 1 | 0.5 |
|  | Missing | 9 | - | 7 | - | 16 | - |
| Solid Tumor diagnosis | Bladder | 1 | 0.9 | 4 | 3.6 | 5 | 2.2 |
|  | Breast | 50 | 44.2 | 51 | 45.5 | 101 | 44.9 |
|  | Colorectal | 24 | 21.2 | 22 | 19.6 | 46 | 20.4 |
|  | Lung | 8 | 7.1 | 11 | 9.8 | 19 | 8.4 |
|  | Melanoma | 1 | 0.9 | 0 | 0.0 | 1 | 0.4 |
|  | Pancreas | 1 | 0.9 | 1 | 0.9 | 2 | 0.9 |
|  | Prostate | 5 | 4.4 | 4 | 3.6 | 9 | 4.0 |
|  | Other^ | 23 | 20.4 | 19 | 17.0 | 42 | 18.7 |
| Performance Status (ECOG) | Fully active* | 91 | 82.7 | 85 | 75.9 | 176 | 79.3 |
|  | Restricted in physically strenuous activity** | 18 | 16.4 | 26 | 23.2 | 44 | 19.8 |
|  | Ambulatory and capable of all selfcare*** | 1 | 0.9 | 1 | 0.9 | 2 | 0.9 |
|  | Missing | 3 | - | 0 | - | 3 | - |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** $=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature,
e.g., light house work, office work
${ }^{* * *}=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.33 Summary of demographic characteristics (ATP cohort for Humoral persistence)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=68 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=70 \end{gathered}$ |  | Total$N=138$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Characteristics | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% |
| Age[years] at vaccination dose:1 | Mean | 54.8 | - | 56.7 | - | 55.8 | - |
|  | SD | 10.7 | - | 11.1 | - | 10.9 | - |
|  | Median | 53.5 | - | 57.0 | - | 55.5 | - |
|  | Minimum | 35.0 | - | 31.0 | - | 31.0 | - |
|  | Maximum | 85.0 | - | 78.0 | - | 85.0 | - |
|  | Missing | 0 | - | 0 | - | 0 | - |
| Gender | Male | 20 | 29.4 | 23 | 32.9 | 43 | 31.2 |
|  | Female | 48 | 70.6 | 47 | 67.1 | 95 | 68.8 |
| Ethnicity | American Hispanic or Latino | 3 | 4.5 | 3 | 4.3 | 6 | 4.4 |
|  | Not American Hispanic or Latino | 64 | 95.5 | 67 | 95.7 | 131 | 95.6 |
|  | Missing | 1 | - | 0 | - | 1 | - |
| Geographic Ancestry | African Heritage / African American | 1 | 1.5 | 1 | 1.4 | 2 | 1.5 |
|  | American Indian or Alaskan Native | 2 | 3.0 | 0 | 0.0 | 2 | 1.5 |
|  | Asian - East Asian Heritage | 6 | 9.0 | 9 | 12.9 | 15 | 10.9 |
|  | White - Arabic / North African Heritage | 1 | 1.5 | 0 | 0.0 | 1 | 0.7 |
|  | White - Caucasian / European Heritage | 57 | 85.1 | 59 | 84.3 | 116 | 84.7 |
|  | Other | 0 | 0.0 | 1 | 1.4 | 1 | 0.7 |
|  | Missing | 1 | - | 0 | - | 1 | - |
| Solid Tumor diagnosis | Bladder | 0 | 0.0 | 1 | 1.4 | 1 | 0.7 |
|  | Breast | 41 | 60.3 | 40 | 57.1 | 81 | 58.7 |
|  | Colorectal | 15 | 22.1 | 18 | 25.7 | 33 | 23.9 |
|  | Lung | 2 | 2.9 | 6 | 8.6 | 8 | 5.8 |
|  | Melanoma | 1 | 1.5 | 0 | 0.0 | 1 | 0.7 |
|  | Prostate | 1 | 1.5 |  | 1.4 | 2 | 1.4 |
|  | Other^ | 8 | 11.8 | 4 | 5.7 | 12 | 8.7 |
| Performance Status (ECOG) | Fully active* | 62 | 92.5 | 62 | 88.6 | 124 | 90.5 |
|  | Restricted in physically strenuous activity* | 5 | 7.5 | 8 | 11.4 | 13 | 9.5 |
|  | Ambulatory and capable of all selfcare*** | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
|  | Missing | 1 | - | 0 | - | 1 | - |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** $=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature,
e.g., light house work, office work
${ }^{* * *}=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.34 Summary of demographic characteristics (ATP cohort for CMI persistence)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=20 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=20 \end{aligned}$ |  | $\begin{aligned} & \text { Total } \\ & \mathrm{N}=40 \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Characteristics | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or n | \% |
| Age[years] at vaccination dose:1 | Mean | 55.4 | - | 59.5 | - | 57.4 | - |
|  | SD | 10.7 | - | 11.0 | - | 10.9 | - |
|  | Median | 54.5 | - | 60.5 | - | 56.0 | - |
|  | Minimum | 43.0 | - | 39.0 | - | 39.0 | - |
|  | Maximum | 85.0 | - | 78.0 | - | 85.0 | - |
|  | Missing | 0 | - | 0 | - | 0 | - |
| Gender | Male | 6 | 30.0 | 8 | 40.0 | 14 | 35.0 |
|  | Female | 14 | 70.0 | 12 | 60.0 | 26 | 65.0 |
| Ethnicity | American Hispanic or Latino | 1 | 5.0 |  | 0.0 | 1 | 2.5 |
|  | Not American Hispanic or Latino | 19 | 95.0 | 20 | 100 | 39 | 97.5 |
| Geographic Ancestry | African Heritage / African American | 1 | 5.0 | 1 | 5.0 | 2 | 5.0 |
|  | American Indian or Alaskan Native | 1 | 5.0 | 0 | 0.0 | 1 | 2.5 |
|  | White - Caucasian / European Heritage | 18 | 90.0 | 19 | 95.0 | 37 | 92.5 |
| Solid Tumor diagnosis | Breast | 10 | 50.0 | 11 | 55.0 | 21 | 52.5 |
|  | Colorectal | 4 | 20.0 | 5 | 25.0 | 9 | 22.5 |
|  | Lung | 0 | 0.0 | 2 | 10.0 | 2 | 5.0 |
|  | Melanoma | 1 | 5.0 | 0 | 0.0 | 1 | 2.5 |
|  | Prostate | 1 | 5.0 | 1 | 5.0 | 2 | 5.0 |
|  | Other ${ }^{\wedge}$ | 4 | 20.0 | 1 | 5.0 | 5 | 12.5 |
| Performance Status (ECOG) | Fully active* | 17 | 85.0 | 17 | 85.0 | 34 | 85.0 |
|  | Restricted in physically strenuous activity** | 3 | 15.0 | - | 15.0 | 6 | 15.0 |
|  | Ambulatory and capable of all selfcare*** | 0 | 0.0 | - | 0.0 | 0 | 0.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** $=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature,
e.g., light house work, office work
${ }^{* * *}=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.35 Summary of demographic characteristics by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  | OnChemo |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=91 \end{aligned}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=24 \end{aligned}$ |  | $\begin{gathered} \begin{array}{c} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=117 \end{array} \end{gathered}$ |  | $\begin{aligned} & \text { Placebo } \\ & N=115 \end{aligned}$ |  |
| Characteristics | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ |  | Value or $n$ |  | Value or $n$ |  |
| Age[years] at vaccination dose:1 | Mean | 57.0 | - | 58.8 | - | 57.3 | - | 57.4 | - | 57.1 |  | 58.5 |  |
|  | SD | 11.0 | - | 11.6 | - | 10.6 | - | 12.5 | - | 10.8 | - | 11.7 |  |
|  | Median | 56.5 | - | 59.0 | - | 59.0 | - | 53.5 | - | 57.0 | - | 59.0 | - |
|  | Minimum | 36.0 | - | 36.0 | - | 35.0 | - | 31.0 | - | 35.0 | - | 31.0 |  |
|  | Maximum | 85.0 | - | 87.0 | - | 77.0 | - | 84.0 | - | 85.0 |  | 87.0 | - |
|  | Missing | 0 |  | 0 | - | 0 | - | 0 | - | 0 | - | 0 |  |
| Gender | Male | 36 | 40.0 | 37 | 40.7 | 11 | 40.7 | 9 | 37.5 | 47 | 40.2 | 46 | 40.0 |
|  | Female | 54 | 60.0 | 54 | 59.3 | 16 | 59.3 | 15 | 62.5 | 70 | 59.8 | 69 | 60.0 |
| Ethnicity | American Hispanic or Latino | 5 | 6.0 | 4 | 4.7 | 0 | 0.0 | 2 | 9.1 | 5 | 4.6 | 6 | 5.6 |
|  | Not American Hispanic or Latino | 78 | 94.0 | 81 | 95.3 | 25 | 100 | 20 | 90.9 | 103 | 95.4 | 101 | 94.4 |
|  | Missing | 7 | - | 6 | - | 2 | - | 2 | - | 9 | - | 8 | - |
| Geographic Ancestry | African Heritage / African American | 2 | 2.4 | 2 | 2.4 | 0 | 0.0 | 0 | 0.0 | 2 | 1.9 | 2 | 1.9 |
|  | American Indian or Alaskan Native | 2 | 2.4 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 2 | 1.9 | 0 | 0.0 |
|  | Asian - East Asian Heritage | 9 | 10.8 | 12 | 14.1 | 2 | 8.0 | 2 | 9.1 | 11 | 10.2 | 14 | 13.1 |
|  | Asian - South East Asian Heritage | 0 | 0.0 | 1 | 1.2 | 0 | 0.0 | 1 | 4.5 | 0 | 0.0 | 2 | 1.9 |
|  | White - Arabic / North African Heritage | 1 | 1.2 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 0.9 | 0 | 0.0 |
|  | White - Caucasian / European Heritage | 69 | 83.1 | 70 | 82.4 | 23 | 92.0 | 18 | 81.8 | 92 | 85.2 | 88 | 82.2 |
|  | Other | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 4.5 | 0 | 0.0 | 1 | 0.9 |
|  | Missing | 7 | - | 6 | - | 2 | - | 2 | - | 9 | - | 8 | - |
| Solid Tumor diagnosis | Bladder | 1 | 1.1 | 3 | 3.3 | 0 | 0.0 | 1 | 4.2 | 1 | 0.9 |  | 3.5 |
|  | Breast | 40 | 44.4 | 41 | 45.1 | 13 | 48.1 | 11 | 45.8 | 53 | 45.3 | 52 | 45.2 |
|  | Colorectal | 19 | 21.1 | 20 | 22.0 | 6 | 22.2 | 2 | 8.3 | 25 | 21.4 | 22 | 19.1 |
|  | Lung | 7 | 7.8 | 10 | 11.0 | 1 | 3.7 | 3 | 12.5 | 8 | 6.8 | 13 | 11.3 |
|  | Melanoma | 1 | 1.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 0.9 | 0 | 0.0 |
|  | Pancreas | 1 | 1.1 | 0 | 0.0 | 0 | 0.0 | 1 | 4.2 | 1 | 0.9 | 1 | 0.9 |
|  | Prostate | 4 | 4.4 | 3 | 3.3 | 1 | 3.7 | 1 | 4.2 | 5 | 4.3 |  | 3.5 |
|  | Other ${ }^{\wedge}$ | 17 | 18.9 | 14 | 15.4 | 6 | 22.2 | 5 | 20.8 | 23 | 19.7 | 19 | 16.5 |
| Performance Status (ECOG) | Fully active* | 72 | 81.8 | 68 | 74.7 | 23 | 88.5 | 18 | 75.0 | 95 | 83.3 | 86 | 74.8 |
|  | Restricted in physically strenuous activity** | 15 | 17.0 | 22 | 24.2 | 3 | 11.5 | 6 | 25.0 | 18 | 15.8 | 28 | 24.3 |


|  |  |  | PreC | hemo |  |  | OnC | hemo |  |  |  | tal |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZI} \\ & \mathrm{~N}= \end{aligned}$ |  |  |  | $\begin{aligned} & \mathrm{HZI} \\ & \mathrm{~N}= \end{aligned}$ |  |  |  | $\begin{gathered} \mathrm{HZ} \\ \mathrm{~N}= \end{gathered}$ |  |  |  |
| Characteristics | Parameters or Categories | Value or $n$ | \% | Value or n | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ |  |
|  | Ambulatory and capable of all selfcare*** | 1 | 1.1 | 1 | 1.1 | 0 | 0.0 | 0 | 0.0 | 1 | 0.9 | 1 | 0.9 |
|  | Missing | 2 | - | 0 | - | 1 | - | 0 | - | 3 | - | 0 | - |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%$ = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
*** $=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.36 Summary of demographic characteristics by PreChemo/OnChemo groups (ATP cohort for Humoral persistence)

|  |  | PreChemo |  |  |  | OnChemo |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=56 \end{gathered}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=17 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=14 \end{gathered}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=68 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=70 \end{aligned}$ |  |
| Characteristics | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ |  | Value or $n$ |  |
| Age[years] at vaccination dose:1 | Mean | 54.5 | - | 57.6 | - | 55.7 | - | 53.1 | - | 54.8 | - | 56.7 | - |
|  | SD | 10.6 | - | 11.1 | - | 11.4 | - | 10.9 | - | 10.7 | - | 11.1 |  |
|  | Median | 53.0 | - | 59.0 | - | 58.0 | - | 50.5 | - | 53.5 | - | 57.0 | - |
|  | Minimum | 36.0 | - | 38.0 | - | 35.0 | - | 31.0 | - | 35.0 | - | 31.0 |  |
|  | Maximum | 85.0 | - | 78.0 | - | 77.0 | - | 73.0 | - | 85.0 | - | 78.0 | - |
|  | Missing | 0 | - | 0 |  | 0 | - | 0 | - | 0 | - | 0 |  |
| Gender | Male | 14 | 27.5 | 19 | 33.9 | 6 | 35.3 | 4 | 28.6 | 20 | 29.4 | 23 | 32.9 |
|  | Female | 37 | 72.5 | 37 | 66.1 | 11 | 64.7 | 10 | 71.4 | 48 | 70.6 | 47 | 67.1 |
| Ethnicity | American Hispanic or Latino | 3 | 6.0 | 2 | 3.6 | 0 | 0.0 | 1 | 7.1 | 3 | 4.5 | 3 | 4.3 |
|  | Not American Hispanic or Latino | 47 | 94.0 | 54 | 96.4 | 17 | 100 | 13 | 92.9 | 64 | 95.5 | 67 | 95.7 |
|  | Missing | 1 | - | 0 | - | 0 | - | 0 | - | 1 | - | 0 | - |
| Geographic Ancestry | African Heritage / African American | 1 | 2.0 | 1 | 1.8 | 0 | 0.0 | 0 | 0.0 | 1 | 1.5 | 1 | 1.4 |
|  | American Indian or Alaskan Native | 2 | 4.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 2 | 3.0 | 0 | 0.0 |
|  | Asian - East Asian Heritage | 5 | 10.0 | 8 | 14.3 | 1 | 5.9 | 1 | 7.1 | 6 | 9.0 | 9 | 12.9 |
|  | White - Arabic / North African Heritage | 1 | 2.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 1.5 | 0 | 0.0 |
|  | White - Caucasian / European Heritage | 41 | 82.0 | 47 | 83.9 | 16 | 94.1 | 12 | 85.7 | 57 | 85.1 | 59 | 84.3 |
|  | Other | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 7.1 | 0 | 0.0 | 1 | 1.4 |
|  | Missing | 1 | - | 0 | - | 0 | - | 0 | - | 1 | - | 0 | - |
| Solid Tumor diagnosis | Bladder | 0 | 0.0 | 1 | 1.8 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 1.4 |
|  | Breast | 32 | 62.7 | 32 | 57.1 | 9 | 52.9 | 8 | 57.1 | 41 | 60.3 | 40 | 57.1 |
|  | Colorectal | 10 | 19.6 | 16 | 28.6 | 5 | 29.4 | 2 | 14.3 | 15 | 22.1 | 18 | 25.7 |
|  | Lung | 2 | 3.9 | 4 | 7.1 | 0 | 0.0 | 2 | 14.3 | 2 | 2.9 | 6 | 8.6 |
|  | Melanoma | 1 | 2.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 1.5 | 0 | 0.0 |
|  | Prostate | 1 | 2.0 | 1 | 1.8 | 0 | 0.0 | 0 | 0.0 | 1 | 1.5 | 1 | 1.4 |
|  | Other ${ }^{\wedge}$ | 5 | 9.8 | 2 | 3.6 | 3 | 17.6 | 2 | 14.3 | 8 | 11.8 | 4 | 5.7 |
| Performance Status (ECOG) | Fully active* | 46 | 92.0 | 50 | 89.3 | 16 | 94.1 | 12 | 85.7 | 62 | 92.5 | 62 | 88.6 |
|  | Restricted in physically strenuous activity** | 4 | 8.0 | 6 | 10.7 | 1 | 5.9 | 2 | 14.3 | 5 | 7.5 | 8 | 11.4 |
|  | Ambulatory and capable of all selfcare ${ }^{* * *}$ | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
|  | Missing | 1 | - | 0 | - | 0 | - | 0 | - | 1 | - | 0 | - |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
*** $=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.37 Summary of demographic characteristics by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=30 \end{gathered}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=85 \end{gathered}$ |  | $\begin{gathered} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=117 \end{gathered}$ |  | $\begin{aligned} & \text { Placebo } \\ & N=115 \end{aligned}$ |  |
| Characteristics <br> Age[years] at vaccination dose:1 | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ |  | Value or $n$ |  |
|  | Mean | 43.4 | - | 43.9 | - | 62.0 | - | 63.7 | - | 57.1 | - | 58.5 | - |
|  | SD | 4.2 | - | 4.6 | - | 7.8 | - | 8.8 | - | 10.8 | - | 11.7 | - |
|  | Median | 44.0 | - | 44.0 | - | 62.0 | - | 64.0 |  | 57.0 | - | 59.0 | - |
|  | Minimum | 35.0 | - | 31.0 | - | 50.0 | - | 50.0 |  | 35.0 | - | 31.0 | - |
|  | Maximum | 49.0 | - | 49.0 | - | 85.0 | - | 87.0 | - | 85.0 | - | 87.0 | - |
|  | Missing | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - |
| Gender | Male | 3 | 9.7 | 5 | 16.7 | 44 | 51.2 | 41 | 48.2 | 47 | 40.2 | 46 | 40.0 |
|  | Female | 28 | 90.3 | 25 | 83.3 | 42 | 48.8 | 44 | 51.8 | 70 | 59.8 | 69 | 60.0 |
| Ethnicity | American Hispanic or Latino | 1 | 3.4 | 3 | 10.3 | 4 | 5.1 | 3 | 3.8 | 5 | 4.6 | 6 | 5.6 |
|  | Not American Hispanic or Latino | 28 | 96.6 | 26 | 89.7 | 75 | 94.9 | 75 | 96.2 | 103 | 95.4 | 101 | 94.4 |
|  | Missing | 2 | - | 1 | - | 7 | - | 7 | - | 9 | - | 8 | - |
| Geographic Ancestry | African Heritage / African American | 1 | 3.4 | 0 | 0.0 | 1 | 1.3 | 2 | 2.6 | 2 | 1.9 | 2 | 1.9 |
|  | American Indian or Alaskan Native | 1 | 3.4 | 0 | 0.0 | 1 | 1.3 | 0 | 0.0 | 2 | 1.9 | 0 | 0.0 |
|  | Asian - East Asian Heritage | 5 | 17.2 | 5 | 17.2 | 6 | 7.6 | 9 | 11.5 | 11 | 10.2 | 14 | 13.1 |
|  | Asian - South East Asian Heritage | 0 | 0.0 | 1 | 3.4 | 0 | 0.0 | 1 | 1.3 | 0 | 0.0 | 2 | 1.9 |
|  | White - Arabic / North African Heritage | 0 | 0.0 | 0 | 0.0 | 1 | 1.3 | 0 | 0.0 | 1 | 0.9 | 0 | 0.0 |
|  | White - Caucasian / European Heritage | 22 | 75.9 | 22 | 75.9 | 70 | 88.6 | 66 | 84.6 | 92 | 85.2 | 88 | 82.2 |
|  | Other | 0 | 0.0 | 1 | 3.4 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 0.9 |
|  | Missing | 2 | - | 1 | - | 7 | - | 7 | - | 9 | - | 8 | - |
| Solid Tumor diagnosis | Bladder | 0 | 0.0 | 0 | 0.0 | 1 | 1.2 | 4 | 4.7 | 1 | 0.9 | 4 | 3.5 |
|  | Breast | 24 | 77.4 | 24 | 80.0 | 29 | 33.7 | 28 | 32.9 | 53 | 45.3 | 52 | 45.2 |
|  | Colorectal | 4 | 12.9 | 2 | 6.7 | 21 | 24.4 | 20 | 23.5 | 25 | 21.4 | 22 | 19.1 |
|  | Lung | 0 | 0.0 | 0 | 0.0 | 8 | 9.3 | 13 | 15.3 | 8 | 6.8 | 13 | 11.3 |
|  | Melanoma | 0 | 0.0 | 0 | 0.0 | 1 | 1.2 | 0 | 0.0 | 1 | 0.9 | 0 | 0.0 |
|  | Pancreas | 0 | 0.0 | 0 | 0.0 |  | 1.2 | 1 | 1.2 | 1 | 0.9 | 1 | 0.9 |
|  | Prostate | 0 | 0.0 | 0 | 0.0 | 5 | 5.8 | 4 | 4.7 | 5 | 4.3 | 4 | 3.5 |
|  | Other^ | 3 | 9.7 | 4 | 13.3 | 20 | 23.3 | 15 | 17.6 | 23 | 19.7 | 19 | 16.5 |
| Performance Status (ECOG) | Fully active* | 28 | 96.6 | 28 | 93.3 | 67 | 78.8 | 58 | 68.2 | 95 | 83.3 | 86 | 74.8 |
|  | Restricted in physically strenuous activity** | 1 | 3.4 | 2 | 6.7 | 17 | 20.0 | 26 | 30.6 | 18 | 15.8 | 28 | 24.3 |


|  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  | Placebo$N=30$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=85 \end{aligned}$ |  | $\begin{gathered} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=117 \end{gathered}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=115 \end{aligned}$ |  |
| Characteristics | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or n | \% | Value or n | \% | Value or n | \% |
|  | Ambulatory and capable of all selfcare** | 0 | 0.0 | 0 | 0.0 | 1 | 1.2 | 1 | 1.2 | 1 | 0.9 | 1 | 0.9 |
|  | Missing | 2 | - | 0 | - | 1 | - | 0 | - | 3 | - | 0 | - |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%$ = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* $=$ Fully active, able to carry on all pre-disease performance without restriction
${ }^{* *}=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
${ }^{* * *}=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.38 Summary of demographic characteristics by age strata (ATP cohort for Humoral immunogenicity)

|  |  | 18-49ys |  |  |  | $\geq 50 \mathrm{ys}$ |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  | Placebo$N=29$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=60 \end{aligned}$ |  | Placebo$N=69$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=87 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=98 \end{gathered}$ |  |
| Characteristics <br> Age[years] at vaccination dose:1 | Parameters or Categories | Value or n | \% | Value or n | \% | Value or $n$ | \% | Value or n | \% | Value or n | \% | Value or $n$ |  |
|  | Mean | 43.0 | - | 43.8 | - | 61.2 | - | 62.5 | - | 55.5 | - | 57.0 | - |
|  | SD | 4.3 | - | 4.6 |  | 8.1 | - | 7.9 |  | 11.0 | - | 11.1 | - |
|  | Median | 43.0 | - | 44.0 |  | 60.0 | - | 63.0 |  | 56.0 | - | 57.0 | - |
|  | Minimum | 35.0 | - | 31.0 | - | 50.0 | - | 50.0 | - | 35.0 | - | 31.0 | - |
|  | Maximum | 49.0 | - | 49.0 | - | 85.0 | - | 78.0 | - | 85.0 | - | 78.0 | - |
|  | Missing | 0 | - | 0 |  | 0 | - | 0 | - | 0 | - | 0 |  |
| Gender | Male | 3 | 11.1 | 5 | 17.2 | 27 | 45.0 | 33 | 47.8 | 30 | 34.5 | 38 | 38.8 |
|  | Female | 24 | 88.9 | 24 | 82.8 | 33 | 55.0 | 36 | 52.2 | 57 | 65.5 | 60 | 61.2 |
| Ethnicity | American Hispanic or Latino | 1 | 4.0 | 3 | 10.7 | 3 | 5.6 | 3 | 4.8 | 4 | 5.1 | 6 | 6.6 |
|  | Not American Hispanic or Latino | 24 | 96.0 | 25 | 89.3 | 51 | 94.4 | 60 | 95.2 | 75 | 94.9 | 85 | 93.4 |
|  | Missing | 2 | - | 1 | - | 6 | - | 6 | - | 8 | - | 7 | - |
| Geographic Ancestry | African Heritage / African American | 1 | 4.0 | 0 | 0.0 | 1 | 1.9 | 2 | 3.2 | 2 | 2.5 | 2 | 2.2 |
|  | American Indian or Alaskan Native | 1 | 4.0 | 0 | 0.0 | 1 | 1.9 | 0 | 0.0 | 2 | 2.5 | 0 | 0.0 |
|  | Asian - East Asian Heritage | 5 | 20.0 | 5 | 17.9 | 3 | 5.6 | 8 | 12.7 | 8 | 10.1 | 13 | 14.3 |
|  | Asian - South East Asian Heritage | 0 | 0.0 | 1 | 3.6 | 0 | 0.0 | 1 | 1.6 | 0 | 0.0 | 2 | 2.2 |
|  | White - Arabic / North African Heritage | 0 | 0.0 | 0 | 0.0 | 1 | 1.9 | 0 | 0.0 | 1 | 1.3 | 0 | 0.0 |
|  | White - Caucasian / European Heritage | 18 | 72.0 | 21 | 75.0 | 48 | 88.9 | 52 | 82.5 | 66 | 83.5 | 73 | 80.2 |
|  | Other | 0 | 0.0 | 1 | 3.6 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 1.1 |
|  | Missing | 2 | - | 1 | - | 6 | - | 6 | - | 8 | - | 7 | - |
| Solid Tumor diagnosis | Bladder | 0 | 0.0 | 0 | 0.0 | 1 | 1.7 | 1 | 1.4 | 1 | 1.1 | 1 | 1.0 |
|  | Breast | 21 | 77.8 | 23 | 79.3 | 26 | 43.3 | 25 | 36.2 | 47 | 54.0 | 48 | 49.0 |
|  | Colorectal | 3 | 11.1 | 2 | 6.9 | 14 | 23.3 | 20 | 29.0 | 17 | 19.5 | 22 | 22.4 |
|  | Lung | 0 | 0.0 | 0 | 0.0 | 4 | 6.7 | 10 | 14.5 | 4 | 4.6 | 10 | 10.2 |
|  | Melanoma | 0 | 0.0 | 0 | 0.0 | 1 | 1.7 | 0 | 0.0 | 1 | 1.1 | 0 | 0.0 |
|  | Pancreas | 0 | 0.0 | 0 | 0.0 | 1 | 1.7 | 1 | 1.4 | 1 | 1.1 | 1 | 1.0 |
|  | Prostate | 0 | 0.0 | 0 | 0.0 | 2 | 3.3 | 2 | 2.9 | 2 | 2.3 | 2 | 2.0 |
|  | Other^ | 3 | 11.1 | 4 | 13.8 | 11 | 18.3 | 10 | 14.5 | 14 | 16.1 | 14 | 14.3 |
| Performance Status (ECOG) | Fully active* | 25 | 100 | 27 | 93.1 | 49 | 83.1 | 50 | 72.5 | 74 | 88.1 | 77 | 78.6 |
|  | Restricted in physically strenuous activity** | 0 | 0.0 | 2 | 6.9 | 10 | 16.9 | 18 | 26.1 | 10 | 11.9 | 20 | 20.4 |


|  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=29 \end{aligned}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=60 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=69 \end{gathered}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=87 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=98 \end{gathered}$ |  |
| Characteristics | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or n | \% | Value or n | \% |
|  | Ambulatory and capable of all selfcare** | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 1.4 | 0 | 0.0 | 1 | 1.0 |
|  | Missing | 2 | - | 0 | - | 1 | - | 0 | - | 3 | - | 0 | - |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%$ = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* $=$ Fully active, able to carry on all pre-disease performance without restriction
${ }^{* *}=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
${ }^{* * *}=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.39 Summary of demographic characteristics by age strata (ATP cohort for CMI immunogenicity)

|  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{gathered} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=9 \end{gathered}$ |  | Placebo $\mathrm{N}=9$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=18 \end{aligned}$ |  | Placebo $\mathrm{N}=22$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=31 \end{gathered}$ |  |
| Characteristics <br> Age[years] at vaccination dose:1 | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% |
|  | Mean | 44.2 | - | 43.7 | - | 63.4 | - | 62.9 | - | 57.0 | - | 57.3 | - |
|  | SD | 2.5 |  | 4.4 |  | 9.5 | - | 8.3 | - | 12.1 |  | 11.5 |  |
|  | Median | 43.0 | - | 44.0 |  | 61.0 | - | 64.0 | - | 56.0 | - | 56.0 |  |
|  | Minimum | 41.0 | - | 36.0 | - | 52.0 | - | 50.0 | - | 41.0 | - | 36.0 | - |
|  | Maximum | 48.0 | - | 49.0 | - | 85.0 | - | 78.0 | - | 85.0 | - | 78.0 |  |
|  | Missing | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - |
| Gender | Male | 1 | 11.1 | 3 | 33.3 | 11 | 61.1 | 11 | 50.0 | 12 | 44.4 | 14 | 45.2 |
|  | Female | 8 | 88.9 | 6 | 66.7 | 7 | 38.9 | 11 | 50.0 | 15 | 55.6 | 17 | 54.8 |
| Ethnicity | American Hispanic or Latino | 0 | 0.0 | 1 | 11.1 | 1 | 7.1 | 0 | 0.0 | 1 | 4.5 | 1 | 3.6 |
|  | Not American Hispanic or Latino | 8 | 100 | 8 | 88.9 | 13 | 92.9 | 19 | 100 | 21 | 95.5 | 27 | 96.4 |
|  | Missing | 1 | - | 0 | - | 4 | - | 3 | - | 5 | - | 3 | - |
| Geographic Ancestry | African Heritage / African American | 1 | 12.5 | 0 | 0.0 | 0 | 0.0 | 1 | 5.3 | 1 | 4.5 | 1 | 3.6 |
|  | American Indian or Alaskan Native | 0 | 0.0 | 0 | 0.0 | 1 | 7.1 | 0 | 0.0 | 1 | 4.5 | 0 | 0.0 |
|  | White - Caucasian / European Heritage | 7 | 87.5 | 9 | 100 | 13 | 92.9 | 18 | 94.7 | 20 | 90.9 | 27 | 96.4 |
|  | Missing | 1 | - | 0 | - | 4 | - | 3 | - | 5 | - | 3 | - |
| Solid Tumor diagnosis | Breast | 6 | 66.7 | 6 | 66.7 | 4 | 22.2 | 9 | 40.9 | 10 | 37.0 | 15 | 48.4 |
|  | Colorectal | 1 | 11.1 | 1 | 11.1 | 3 | 16.7 | 4 | 18.2 | 4 | 14.8 | 5 | 16.1 |
|  | Lung | 0 | 0.0 | 0 | 0.0 | 2 | 11.1 | 4 | 18.2 | 2 | 7.4 | 4 | 12.9 |
|  | Melanoma | 0 | 0.0 | 0 | 0.0 | 1 | 5.6 |  | 0.0 | 1 | 3.7 | 0 | 0.0 |
|  | Prostate | 0 | 0.0 | 0 | 0.0 | 2 | 11.1 | 1 | 4.5 | 2 | 7.4 | 1 | 3.2 |
|  | Other^ | 2 | 22.2 | 2 | 22.2 | 6 | 33.3 | 4 | 18.2 | 8 | 29.6 | 6 | 19.4 |
| Performance Status (ECOG) | Fully active* | 9 | 100 | 7 | 77.8 | 12 | 66.7 | 15 | 68.2 | 21 | 77.8 | 22 | 71.0 |
|  | Restricted in physically strenuous activity** | 0 | 0.0 | 2 | 22.2 | 6 | 33.3 | 6 | 27.3 | 6 | 22.2 | 8 | 25.8 |
|  | Ambulatory and capable of all selfcare*** | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 4.5 | 0 | 0.0 | 1 | 3.2 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects

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$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
${ }^{* *}=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
$* * *=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.40 Summary of demographic characteristics by age strata (ATP cohort for Humoral persistence)

|  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=22 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=22 \end{aligned}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=46 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=48 \end{gathered}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=68 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=70 \end{aligned}$ |  |
| Characteristics | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ |  | Value or $n$ |  |
| Age[years] at vaccination dose:1 | Mean | 43.0 | - | 43.9 | - | 60.4 | - | 62.6 | - | 54.8 | - | 56.7 | - |
|  | SD | 4.5 | - | 4.7 | - | 7.9 | - | 7.7 | - | 10.7 | - | 11.1 |  |
|  | Median | 43.5 | - | 43.5 | - | 59.0 | - | 64.0 | - | 53.5 | - | 57.0 | - |
|  | Minimum | 35.0 | - | 31.0 | - | 50.0 | - | 50.0 | - | 35.0 | - | 31.0 | - |
|  | Maximum | 49.0 | - | 49.0 | - | 85.0 | - | 78.0 | - | 85.0 | - | 78.0 | - |
|  | Missing | 0 | - | 0 |  | 0 | - | 0 | - | 0 | - | 0 |  |
| Gender | Male | 1 | 4.5 | 2 | 9.1 | 19 | 41.3 | 21 | 43.8 | 20 | 29.4 | 23 | 32.9 |
|  | Female | 21 | 95.5 | 20 | 90.9 | 27 | 58.7 | 27 | 56.3 | 48 | 70.6 | 47 | 67.1 |
| Ethnicity | American Hispanic or Latino | 1 | 4.5 | 2 | 9.1 | 2 | 4.4 | 1 | 2.1 | 3 | 4.5 | 3 | 4.3 |
|  | Not American Hispanic or Latino | 21 | 95.5 | 20 | 90.9 | 43 | 95.6 | 47 | 97.9 | 64 | 95.5 | 67 | 95.7 |
|  | Missing | 0 | - | 0 | - | 1 | - | 0 | - | 1 | - | 0 | - |
| Geographic Ancestry | African Heritage / African American | 1 | 4.5 | 0 | 0.0 | 0 | 0.0 | 1 | 2.1 | 1 | 1.5 | 1 | 1.4 |
|  | American Indian or Alaskan Native | 1 | 4.5 | 0 | 0.0 | 1 | 2.2 | 0 | 0.0 | 2 | 3.0 | 0 | 0.0 |
|  | Asian - East Asian Heritage | 4 | 18.2 | 4 | 18.2 | 2 | 4.4 | 5 | 10.4 | 6 | 9.0 | 9 | 12.9 |
|  | White - Arabic / North African Heritage | 0 | 0.0 | 0 | 0.0 | 1 | 2.2 | 0 | 0.0 | 1 | 1.5 | 0 | 0.0 |
|  | White - Caucasian / European Heritage | 16 | 72.7 | 17 | 77.3 | 41 | 91.1 | 42 | 87.5 | 57 | 85.1 | 59 | 84.3 |
|  | Other | 0 | 0.0 |  | 4.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 1.4 |
|  | Missing | 0 | - | 0 | - | 1 | - | 0 | - | 1 | - | 0 | - |
| Solid Tumor diagnosis | Bladder | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 2.1 | 0 | 0.0 | 1 | 1.4 |
|  | Breast | 20 | 90.9 | 20 | 90.9 | 21 | 45.7 | 20 | 41.7 | 41 | 60.3 | 40 | 57.1 |
|  | Colorectal | 2 | 9.1 | 2 | 9.1 | 13 | 28.3 | 16 | 33.3 | 15 | 22.1 | 18 | 25.7 |
|  | Lung | 0 | 0.0 | O | 0.0 | 2 | 4.3 | 6 | 12.5 | 2 | 2.9 | 6 | 8.6 |
|  | Melanoma | 0 | 0.0 | 0 | 0.0 | 1 | 2.2 | 0 | 0.0 | 1 | 1.5 | 0 | 0.0 |
|  | Prostate | 0 | 0.0 | 0 | 0.0 | 1 | 2.2 | 1 | 2.1 | 1 | 1.5 | 1 | 1.4 |
|  | Other ${ }^{\wedge}$ | 0 | 0.0 | 0 | 0.0 | 8 | 17.4 | 4 | 8.3 | 8 | 11.8 | 4 | 5.7 |
| Performance Status (ECOG) | Fully active* | 21 | 100 | 22 | 100 | 41 | 89.1 | 40 | 83.3 | 62 | 92.5 | 62 | 88.6 |
|  | Restricted in physically strenuous activity** | 0 | 0.0 | 0 | 0.0 | 5 | 10.9 | 8 | 16.7 | 5 | 7.5 | 8 | 11.4 |
|  | Ambulatory and capable of all selfcare ${ }^{* * *}$ | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
|  | Missing | 1 | - | 0 | - | 0 | - | 0 | - | 1 | - | 0 | - |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
*** $=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.41 Summary of demographic characteristics by age strata (ATP cohort for CMI persistence)

|  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=7 \end{aligned}$ |  | Placebo $\mathrm{N}=5$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=13 \end{aligned}$ |  | Placebo$N=15$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=20 \end{aligned}$ |  | Placebo$N=20$ |  |
| Characteristics <br> Age[years] at vaccination dose:1 | Parameters or Categories | Value or n | \% | Value or n | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ |  | Value or $n$ | \% |
|  | Mean | 45.0 | - | 45.2 | - | 60.9 | - | 64.3 | - | 55.4 | - | 59.5 | - |
|  | SD | 2.2 | - | 4.1 | - | 9.1 | - | 7.9 |  | 10.7 | - | 11.0 |  |
|  | Median | 44.0 | - | 47.0 | - | 58.0 | - | 65.0 |  | 54.5 | - | 60.5 |  |
|  | Minimum | 43.0 | - | 39.0 | - | 52.0 | - | 53.0 |  | 43.0 | - | 39.0 | - |
|  | Maximum | 48.0 | - | 49.0 | - | 85.0 |  | 78.0 |  | 85.0 | - | 78.0 | - |
|  | Missing | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - |
| Gender | Male | 1 | 14.3 | 1 | 20.0 | 5 | 38.5 | 7 | 46.7 | 6 | 30.0 | 8 | 40.0 |
|  | Female | 6 | 85.7 | 4 | 80.0 | 8 | 61.5 | 8 | 53.3 | 14 | 70.0 | 12 | 60.0 |
| Ethnicity | American Hispanic or Latino | 0 | 0.0 | 0 | 0.0 | 1 | 7.7 | 0 | 0.0 | 1 | 5.0 | 0 | 0.0 |
|  | Not American Hispanic or Latino | 7 | 100 | 5 | 100 | 12 | 92.3 | 15 | 100 | 19 | 95.0 | 20 | 100 |
| Geographic Ancestry | African Heritage / African American | 1 | 14.3 | 0 | 0.0 | 0 | 0.0 | 1 | 6.7 | 1 | 5.0 | 1 | 5.0 |
|  | American Indian or Alaskan Native | 0 | 0.0 | 0 | 0.0 | 1 | 7.7 | 0 | 0.0 | 1 | 5.0 | 0 | 0.0 |
|  | White - Caucasian / European Heritage | 6 | 85.7 | 5 | 100 | 12 | 92.3 | 14 | 93.3 | 18 | 90.0 | 19 | 95.0 |
| Solid Tumor diagnosis | Breast | 6 | 85.7 | 4 | 80.0 | 4 | 30.8 | 7 | 46.7 | 10 | 50.0 | 11 | 55.0 |
|  | Colorectal | 1 | 14.3 | 1 | 20.0 | 3 | 23.1 | 4 | 26.7 | 4 | 20.0 | 5 | 25.0 |
|  | Lung | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 2 | 13.3 | 0 | 0.0 | 2 | 10.0 |
|  | Melanoma | 0 | 0.0 | 0 | 0.0 | 1 | 7.7 | 0 | 0.0 | 1 | 5.0 | 0 | 0.0 |
|  | Prostate | 0 | 0.0 | 0 | 0.0 | 1 | 7.7 | 1 | 6.7 | 1 | 5.0 | 1 | 5.0 |
|  | Other ${ }^{\wedge}$ | 0 | 0.0 | 0 | 0.0 | 4 | 30.8 | 1 | 6.7 | 4 | 20.0 | 1 | 5.0 |
| Performance Status (ECOG) | Fully active* | 7 | 100 | 5 | 100 | 10 | 76.9 | 12 | 80.0 | 17 | 85.0 | 17 | 85.0 |
|  | Restricted in physically strenuous activity** | 0 | 0.0 | 0 | 0.0 | 3 | 23.1 | 3 | 20.0 | 3 | 15.0 | 3 | 15.0 |
|  | Ambulatory and capable of all selfcare** | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value $=$ value of the considered parameter

SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
${ }^{* *}=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
*** $=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.42 Summary of demographic characteristics by age strata in PreChemo Groups only (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=23 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=23 \end{aligned}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=67 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=68 \end{gathered}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=91 \end{gathered}$ |  |
| Characteristics | Parameters or Categories | Value or $n$ | \% | Value or n | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or n | \% |
| Age[years] at vaccination dose:1 | Mean | 43.1 | - | 43.6 | - | 61.8 | - | 64.0 |  | 57.0 | - | 58.8 |  |
|  | SD | 4.0 | - | 3.9 | - 8 | 8.1 | - | 8.3 |  | 11.0 | - | 11.6 | - |
|  | Median | 43.0 | - | 43.0 | - | 62.0 | - | 65.0 | - | 56.5 | - | 59.0 | - |
|  | Minimum | 36.0 | - | 36.0 | - | 50.0 | - | 50.0 | - | 36.0 | - | 36.0 | - |
|  | Maximum | 49.0 | - | 49.0 | - | 85.0 | - | 87.0 | - | 85.0 | - | 87.0 | - |
|  | Missing | 0 | - 0 | 0 | - 0 | 0 | - | 0 |  | 0 | - | 0 | - |
| Gender | Male | 2 | 8.7 | 5 | 21.7 | 34 | 50.7 | 32 | 47.1 | 36 | 40.0 | 37 | 40.7 |
|  | Female | 21 | 91.3 | 18 | 78.3 | 33 | 49.3 | 36 | 52.9 | 54 | 60.0 | 54 | 59.3 |
| Ethnicity | American Hispanic or Latino | 1 | 4.5 | 2 | 9.1 | 4 | 6.6 | 2 | 3.2 | 5 | 6.0 | 4 | 4.7 |
|  | Not American Hispanic or Latino | 21 | 95.5 | 20 | 90.9 | 57 | 93.4 | 61 | 96.8 | 78 | 94.0 | 81 | 95.3 |
|  | Missing | 1 | - | 1 | - 6 | 6 | - | 5 | - | 7 | - | 6 | - |
| Geographic Ancestry | African Heritage / African American | 1 | 4.5 | 0 | 0.0 | 1 | 1.6 | 2 | 3.2 | 2 | 2.4 | 2 | 2.4 |
|  | American Indian or Alaskan Native | 1 | 4.5 | 0 | 0.0 | 1 | 1.6 | 0 | 0.0 | 2 | 2.4 | 0 | 0.0 |
|  | Asian - East Asian Heritage | 4 | 18.2 | 4 | 18.2 | 5 | 8.2 | 8 | 12.7 | 9 | 10.8 | 12 | 14.1 |
|  | Asian - South East Asian Heritage | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 1.6 | 0 | 0.0 | 1 | 1.2 |
|  | White - Arabic / North African Heritage | 0 | 0.0 | 0 | 0.0 | 1 | 1.6 | 0 | 0.0 | 1 | 1.2 | 0 | 0.0 |
|  | White - Caucasian / European Heritage | 16 | 72.7 | 18 | 81.8 | 53 | 86.9 | 52 | 82.5 | 69 | 83.1 | 70 | 82.4 |
|  | Missing | 1 | - | 1 | - | 6 | - | 5 | - | 7 | - | 6 | - |
| Solid Tumor diagnosis | Bladder | 0 | 0.0 | 0 | 0.0 | 1 | 1.5 | 3 | 4.4 | 1 | 1.1 | 3 | 3.3 |
|  | Breast | 18 | 78.3 | 17 | 73.9 | 22 | 32.8 | 24 | 35.3 | 40 | 44.4 | 41 | 45.1 |
|  | Colorectal | 3 | 13.0 | 2 | 8.7 | 16 | 23.9 | 18 | 26.5 | 19 | 21.1 | 20 | 22.0 |
|  | Lung | 0 | 0.0 | 0 | 0.0 | 7 | 10.4 | 10 | 14.7 | 7 | 7.8 | 10 | 11.0 |
|  | Melanoma | 0 | 0.0 | 0 | 0.0 | 1 | 1.5 | 0 | 0.0 | 1 | 1.1 | 0 | 0.0 |
|  | Pancreas | 0 | 0.0 | 0 | 0.0 | 1 | 1.5 | 0 | 0.0 | 1 | 1.1 | 0 | 0.0 |
|  | Prostate | 0 | 0.0 | 0 | 0.0 | 4 | 6.0 | 3 | 4.4 | 4 | 4.4 | 3 | 3.3 |
|  | Other^ | 2 | 8.7 | 4 | 17.4 | 15 | 22.4 | 10 | 14.7 | 17 | 18.9 | 14 | 15.4 |
| Performance Status (ECOG) | Fully active* | 21 | 95.5 | 21 | 91.3 | 51 | 77.3 | 47 | 69.1 | 72 | 81.8 | 68 | 74.7 |
|  | Restricted in physically strenuous activity** | 1 | 4.5 | 2 | 8.7 | 14 | 21.2 | 20 | 29.4 | 15 | 17.0 | 22 | 24.2 |
|  | Ambulatory and capable of all selfcare** | 0 | 0.0 | 0 | 0.0 | 1 | 1.5 | 1 | 1.5 | 1 | 1.1 | 1 | 1.1 |


|  |  | 18-49ys |  | $\geq 50 y s$ |  |  | Total |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=23 \end{aligned}$ | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=23 \end{aligned}$ | $\begin{aligned} & \mathrm{HZ} / \mathrm{s} \\ & \mathrm{~N}=6 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=68 \end{gathered}$ | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=91 \end{gathered}$ |
| Characteristics | Parameters or Categories | $\text { Value } \%$ <br> or $n$ | Value $\%$ or $n$ | Value or $n$ | \% | Value $\%$ or $n$ | Value \% or $n$ | Value $\%$ or $n$ |
|  | Missing | 1 - | - | 1 - |  | 0 | 2 | 0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
${ }^{* *}=$ Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
${ }^{* * *}=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.43 Summary of demographic characteristics by age strata in PreChemo Groups only (ATP cohort for Humoral immunogenicity)

|  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=19 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=23 \end{aligned}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=46 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=55 \end{gathered}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=65 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ N=78 \end{gathered}$ |  |
| Characteristics <br> Age[years] at vaccination dose:1 | Parameters or Categories | Value or n | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ |  | Value or n |  | Value or $n$ |  |
|  | Mean | 42.5 | - | 43.6 |  | 60.9 |  | 62.5 |  | 55.5 |  | 56.9 |  |
|  | SD | 3.9 | - | 3.9 | - | 8.6 |  | 7.7 |  | 11.3 | - | 11.0 | - |
|  | Median | 43.0 | - | 43.0 | - | 59.5 | - | 64.0 | - | 55.0 | - | 57.0 | - |
|  | Minimum | 36.0 | - | 36.0 | - | 50.0 | - | 50.0 | - | 36.0 | - | 36.0 | - |
|  | Maximum | 48.0 | - | 49.0 |  | 85.0 | - | 78.0 |  | 85.0 | - | 78.0 | - |
|  | Missing | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - |
| Gender | Male | 2 | 10.5 | 5 | 21.7 | 21 | 45.7 | 26 | 47.3 | 23 | 35.4 | 31 | 39.7 |
|  | Female | 17 | 89.5 | 18 | 78.3 | 25 | 54.3 | 29 | 52.7 | 42 | 64.6 | 47 | 60.3 |
| Ethnicity | American Hispanic or Latino | 1 | 5.6 | 2 | 9.1 | 3 | 7.3 | 2 | 3.9 | 4 | 6.8 | 4 | 5.5 |
|  | Not American Hispanic or Latino | 17 | 94.4 | 20 | 90.9 | 38 | 92.7 | 49 | 96.1 | 55 | 93.2 | 69 | 94.5 |
|  | Missing | 1 | - | 1 | - | 5 | - | 4 | - | 6 | - | 5 | - |
| Geographic Ancestry | African Heritage / African American | 1 | 5.6 | 0 | 0.0 | 1 | 2.4 | 2 | 3.9 | 2 | 3.4 | 2 | 2.7 |
|  | American Indian or Alaskan Native | 1 | 5.6 | 0 | 0.0 | 1 | 2.4 | 0 | 0.0 | 2 | 3.4 | 0 | 0.0 |
|  | Asian - East Asian Heritage | 4 | 22.2 | 4 | 18.2 | 2 | 4.9 | 7 | 13.7 | 6 | 10.2 | 11 | 15.1 |
|  | Asian - South East Asian Heritage | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 2.0 | 0 | 0.0 | 1 | 1.4 |
|  | White - Arabic / North African Heritage | 0 | 0.0 | 0 | 0.0 | 1 | 2.4 | 0 | 0.0 | 1 | 1.7 | 0 | 0.0 |
|  | White - Caucasian / European Heritage | 12 | 66.7 | 18 | 81.8 | 36 | 87.8 | 41 | 80.4 | 48 | 81.4 | 59 | 80.8 |
|  | Missing | 1 | - | 1 | - | 5 | - | 4 | - | 6 | - | 5 | - |
| Solid Tumor diagnosis | Bladder | 0 | 0.0 | 0 | 0.0 | 1 | 2.2 | 1 | 1.8 | 1 | 1.5 | 1 | 1.3 |
|  | Breast | 15 | 78.9 | 17 | 73.9 | 19 | 41.3 | 22 | 40.0 | 34 | 52.3 | 39 | 50.0 |
|  | Colorectal | 2 | 10.5 | 2 | 8.7 | 10 | 21.7 | 18 | 32.7 | 12 | 18.5 | 20 | 25.6 |
|  | Lung | 0 | 0.0 | 0 | 0.0 | 4 | 8.7 | 7 | 12.7 | 4 | 6.2 | 7 | 9.0 |
|  | Melanoma | 0 | 0.0 | 0 | 0.0 | 1 | 2.2 | 0 | 0.0 | 1 | 1.5 | 0 | 0.0 |
|  | Pancreas | 0 | 0.0 | 0 | 0.0 | 1 | 2.2 | 0 | 0.0 | 1 | 1.5 | 0 | 0.0 |
|  | Prostate | 0 | 0.0 | 0 | 0.0 | 2 | 4.3 | 1 | 1.8 | 2 | 3.1 | 1 | 1.3 |
|  | Other^ | 2 | 10.5 | 4 | 17.4 | 8 | 17.4 | 6 | 10.9 | 10 | 15.4 | 10 | 12.8 |
| Performance Status (ECOG) | Fully active* | 18 | 100 | 21 | 91.3 | 37 | 82.2 | 41 | 74.5 | 55 | 87.3 | 62 | 79.5 |
|  | Restricted in physically strenuous activity** | 0 | 0.0 | 2 | 8.7 | 8 | 17.8 | 13 | 23.6 | 8 | 12.7 | 15 | 19.2 |


|  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=19 \end{aligned}$ |  | Placebo$N=23$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=46 \end{aligned}$ |  | Placebo$N=55$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=65 \end{aligned}$ |  | Placebo <br> $\mathrm{N}=78$ |  |
| Characteristics | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% |
|  | Ambulatory and capable of all selfcare*** | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 1.8 | 0 | 0.0 | 1 | 1.3 |
|  | Missing |  | - | 0 | - | 1 | - | 0 | - | 2 | - | 0 | - |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%$ = number / percentage of subjects in a given category
Value $=$ value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
*** $=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.

Table 6.44 Summary of demographic characteristics by age strata in PreChemo Groups only (ATP cohort for Humoral persistence)

|  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=16 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=16 \end{gathered}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=35 \end{aligned}$ |  | Placebo$N=40$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=56 \end{aligned}$ |  |
| Characteristics | Parameters or Categories | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% | Value or $n$ | \% |
| Age[years] at vaccination dose:1 | Mean | 42.8 | - | 43.8 | - | 59.8 | - | 63.2 | - | 54.5 | - | 57.6 |  |
|  | SD | 4.2 | - | 3.9 | - | 8.0 | - | 7.6 | - | 10.6 |  | 11.1 |  |
|  | Median | 43.0 | - | 43.0 | - | 57.0 | - | 64.5 | - | 53.0 |  | 59.0 |  |
|  | Minimum | 36.0 | - | 38.0 | - | 50.0 | - | 50.0 | - | 36.0 | - | 38.0 | - |
|  | Maximum | 48.0 | - | 49.0 | - | 85.0 | - | 78.0 | - | 85.0 | - | 78.0 |  |
|  | Missing | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - | 0 |  |
| Gender | Male | 1 | 6.3 | 2 | 12.5 | 13 | 37.1 | 17 | 42.5 | 14 | 27.5 | 19 | 33.9 |
|  | Female | 15 | 93.8 | 14 | 87.5 | 22 | 62.9 | 23 | 57.5 | 37 | 72.5 | 37 | 66.1 |
| Ethnicity | American Hispanic or Latino | 1 | 6.3 | 1 | 6.3 | 2 | 5.9 | 1 | 2.5 | 3 | 6.0 | 2 | 3.6 |
|  | Not American Hispanic or Latino | 15 | 93.8 | 15 | 93.8 | 32 | 94.1 | 39 | 97.5 | 47 | 94.0 | 54 | 96.4 |
|  | Missing | 0 | - | 0 | - | 1 | - | 0 | - | 1 | - | 0 |  |
| Geographic Ancestry | African Heritage / African American | 1 | 6.3 | 0 | 0.0 | 0 | 0.0 | 1 | 2.5 | 1 | 2.0 | 1 | 1.8 |
|  | American Indian or Alaskan Native | 1 | 6.3 | 0 | 0.0 | 1 | 2.9 | 0 | 0.0 | 2 | 4.0 | 0 | 0.0 |
|  | Asian - East Asian Heritage | 4 | 25.0 | 3 | 18.8 | 1 | 2.9 | 5 | 12.5 | 5 | 10.0 | 8 | 14.3 |
|  | White - Arabic / North African Heritage | 0 | 0.0 | 0 | 0.0 | 1 | 2.9 | 0 | 0.0 | 1 | 2.0 | 0 | 0.0 |
|  | White - Caucasian / European Heritage | 10 | 62.5 | 13 | 81.3 | 31 | 91.2 | 34 | 85.0 | 41 | 82.0 | 47 | 83.9 |
|  | Missing | 0 | - | 0 | - | 1 | - | 0 | - | 1 | - | 0 | - |
| Solid Tumor diagnosis | Bladder | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 2.5 | 0 | 0.0 | 1 | 1.8 |
|  | Breast | 15 | 93.8 | 14 | 87.5 | 17 | 48.6 | 18 | 45.0 | 32 | 62.7 | 32 | 57.1 |
|  | Colorectal | 1 | 6.3 | 2 | 12.5 | 9 | 25.7 | 14 | 35.0 | 10 | 19.6 | 16 | 28.6 |
|  | Lung | 0 | 0.0 | 0 | 0.0 | 2 | 5.7 | 4 | 10.0 | 2 | 3.9 | 4 | 7.1 |
|  | Melanoma | 0 | 0.0 | 0 | 0.0 | 1 | 2.9 | 0 | 0.0 | 1 | 2.0 | 0 | 0.0 |
|  | Prostate | 0 | 0.0 | 0 | 0.0 | 1 | 2.9 | 1 | 2.5 | 1 | 2.0 | 1 | 1.8 |
|  | Other ${ }^{\wedge}$ | 0 | 0.0 | 0 | 0.0 | 5 | 14.3 | 2 | 5.0 | 5 | 9.8 | 2 | 3.6 |
| Performance Status (ECOG) | Fully active* | 15 | 100 | 16 | 100 | 31 | 88.6 | 634 | 85.0 | 46 | 92.0 | 50 | 89.3 |
|  | Restricted in physically strenuous activity** | 0 | 0.0 | 0 | 0.0 | 4 | 11.4 | 6 | 15.0 | 4 | 8.0 | 6 | 10.7 |
|  | Ambulatory and capable of all selfcare*** | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
|  | Missing | 1 | - | 0 | - | 0 | - | 0 | - | 1 | - | 0 | - |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ total number of subjects
$\mathrm{n} / \%=$ number / percentage of subjects in a given category
Value = value of the considered parameter
SD = Standard deviation
ECOG = Eastern Cooperative Oncology Group
${ }^{\wedge}$ Other includes gastric, endometrial, ovarian, head and neck, larynx, mouth, sinus, tonsil, liposarcoma mixoid, liver, oesophadeal, renal, sarcoma, stomach, testicular embryonic carcinoma, thyroid, tongue, cervix, urotelial, uterine leiomyrsarcoma

* = Fully active, able to carry on all pre-disease performance without restriction
** = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
*** $=$ Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.


## Table 6.45 List of subjects withdrawn from vaccination with reason for withdrawal (Total Vaccinated Cohort)

| Group | Subject number | Dose | Decision | Reason | Comment |
| :---: | :---: | :---: | :---: | :---: | :---: |
| HZ/su | PPD | 2 |  | VISIT NOT DONE |  |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 | SUBJECT | OTHER | SUBJECT WITHDREW FROM SECOND INJECTION |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 | INVESTIGATOR | NON-SERIOUS ADVERSE EVENT | AE1 |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 | INVESTIGATOR | NON-SERIOUS ADVERSE EVENT | AE3 |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 | SUBJECT | OTHER | CONSENT WITHDRAWAL |
|  |  | 2 |  | VISIT NOT DONE |  |
| Placebo |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 |  | VISIT NOT DONE |  |
|  |  | 2 |  | VISIT NOT DONE |  |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Table 7.1 Seropositivity rates and geometric mean concentrations (GMCs) of anti-gE antibody at Month 0, 1, 2, 6 and 13 (adapted ATP cohort for Humoral immunogenicity)


HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
GMC = geometric mean antibody concentration calculated on all subjects
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration equal to or above specified value
$95 \% \mathrm{Cl}=95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.2 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 (adapted ATP cohort for Humoral immunogenicity)

|  |  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 95\% Cl |  |
| Test description | Group | Timing | N | n | \% | LL | UL |
| VZV.gE Ab.lgG | HZ/su | Pl(M1) | 85 | 73 | 85.9 | 76.6 | 92.5 |
|  |  | PlI(M2) | 87 | 75 | 86.2 | 77.1 | 92.7 |
|  |  | PII(M6) 42 | 42 | 31 | 73.8 | 58.0 | 86.1 |
|  |  | PII(M13) | 68 | 35 | 51.5 | 39.0 | 63.8 |
|  | Placebo | Pl(M1) | 93 | 0 | 0.0 | 0.0 | 3.9 |
|  |  | PlI(M2) | 94 | - | 0.0 | 0.0 | 3.8 |
|  |  | PlI(M6) | 42 | 1 | 2.4 | 0.1 | 12.6 |
|  |  | PII(M13) 6 | 69 | 0 | 0.0 | 0.0 | 5.2 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination $\geq 4$ fold the cut-off for Anti-gE ( $4 \times 97$ $\mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at post-vaccination $\geq 4$ fold the pre-vaccination antibody concentration
$N=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
$95 \% \mathrm{Cl}=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

## Table 7.3 Mean Geometric Increase (MGI) of anti-gE antibody ELISA

 concentrations at Month 1, 2, 6 and 13 (adapted ATP cohort for Humoral immunogenicity)|  |  |  |  |  |  | MGI |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |  | 95\% CI |  |
| Group | N | Time point description | GMC | Time point description | GMC | Ratio order | Value | LL | UL |
| HZ/su | 85 | Pl(M1) | 24793.1 | PRE | 1027.5 | PI(M1) / PRE | 24.1 | 17.7 | 33.0 |
|  | 87 | PII(M2) | 18291.7 | PRE | 1049.8 | PII(M2) / PRE | 17.4 | 13.2 | 23.0 |
|  | 42 | PII(M6) | 7730.4 | PRE | 893.3 | PII(M6) / PRE | 8.7 | 5.8 | 12.8 |
|  | 68 | PII(M13) | 4477.3 | PRE | 1034.6 | PlI(M13) / PRE | 4.3 | 3.4 | 5.6 |
| Placebo | 93 | Pl(M1) | 1117.4 | PRE | 1115.1 | Pl(M1) / PRE | 1.0 | 1.0 | 1.0 |
|  | 94 | PII(M2) | 1063.0 | PRE | 1116.7 | PII(M2) / PRE | 1.0 | 0.9 | 1.0 |
|  | 42 | PII(M6) | 1389.9 | PRE | 1475.6 | PII(M6) / PRE | 0.9 | 0.8 | 1.1 |
|  | 69 | Pl(M13) | 1084.1 | PRE | 1188.3 | PlI(M13) / PRE | 0.9 | 0.8 | 1.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ Number of subjects with available results at the two considered time points
MGI = Geometric mean of the within subject ratios of the post-vaccination reciprocal anti-gE concentration to the Month
0 reciprocal anti-gE concentration
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)
Table 7.4 Descriptive statistics of the fold increase for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 (adapted ATP cohort for Humoral immunogenicity)

| Antibody | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| VZV.gE Ab.lgG | HZ/su | PI(M1) | 85 | 0 | 59.65 | 96.14 | 1.0 | 10.6 | 27.5 | 66.8 | 508.5 |
|  |  | PlI(M2) | 87 |  | 34.76 | 46.07 | 0.5 | 7.0 | 21.5 | 45.2 | 286.2 |
|  |  | Pll(M6) | 42 | 0 | 17.69 | 23.14 | 0.4 | 3.7 | 8.8 | 21.9 | 95.6 |
|  |  | PlI(M13) | 68 | 0 | 7.46 | 9.27 | 0.6 | 2.1 | 4.1 | 7.9 | 45.1 |
|  | Placebo | Pl(M1) | 93 | 4 | 1.02 | 0.20 | 0.6 | 0.9 | 1.0 | 1.1 | 2.1 |
|  |  | PII(M2) | 94 | 4 | 0.99 | 0.27 | 0.5 | 0.8 | 1.0 | 1.1 | 1.8 |
|  |  | PlI(M6) | 42 | 1 | 1.05 | 0.70 | 0.5 | 0.7 | 0.9 | 1.0 | 4.1 |
|  |  | PII(M13) |  |  | 0.97 | 0.38 | 0.4 | 0.8 | 0.9 | 1.1 | 2.4 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1,Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.5 Distribution of fold increase from baseline for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 (adapted ATP cohort for Humoral immunogenicity)

|  |  |  | $\geq 2$ fold |  |  |  | $\geq 4$ fold |  |  |  | $\geq 6$ fold |  |  |  |  | $\geq 8$ fold |  |  |  | $\geq 10$ fold |  |  | $\geq 12$ fold |  |  |  | $\geq 14$ fold |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  |  |
| Antib ody | $\begin{aligned} & \text { Grou } \\ & \mathrm{p} \\ & \hline \end{aligned}$ | Timi ng | N | n \% | $\mathbf{L L}$ | $\begin{aligned} & \mathrm{U} \\ & \mathrm{~L} \end{aligned}$ |  | \% | LL | $\begin{aligned} & \mathrm{U} \\ & \mathrm{~L} \end{aligned}$ |  | \% |  | $-\mathrm{L}, \begin{aligned} & \mathrm{U} \\ & \mathrm{~L} \end{aligned}$ |  | n \% |  | $\mathrm{L} \mathrm{U}$ |  | \% | LL | $\begin{aligned} & \mathrm{U} \\ & \mathrm{~L} \end{aligned}$ | n | \% |  | $\begin{aligned} & \mathrm{U} \\ & \mathrm{~L} \end{aligned}$ |  | \% | $\mathrm{LL} \left\lvert\, \begin{aligned} & \mathrm{U} \\ & \mathrm{~L} \end{aligned}\right.$ |
| $\begin{aligned} & \text { VZV.g } \\ & \text { E } \\ & \text { Ab.lg } \\ & \text { G } \end{aligned}$ | $\begin{aligned} & \mathrm{HZ} / \mathrm{s} \\ & \mathrm{u} \end{aligned}$ | PI(M <br> 1) | 8 7 <br> 5 9 | 7 9 9 | 85 . | 97 | 7 |  | 76 | 92 | 7 | 82 | 72 | 2 89 <br> 6 8 |  | 61 9 . | 71 | $\begin{array}{l\|l} 1 & 88 \\ 2 & .8 \end{array}$ | 6 4 | 75 | 64 .7 | 84 .0 |  | 71 | $\begin{aligned} & 61 \\ & .0 \end{aligned}$ | 81 .0 | 5 | 68 | $\begin{array}{l\|l} 57 & 77 \\ .2 & .9 \end{array}$ |
|  |  | PII(M <br> 2) |  | 8  <br> 1 93 <br> 1  | $\begin{aligned} & 85 \\ & .6 \end{aligned}$ | $\begin{aligned} & 97 \\ & 4 \end{aligned}$ |  |  | $\begin{aligned} & 77 \\ & . \end{aligned}$ | $\begin{aligned} & 92 \\ & .7 \end{aligned}$ |  | $\begin{aligned} & 78 \\ & .2 \end{aligned}$ |  | $\begin{array}{c\|c} \hline 8 & 86 \\ 0 & .3 \end{array}$ |  |  |  | $\begin{array}{l\|l} 3 & 82 \\ 0 & .4 \end{array}$ | $2 \begin{aligned} & 6 \\ & 0 \end{aligned}$ |  |  | $\begin{aligned} & 78 \\ & \hline \end{aligned}$ |  |  | $\begin{aligned} & 54 \\ & 6 \end{aligned}$ | $\begin{aligned} & 75 \\ & .4 \end{aligned}$ |  |  | $\begin{array}{l\|l} 52 & 73 \\ .2 & .3 \end{array}$ |
|  |  | $\begin{aligned} & \text { PII(M } \\ & 6) \\ & \hline \end{aligned}$ | $\begin{array}{l\|l} 4 & 3 \\ 2 & 7 \\ \hline \end{array}$ | 3 88 <br> 7  | $\begin{aligned} & 74 \\ & .4 \end{aligned}$ | $\begin{aligned} & 96 \\ & .0 \end{aligned}$ | 3 1 |  | $\begin{aligned} & 58 \\ & .0 \\ & \hline \end{aligned}$ | $\begin{aligned} & 86 \\ & .1 \\ & \hline \end{aligned}$ | 2 | $\begin{aligned} & 261 \\ & 6.9 \\ & \hline . \end{aligned}$ |  | $\begin{array}{l\|l} \hline 15 & 76 \\ 6 & 4 \\ \hline \end{array}$ | 2 | 2 <br> 22 <br> 2 |  | $\begin{array}{l\|l} \hline 6 & 68 \\ 4 & .0 \\ \hline \end{array}$ |  |  | 27 | 59 .0 | 1 |  | $\begin{aligned} & 25 \\ & .6 \end{aligned}$ | $\begin{aligned} & 56 \\ & . \\ & \hline \end{aligned}$ |  |  | $\begin{array}{l\|l} \hline 19 & 49 \\ .6 & .5 \\ \hline \end{array}$ |
|  |  | $\begin{aligned} & \mathrm{PII}(\mathrm{M} \\ & 13) \end{aligned}$ | $\begin{array}{l\|l} \hline 6 & 5 \\ 8 & 2 \\ \hline \end{array}$ | 5 76 <br> 2 . | $\begin{array}{ll} 64 \\ .6 \end{array}$ | $\begin{aligned} & 85 \\ & .9 \\ & \hline \end{aligned}$ | 3 | $\begin{aligned} & 51 \\ & .5 \\ & \hline \end{aligned}$ | $\begin{aligned} & 39 \\ & .0 \\ & \hline \end{aligned}$ | $\begin{aligned} & 63 \\ & 8 \\ & \hline \end{aligned}$ |  | $\begin{aligned} & 233 \\ & 3 \\ & 3 \\ & \hline \end{aligned}$ |  | $\begin{array}{l\|l} 2 & 46 \\ 8 & .3 \\ \hline \end{array}$ |  |  | $\begin{array}{\|l\|} \hline 14 \\ . \\ \hline \end{array}$ | $\begin{array}{ll} 4 & 35 \\ 1 & .4 \\ \hline \end{array}$ | 1 <br> 4 |  | 11 . 7 | $\begin{array}{\|c} 32 \\ . \\ \hline \end{array}$ |  | $\begin{array}{\|l} \hline 19 \\ .1 \\ \hline \end{array}$ | $\begin{aligned} & 10 \\ & \hline \end{aligned}$ | $\begin{aligned} & 30 \\ & .5 \\ & \hline \end{aligned}$ |  | $\begin{aligned} & 14 \\ & .7 \\ & \hline \end{aligned}$ | $\begin{array}{lll} \text { 7. } & 25 \\ 3 & .4 \end{array}$ |
|  | Plac ebo | $\begin{aligned} & \mathrm{Pl}(\mathrm{M} \\ & 1) \\ & \hline \end{aligned}$ | $\begin{array}{l\|l} 9 & 1 \\ 3 \end{array}$ | $1 \begin{gathered} 1 . \\ 1 \\ \hline \end{gathered}$ | $\begin{array}{l\|l} 0 . & 5 \\ 0 & 8 \\ \hline \end{array}$ | $\begin{aligned} & 5 . \\ & 8 \\ & \hline \end{aligned}$ | 0 | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 3 . \\ & 9 \end{aligned}$ |  | $0 \begin{aligned} & 0 . \\ & 0 \end{aligned}$ |  | $\begin{aligned} & 3 . \\ & 9 \end{aligned}$ |  | $0 \begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 3 \\ & 9 \end{aligned}$ |  | $0 .$ | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 3 . \\ & 9 \end{aligned}$ | 0 | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 3 . \\ & 9 \end{aligned}$ | 0 | $\begin{aligned} & 0 . \\ & 0 \\ & \hline \end{aligned}$ | $\begin{array}{l\|l} 0 . & 3 . \\ 0 & 9 \\ \hline \end{array}$ |
|  |  | PII(M <br> 2) |  | $0 \begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{array}{\|l} \hline 3 . \\ 8 \\ \hline \end{array}$ | 0 |  | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 3 . \\ & 8 \end{aligned}$ | 0 | $0 .$ |  |  |  |  | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ |  |  | $0 .$ | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 3 . \\ & 8 \end{aligned}$ | 0 | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $0 .$ | $\begin{aligned} & 3 . \\ & 8 \\ & \hline \end{aligned}$ | 0 |  | $\begin{array}{l\|l} \hline 0 & 3 . \\ 0 & 8 \\ \hline \end{array}$ |
|  |  | PII(M <br> 6) | $\begin{array}{l\|l} 4 \\ 2 \end{array} 2^{2}$ | $2 \begin{aligned} & 4 . \\ & 8 \end{aligned}$ | $\begin{array}{l\|l} 0 . & 1 \\ 6 & . \end{array}$ | $\begin{aligned} & 16 \\ & \hline \end{aligned}$ | 1 | $\begin{aligned} & 2 . \\ & 4 \end{aligned}$ | $\begin{aligned} & 0 . \\ & 1 \end{aligned}$ | $\begin{aligned} & 12 \\ & 6 \end{aligned}$ |  | $0 .$ | $0 .$ | $\begin{aligned} & 8 . \\ & 4 \end{aligned}$ |  | $0 \begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $0 .$ | $\begin{aligned} & 8 \\ & 4 \end{aligned}$ |  | $0 .$ | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 8 . \\ & 4 \end{aligned}$ | 0 | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $0 .$ | $\begin{aligned} & 8 . \\ & 4 \end{aligned}$ | 0 | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{array}{l\|l} 0 . & 8 . \\ 0 & 4 \end{array}$ |
|  |  | $\begin{aligned} & \text { PII(M } \\ & 13) \end{aligned}$ | $\begin{array}{l\|l} 6 \\ 9 \end{array}{ }^{4}$ | $4 \begin{aligned} & 5 . \\ & 8 \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 1 . \\ & 6 \\ & \hline \end{aligned}$ | $\begin{aligned} & 14 \\ & .2 \end{aligned}$ | 0 | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 5 . \\ & 2 \end{aligned}$ | 0 | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 . \\ & 0 \\ & \hline \end{aligned}$ | $\begin{aligned} & 5 . \\ & \hline \end{aligned}$ | 0 | $0 \begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $0 .$ | $\begin{aligned} & 5 \\ & 2 \\ & \hline \end{aligned}$ |  | $0 .$ | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 5 . \\ & 2 \end{aligned}$ | 0 | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 5 . \\ & 2 \end{aligned}$ | 0 | $\begin{aligned} & 0 \\ & 0 \\ & 0 \end{aligned}$ | $\begin{array}{l\|l} 0 . & 5 . \\ 0 & 2 \\ \hline \end{array}$ |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration within the specified range
$95 \% \mathrm{Cl}=95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Figure 7.1 Reverse cumulative curve for anti-gE antibody concentrations at Month 0 (ATP cohort for Humoral immunogenicity)


HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.2 Reverse cumulative curve for anti-gE antibody concentrations at Month 1 (ATP cohort for Humoral immunogenicity)


HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.3 Reverse cumulative curve for anti-gE antibody concentrations at Month 2 (ATP cohort for Humoral immunogenicity)


HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.4 Reverse cumulative curve for anti-gE antibody concentrations at Month 6 (ATP cohort for Humoral persistence)

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.5 Reverse cumulative curve for anti-gE antibody concentrations at Month 13 (ATP cohort for Humoral persistence)

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

## Table 7.6 Seropositivity rates and geometric mean concentrations (GMCs) of

 anti-gE antibody at Month 0, 1, 2, 6 and 13 by PreChemo/OnChemo groups (adapted ATP cohort for Humoral immunogenicity)

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
GMC = geometric mean antibody concentration calculated on all subjects
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration equal to or above specified value
$95 \% \mathrm{CI}=95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.7 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by PreChemo/OnChemo groups (adapted ATP cohort for Humoral immunogenicity)

| Vaccine response |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | \% CI |
| Test description VZV.gE Ab.lgG | Sub-group | Group | Timing | N | n \% | LL | UL |
|  | PreChemo | HZ/su | Pl(M1) | 64 | 6093.8 | 84.8 | 98.3 |
|  |  |  | PII(M2) | 656 | 6193.8 | 85.0 | 98.3 |
|  |  |  | Pll(M6) | 32 | 2475.0 | 56.6 | 88.5 |
|  |  |  | PlI(M13) | 51 | 2752.9 | 38.5 | 67.1 |
|  |  | Placebo | PI(M1) | 750 | 00.0 | 0.0 | 4.8 |
|  |  |  | Pll(M2) | 760 | 00.0 | 0.0 | 4.7 |
|  |  |  | PII(M6) | 360 | 00.0 | 0.0 | 9.7 |
|  |  |  | PlI(M13) | 550 | 00.0 | 0.0 | 6.5 |
|  | OnChemo | HZ/su | Pl(M1) | 21 | 1361.9 | 38.4 | 81.9 |
|  |  |  | PlI(M2) | 22 | 1463.6 | 40.7 | 82.8 |
|  |  |  | Pll(M6) | 10 | 770.0 | 34.8 | 93.3 |
|  |  |  | PlI(M13) | 178 | 847.1 | 23.0 | 72.2 |
|  |  | Placebo | Pl(M1) | 18 | 00.0 | 0.0 | 18.5 |
|  |  |  | PlI(M2) | 18 | 00.0 | 0.0 | 18.5 |
|  |  |  | Pll(M6) | 6 | 116.7 | 0.4 | 64.1 |
|  |  |  | PlI(M13) | 14 | 00.0 | 0.0 | 23.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination $\geq 4$ fold the cut-off for Anti-gE ( $4 \times 97$ $\mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at post-vaccination $\geq 4$ fold the pre-vaccination antibody concentration
$N=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
$95 \% \mathrm{Cl}=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
Pl(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

## Table 7.8 Mean Geometric Increase (MGI) of anti-gE antibody ELISA

 concentrations at Month 1, 2, 6 and 13 by PreChemo/OnChemo groups (adapted ATP cohort for Humoral immunogenicity)|  |  |  |  |  |  |  | MGI |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |  |  | 95\% CI |  |
| Sub-group | Group | N | Time point description | GMC | Time point description | GMC | Ratio order | Value | LL | UL |
| PreChemo | HZ/su | 64 | PI(M1) | 34729.8 | PRE | 1010.6 | Pl(M1) / PRE | 34.4 | 25.3 | 46.6 |
|  |  | 65 | PII(M2) | 22974.3 | PRE | 1032.3 | PII(M2) / PRE | 22.3 | 17.1 | 29.0 |
|  |  | 32 | PII(M6) | 8528.2 | PRE | 923.5 | PII(M6) / PRE | 9.2 | 6.2 | 13.8 |
|  |  | 51 | Pl(M13) | 4563.0 | PRE | 991.8 | PII(M13) / PRE | 4.6 | 3.5 | 6.1 |
|  | Placebo | 75 | Pl(M1) | 1173.1 | PRE | 1184.2 | PI(M1) / PRE | 1.0 | 0.9 | 1.0 |
|  |  | 76 | PII(M2) | 1126.4 | PRE | 1185.4 | PII(M2) / PRE | 1.0 | 0.9 | 1.0 |
|  |  | 36 | PII(M6) | 1335.3 | PRE | 1481.3 | PII(M6) / PRE | 0.9 | 0.8 | 1.0 |
|  |  | 55 | PII(M13) | 1208.1 | PRE | 1327.3 | PII(M13) / PRE | 0.9 | 0.8 | 1.0 |
| OnChemo | HZ/su | 21 | Pl(M1) | 8876.6 | PRE | 1080.5 | PI(M1) / PRE | 8.2 | 4.0 | 16.7 |
|  |  | 22 | PII(M2) | 9328.0 | PRE | 1103.4 | PII(M2) / PRE | 8.5 | 4.1 | 17.5 |
|  |  | 10 | PII(M6) | 5645.4 | PRE | 803.2 | PII(M6) / PRE | 7.0 | 2.1 | 23.7 |
|  |  | 17 | PII(M13) | 4229.5 | PRE | 1174.4 | PII(M13) / PRE | 3.6 | 2.0 | 6.4 |
|  | Placebo | 18 | Pl(M1) | 912.2 | PRE | 868.2 | PI(M1) / PRE | 1.1 | 1.0 | 1.1 |
|  |  | 18 | PII(M2) | 832.3 | PRE | 868.2 | PII(M2) / PRE | 1.0 | 0.8 | 1.1 |
|  |  | 6 | Pll(M6) | 1768.2 | PRE | 1442.2 | PII(M6) / PRE | 1.2 | 0.6 | 2.6 |
|  |  | 14 | PlI(M13) | 708.5 | PRE | 769.5 | PII(M13) / PRE | 0.9 | 0.8 | 1.1 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ Number of subjects with available results at the two considered time points
$\mathrm{MGI}=$ Geometric mean of the within subject ratios of the post-vaccination reciprocal anti-gE concentration to the Month 0 reciprocal anti-gE concentration
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

## Table 7.9 Descriptive statistics of the fold increase for anti-gE antibody ELISA

 concentrations at Month 1, 2, 6 and 13 by PreChemo/OnChemo groups (adapted ATP cohort for Humoral immunogenicity)| Antibody | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| VZV.gE Ab.lgG | PreChemo | HZ/su | Pl(M1) | 64 | 0 | 70.64 | 105.22 | 2.7 | 16.9 | 34.3 | 81.7 | 508.5 |
|  |  |  | PlI(M2) | 65 | 0 | 37.83 | 48.27 | 1.6 | 11.3 | 24.7 | 45.7 | 286.2 |
|  |  |  | PlI(M6) | 32 | 0 | 17.13 | 22.85 | 1.2 | 3.9 | 9.2 | 20.2 | 95.6 |
|  |  |  | PlI(M13) 51 | 51 | 0 | 7.68 | 9.44 | 0.8 | 2.3 | 4.4 | 8.5 | 45.1 |
|  |  | Placebo | Pl(M1) | 75 | 2 | 1.01 | 0.21 | 0.6 | 0.9 | 1.0 | 1.1 | 2.1 |
|  |  |  | PlI(M2) | 76 | 2 | 0.99 | 0.27 | 0.5 | 0.8 | 1.0 | 1.1 | 1.8 |
|  |  |  | Pll(M6) 36 | 36 | 1 | 0.97 | 0.52 | 0.5 | 0.7 | 0.9 | 1.0 | 3.6 |
|  |  |  | PlI(M13) 55 | 55 | 1 | 0.98 | 0.41 | 0.4 | 0.8 | 0.9 | 1.1 | 2.4 |
|  | OnChemo | HZ/su | Pl(M1) | 21 | 0 | 26.18 | 48.80 | 1.0 | 1.9 | 8.7 | 25.3 | 201.1 |
|  |  |  | PII(M2) | 22 | 0 | 25.69 | 38.42 | 0.5 | 3.1 | 5.6 | 32.3 | 152.9 |
|  |  |  | PII(M6) | 10 | 0 | 19.47 | 25.22 | 0.4 | 1.9 | 6.9 | 33.6 | 68.9 |
|  |  |  | Pll(M13) | 17 | 0 | 6.80 | 8.98 | 0.6 | 1.3 | 3.8 | 5.7 | 30.1 |
|  |  | Placebo | Pl(M1) | 18 | 2 | 1.06 | 0.16 | 0.7 | 0.9 | 1.1 | 1.2 | 1.3 |
|  |  |  | PII(M2) | 18 | 2 | 0.99 | 0.25 | 0.5 | 0.8 | 1.0 | 1.1 | 1.5 |
|  |  |  | Plı(M6) 6 | 6 | 0 | 1.55 | 1.33 | 0.6 | 0.9 | 0.9 | 1.9 | 4.1 |
|  |  |  | Plı(M13) | 14 | 0 | 0.94 | 0.23 | 0.6 | 0.8 | 0.9 | 1.1 | 1.5 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1,Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

## Table 7.10 Distribution of fold increase from baseline for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by <br> PreChemo/OnChemo groups (adapted ATP cohort for Humoral immunogenicity)



|  |  |  |  |  | $\geq 14$ fold |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | 95\% CI |  |
| Antibody | Sub-group | Group | Timing | N | n | \% | LL | UL |
| VZV.gE Ab.lgG | PreChemo | HZ/su | Pl(M1) | 64 | 50 | 78.1 | 66.0 | 87.5 |
|  |  |  | PlI(M2) | 65 | 45 | 69.2 | 56.6 | 80.1 |
|  |  |  | Pll(M6) | 32 | 11 | 34.4 | 18.6 | 53.2 |
|  |  |  | PII(M13) 5 | 51 | 8 | 15.7 | 7.0 | 28.6 |
|  |  | Placebo | Pl(M1) | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  |  |  | PlI(M2) | 76 | 0 | 0.0 | 0.0 | 4.7 |
|  |  |  | Pll(M6) | 36 | 0 | 0.0 | 0.0 | 9.7 |
|  |  |  | PlI(M13) 5 | 55 | 0 | 0.0 | 0.0 | 6.5 |
|  | OnChemo | HZ/su | Pl(M1) | 21 | 8 | 38.1 | 18.1 | 61.6 |
|  |  |  | PII(M2) | 22 | 10 | 45.5 | 24.4 | 67.8 |
|  |  |  | Pll(M6) | 10 | 3 | 30.0 | 6.7 | 65.2 |
|  |  |  | PII(M13) | 17 | 2 | 11.8 | 1.5 | 36.4 |
|  |  | Placebo | Pl(M1) | 18 | 0 | 0.0 | 0.0 | 18.5 |
|  |  |  | PlI(M2) | 18 | 0 | 0.0 | 0.0 | 18.5 |
|  |  |  | PII(M6) 6 | 6 | 0 | 0.0 | 0.0 | 45.9 |
|  |  |  | PII(M13) | 14 | 0 | 0.0 | 0.0 | 23.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration within the specified range
$95 \% \mathrm{CI}=95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Figure 7.6 Reverse cumulative curve for anti-gE antibody concentrations at Month 0 by PreChemo/OnChemo groups (ATP cohort for Humoral immunogenicity)


PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.7 Reverse cumulative curve for anti-gE antibody concentrations at Month 1 by PreChemo/OnChemo groups (ATP cohort for Humoral immunogenicity)


PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.8 Reverse cumulative curve for anti-gE antibody concentrations at Month 2 by PreChemo/OnChemo groups (ATP cohort for Humoral immunogenicity)


PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.9 Reverse cumulative curve for anti-gE antibody concentrations at Month 6 by PreChemo/OnChemo groups (ATP cohort for Humoral persistence)


PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.10 Reverse cumulative curve for anti-gE antibody concentrations at Month 13 by PreChemo/OnChemo groups (ATP cohort for Humoral persistence)


PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

## Table 7.11 Seropositivity rates and geometric mean concentrations (GMCs) of anti-gE antibody at Month 0, 1, 2, 6 and 13 by age strata (adapted

 ATP cohort for Humoral immunogenicity)

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
GMC = geometric mean antibody concentration calculated on all subjects
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration equal to or above specified value
$95 \% \mathrm{Cl}=95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.12 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata (adapted ATP cohort for Humoral immunogenicity)

|  |  |  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | 95\% | CI |
| Test description | Sub-group | Group | Timing | N | n | \% | LL | UL |
| VZV.gE Ab.lgG | 18-49ys | HZ/su | Pl(M1) | 27 | 23 | 85.2 | 66.3 | 95.8 |
|  |  |  | PlI(M2) | 27 | 23 | 85.2 | 66.3 | 95.8 |
|  |  |  | PII(M6) | 16 | 11 | 68.8 | 41.3 | 89.0 |
|  |  |  | PlI(M13) | 22 | 10 | 45.5 | 24.4 | 67.8 |
|  |  | Placebo | Pl(M1) | 27 | 0 | 0.0 | 0.0 | 12.8 |
|  |  |  | PlI(M2) | 28 | 0 | 0.0 | 0.0 | 12.3 |
|  |  |  | PII(M6) | 12 | 1 | 8.3 | 0.2 | 38.5 |
|  |  |  | PII(M13) | 21 | 0 | 0.0 | 0.0 | 16.1 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 58 | 50 | 86.2 | 74.6 | 93.9 |
|  |  |  | PlI(M2) | 60 | 52 | 86.7 | 75.4 | 94.1 |
|  |  |  | Pll(M6) | 26 | 20 | 76.9 | 56.4 | 91.0 |
|  |  |  | PlI(M13) | 46 | 25 | 54.3 | 39.0 | 69.1 |
|  |  | Placebo | Pl(M1) | 66 | 0 | 0.0 | 0.0 | 5.4 |
|  |  |  | PII(M2) | 66 | 0 | 0.0 | 0.0 | 5.4 |
|  |  |  | PII(M6) | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  |  |  | PlI(M13) | 48 | 0 | 0.0 | 0.0 | 7.4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination $\geq 4$ fold the cut-off for Anti-gE (4x97 $\mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at post-vaccination $\geq 4$ fold the pre-vaccination antibody concentration
$N=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit
Pl(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

## Table 7.13 Mean Geometric Increase (MGI) of anti-gE antibody ELISA

 concentrations at Month 1, 2, 6 and 13 by age strata (adapted ATP cohort for Humoral immunogenicity)|  |  |  |  |  |  |  | MGI |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |  |  | 95\% | CI |
| Sub-group | Group | N | Time point description | GMC | Time point description | GMC | Ratio order | Value | LL | UL |
| 18-49ys | HZ/su | 27 | Pl(M1) | 24450.8 | PRE | 992.1 | PI(M1) / PRE | 24.6 | 13.9 | 43.5 |
|  |  | 27 | PII(M2) | 15710.4 | PRE | 992.1 | PII(M2) / PRE | 15.8 | 10.0 | 25.1 |
|  |  | 16 | PII(M6) | 5591.3 | PRE | 885.2 | PII(M6) / PRE | 6.3 | 4.0 | 10.0 |
|  |  | 22 | PII(M13) | 3328.5 | PRE | 932.1 | PII(M13) / PRE | 3.6 | 2.4 | 5.2 |
|  | Placebo 27 | 27 | PI(M1) | 1050.4 | PRE | 1060.0 | PI(M1) / PRE | 1.0 | 0.9 | 1.0 |
|  |  | 28 | PII(M2) | 959.9 | PRE | 1067.1 | PII(M2) / PRE | 0.9 | 0.8 | 1.0 |
|  |  | 12 | PII(M6) | 981.4 | PRE | 1042.8 | PII(M6) / PRE | 0.9 | 0.7 | 1.3 |
|  |  | 21 | PII(M13) | 860.8 | PRE | 991.9 | PII(M13) / PRE | 0.9 | 0.7 | 1.0 |
| $\geq 50 y s$ | HZ/su | 58 | PI(M1) | 24954.0 | PRE | 1044.4 | PI(M1) / PRE | 23.9 | 16.3 | 35.1 |
|  |  | 60 | Plı(M2) | 19587.7 | PRE | 1076.9 | PII(M2) / PRE | 18.2 | 12.8 | 25.9 |
|  |  | 26 | PII(M6) | 9435.8 | PRE | 898.3 | PlI(M6) / PRE | 10.5 | 5.9 | 18.8 |
|  |  | 46 | PlI(M13) | 5159.3 | PRE | 1087.5 | PII(M13) / PRE | 4.7 | 3.4 | 6.6 |
|  | Placebo | 66 | PI(M1) | 1146.0 | PRE | 1138.5 | PI(M1) / PRE | 1.0 | 1.0 | 1.1 |
|  |  | 66 | PlI(M2) | 1110.0 | PRE | 1138.5 | PII(M2) / PRE | 1.0 | 0.9 | 1.0 |
|  |  | 30 | Pll(M6) | 1597.5 | PRE | 1695.5 | PII(M6) / PRE | 0.9 | 0.8 | 1.1 |
|  |  | 48 | PII(M13) | 1199.3 | PRE | 1286.0 | PII(M13) / PRE | 0.9 | 0.8 | 1.0 |

18-49ys $=$ Subjects aged between 18 and 49 years
$\geq 50$ ys $=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ Number of subjects with available results at the two considered time points
$\mathrm{MGI}=$ Geometric mean of the within subject ratios of the post-vaccination reciprocal anti-gE concentration to the Month 0 reciprocal anti-gE concentration
$95 \% \mathrm{CI}=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.14 Descriptive statistics of the fold increase for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata (adapted ATP cohort for Humoral immunogenicity)

| Antibody | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| VZV.gE Ab.lgG | 18-49ys | HZ/su | Pl(M1) | 27 | 0 | 54.66 | 77.72 | 1.4 | 8.8 | 31.1 | 66.8 | 346.0 |
|  |  |  | PlI(M2) | 27 | 0 | 26.87 | 25.23 | 1.3 | 7.0 | 17.9 | 45.2 | 96.3 |
|  |  |  | Pll(M6) | 16 | 0 | 8.55 | 6.32 | 1.1 | 3.5 | 7.2 | 12.6 | 21.9 |
|  |  |  | PlI(M13) | 22 | 0 | 4.93 | 3.96 | 0.8 | 2.0 | 3.6 | 7.8 | 15.7 |
|  |  | Placebo | Pl(M1) | 27 | 1 | 1.00 | 0.14 | 0.8 | 0.9 | 1.0 | 1.1 | 1.4 |
|  |  |  | PII(M2) | 28 | 1 | 0.92 | 0.17 | 0.5 | 0.8 | 0.9 | 1.0 | 1.2 |
|  |  |  | Pll(M6) | 12 | 1 | 1.11 | 0.96 | 0.6 | 0.7 | 0.9 | 1.0 | 4.1 |
|  |  |  | PII(M13) | 21 | 1 | 0.93 | 0.42 | 0.6 | 0.7 | 0.8 | 0.9 | 2.3 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 58 | 0 | 61.98 | 104.15 | 1.0 | 10.6 | 25.4 | 72.6 | 508.5 |
|  |  |  | PII(M2) | 60 | 0 | 38.31 | 52.65 | 0.5 | 7.4 | 22.4 | 44.8 | 286.2 |
|  |  |  | Pll(M6) | 26 | 0 | 23.31 | 27.70 | 0.4 | 4.1 | 10.5 | 33.6 | 95.6 |
|  |  |  | PII(M13) | 46 | 0 | 8.66 | 10.77 | 0.6 | 2.3 | 4.5 | 10.4 | 45.1 |
|  |  | Placebo | Pl(M1) | 66 | 3 | 1.03 | 0.22 | 0.6 | 0.9 | 1.0 | 1.2 | 2.1 |
|  |  |  | PII(M2) | 66 | 3 | 1.02 | 0.30 | 0.5 | 0.8 | 1.0 | 1.2 | 1.8 |
|  |  |  | PII(M6) | 30 | 0 | 1.03 | 0.58 | 0.5 | 0.7 | 0.9 | 1.0 | 3.6 |
|  |  |  | PII(M13) | 48 | 0 | 0.99 | 0.37 | 0.4 | 0.8 | 0.9 | 1.1 | 2.4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1, Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.15 Distribution of fold increase from baseline for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata (adapted ATP cohort for Humoral immunogenicity)


|  |  |  |  |  | $\geq 14$ fold |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | 95\% CI |  |
| Antibody | Sub-group | Group | Timing | N | n | \% | LL | UL |
| VZV.gE Ab.IgG | 18-49ys | HZ/su | Pl(M1) | 27 | 20 | 74.1 | 53.7 | 88.9 |
|  |  |  | PlI(M2) | 27 | 16 | 59.3 | 38.8 | 77.6 |
|  |  |  | PII(M6) | 16 | 3 | 18.8 | 4.0 | 45.6 |
|  |  |  | PlI(M13) 22 | 22 | 1 | 4.5 | 0.1 | 22.8 |
|  |  | Placebo | Pl(M1) | 27 | - | 0.0 | 0.0 | 12.8 |
|  |  |  | PII(M2) 28 | 28 | 0 | 0.0 | 0.0 | 12.3 |
|  |  |  | PII(M6) 12 | 12 | 0 | 0.0 | 0.0 | 26.5 |
|  |  |  | Plı(M13) 21 | 21 | 0 | 0.0 | 0.0 | 16.1 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 58 | 38 | 65.5 | 51.9 | 77.5 |
|  |  |  | PII(M2) 60 | 60 | 39 | 65.0 | 51.6 | 76.9 |
|  |  |  | PII(M6) 26 | 26 | 11 | 42.3 | 23.4 | 63.1 |
|  |  |  | Pll(M13) 4 | 46 |  | 19.6 | 9.4 | 33.9 |
|  |  | Placebo | Pl(M1) | 66 | 0 | 0.0 | 0.0 | 5.4 |
|  |  |  | Plı(M2) 66 | 66 | 0 | 0.0 | 0.0 | 5.4 |
|  |  |  | Pll(M6) 30 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  |  |  | PII(M13) 48 | 48 | 0 | 0.0 | 0.0 | 7.4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration within the specified range
95\% CI = 95\% confidence interval; LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Figure 7.11 Reverse cumulative curve for anti-gE antibody concentrations at Month 0 by age strata (ATP cohort for Humoral immunogenicity)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.12 Reverse cumulative curve for anti-gE antibody concentrations at Month 1 by age strata (ATP cohort for Humoral immunogenicity)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.13 Reverse cumulative curve for anti-gE antibody concentrations at Month 2 by age strata (ATP cohort for Humoral immunogenicity)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.14 Reverse cumulative curve for anti-gE antibody concentrations at Month 6 by age strata (ATP cohort for Humoral persistence)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.15 Reverse cumulative curve for anti-gE antibody concentrations at Month 13 by age strata (ATP cohort for Humoral persistence)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

## Table 7.16 Seropositivity rates and geometric mean concentrations (GMCs) of anti-gE antibody at Month 0, 1, 2, 6 and 13 by age strata in PreChemo Groups only (adapted ATP cohort for Humoral immunogenicity)



18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
GMC = geometric mean antibody concentration calculated on all subjects
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration equal to or above specified value $95 \% \mathrm{CI}=95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.17 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata in PreChemo Groups only (adapted ATP cohort for Humoral immunogenicity)

|  |  |  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | 95\% | Cl |
| Test description | Sub-group | Group | Timing | N | n | \% | LL | UL |
| VZV.gE Ab.lgG | 18-49ys | HZ/su | Pl(M1) | 19 | 19 | 100 | 82.4 | 100 |
|  |  |  | PlI(M2) | 19 | 18 | 94.7 | 74.0 | 99.9 |
|  |  |  | Pll(M6) | 12 | 9 | 75.0 | 42.8 | 94.5 |
|  |  |  | PlI(M13) | 16 | 8 | 50.0 | 24.7 | 75.3 |
|  |  | Placebo | Pl(M1) | 21 | 0 | 0.0 | 0.0 | 16.1 |
|  |  |  | PII(M2) | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  |  |  | Pll(M6) | 9 | 0 | 0.0 | 0.0 | 33.6 |
|  |  |  | PII(M13) | 15 | 0 | 0.0 | 0.0 | 21.8 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 45 | 41 | 91.1 | 78.8 | 97.5 |
|  |  |  | PII(M2) | 46 | 43 | 93.5 | 82.1 | 98.6 |
|  |  |  | Pll(M6) | 20 | 15 | 75.0 | 50.9 | 91.3 |
|  |  |  | Pll(M13) | 35 | 19 | 54.3 | 36.6 | 71.2 |
|  |  | Placebo | Pl(M1) | 54 | 0 | 0.0 | 0.0 | 6.6 |
|  |  |  | PII(M2) | 54 | 0 | 0.0 | 0.0 | 6.6 |
|  |  |  | PII(M6) | 27 | 0 | 0.0 | 0.0 | 12.8 |
|  |  |  | Pll(M13) | 40 | 0 | 0.0 | 0.0 | 8.8 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination $\geq 4$ fold the cut-off for Anti-gE ( $4 \times 97$ $\mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at post-vaccination $\geq 4$ fold the pre-vaccination antibody concentration
$N=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
95\% CI $=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

## Table 7.18 Mean Geometric Increase (MGI) of anti-gE antibody ELISA

 concentrations at Month 1, 2, 6 and 13 by age strata in PreChemo Groups only (adapted ATP cohort for Humoral immunogenicity)|  |  |  |  |  |  |  | MGI |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |  |  | 95\% CI |  |
| Sub-group | Group | N | Time point description | GMC | Time point description | GMC | Ratio order | Value | LL | UL |
| 18-49ys | HZ/su | 19 | PI(M1) | 41519.9 | PRE | 930.2 | PI(M1) / PRE | 44.6 | 27.9 | 71.5 |
|  |  | 19 | PII(M2) | 20955.9 | PRE | 930.2 | PII(M2) / PRE | 22.5 | 14.3 | 35.5 |
|  |  | 12 | PII(M6) | 5893.1 | PRE | 779.0 | PII(M6) / PRE | 7.6 | 4.8 | 12.0 |
|  |  | 16 | PII(M13) | 3785.9 | PRE | 861.4 | PlI(M13) / PRE | 4.4 | 2.9 | 6.7 |
|  | Placebo | 21 | Pl(M1) | 1039.5 | PRE | 1080.4 | PI(M1) / PRE | 1.0 | 0.9 | 1.0 |
|  |  | 22 | PII(M2) | 970.9 | PRE | 1088.7 | PII(M2) / PRE | 0.9 | 0.8 | 1.0 |
|  |  | 9 | PII(M6) | 878.0 | PRE | 1032.9 | PII(M6) / PRE | 0.9 | 0.7 | 1.0 |
|  |  | 15 | PII(M13) | 915.9 | PRE | 1009.6 | PII(M13) / PRE | 0.9 | 0.7 | 1.1 |
| $\geq 50 y s$ | HZ/su | 45 | PI(M1) | 32207.5 | PRE | 1046.7 | PI(M1) / PRE | 30.8 | 20.8 | 45.5 |
|  |  | 46 | PII(M2) | 23863.7 | PRE | 1077.7 | PII(M2) / PRE | 22.1 | 15.8 | 31.0 |
|  |  | 20 | PII(M6) | 10645.5 | PRE | 1022.7 | PII(M6) / PRE | 10.4 | 5.7 | 19.2 |
|  |  | 35 | PII(M13) | 4969.6 | PRE | 1057.8 | PII(M13) / PRE | 4.7 | 3.2 | 6.8 |
|  | Placebo | 54 | PI(M1) | 1229.6 | PRE | 1227.2 | Pl(M1) / PRE | 1.0 | 0.9 | 1.1 |
|  |  | 54 | PII(M2) | 1196.6 | PRE | 1227.2 | PII(M2) / PRE | 1.0 | 0.9 | 1.1 |
|  |  | 27 | PII(M6) | 1535.5 | PRE | 1670.4 | PII(M6) / PRE | 0.9 | 0.8 | 1.1 |
|  |  | 40 | PII(M13) | 1340.3 | PRE | 1470.6 | PII(M13) / PRE | 0.9 | 0.8 | 1.0 |

18-49ys $=$ Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ Number of subjects with available results at the two considered time points
$\mathrm{MGI}=$ Geometric mean of the within subject ratios of the post-vaccination reciprocal anti-gE concentration to the Month 0 reciprocal anti-gE concentration
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.19 Descriptive statistics of the fold increase for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata in PreChemo Groups only (adapted ATP cohort for Humoral immunogenicity)

| Antibody | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| VZV.gE Ab.lgG | 18-49ys | HZ/su | Pl(M1) | 190 | 0 | 72.03 | 86.91 | 8.2 | 25.4 | 40.3 | 82.1 | 346.0 |
|  |  |  | PlI(M2) | 190 | 0 | 32.08 | 25.33 | 2.6 | 10.4 | 24.8 | 46.5 | 96.3 |
|  |  |  | Pll(M6) | 120 | 0 | 9.50 | 6.50 | 2.7 | 3.9 | 8.5 | 14.3 | 21.9 |
|  |  |  | PII(M13) | 160 | 0 | 5.71 | 4.14 | 0.8 | 2.8 | 3.8 | 8.2 | 15.7 |
|  |  | Placebo | Pl(M1) | 21 | 1 | 0.97 | 0.13 | 0.8 | 0.9 | 0.9 | 1.0 | 1.4 |
|  |  |  | PlI(M2) | 22 | 1 | 0.91 | 0.17 | 0.5 | 0.8 | 0.9 | 1.0 | 1.2 |
|  |  |  | Pll(M6) 9 | 9 | 1 | 0.87 | 0.18 | 0.6 | 0.8 | 0.9 | 0.9 | 1.2 |
|  |  |  | PII(M13) | 15 | 1 | 0.98 | 0.49 | 0.6 | 0.7 | 0.8 | 0.9 | 2.3 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 450 | 0 | 70.05 | 112.96 | 2.7 | 12.5 | 33.5 | 81.3 | 508.5 |
|  |  |  | PlI(M2) | 460 | 0 | 40.21 | 55.11 | 1.6 | 11.3 | 23.8 | 45.7 | 286.2 |
|  |  |  | PII(M6) 20 | 20 | 0 | 21.71 | 27.72 | 1.2 | 3.9 | 10.5 | 29.6 | 95.6 |
|  |  |  | PII(M13) 3 | 350 | 0 | 8.57 | 11.00 | 0.9 | 2.1 | 4.7 | 10.4 | 45.1 |
|  |  | Placebo | Pl(M1) | 54 | 1 | 1.02 | 0.24 | 0.6 | 0.9 | 1.0 | 1.1 | 2.1 |
|  |  |  | PlI(M2) | 54 | 1 | 1.02 | 0.30 | 0.5 | 0.8 | 1.0 | 1.2 | 1.8 |
|  |  |  | PlI(M6) 27 | 270 | 0 | 1.01 | 0.59 | 0.5 | 0.7 | 0.9 | 1.0 | 3.6 |
|  |  |  | PII(M13) | 40 | 0 | 0.97 | 0.39 | 0.4 | 0.8 | 0.9 | 1.1 | 2.4 |

[^7]Table 7.20 Distribution of fold increase from baseline for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata in PreChemo Groups only (adapted ATP cohort for Humoral immunogenicity)

|  |  |  |  | $\geq 2$ fold |  |  | $\geq 4$ fold |  |  | $\geq 6$ fold |  |  |  | $\geq 8$ fold |  |  |  | $\geq 10$ fold |  |  |  | $\geq 12$ fold |  |  | $\geq 14$ fold |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  | $\begin{gathered} 95 \% \\ \text { CI } \end{gathered}$ |  |  | 95 | \% |  |  | 95\% |  |  |  | $95 \%$ Cl |  |  |  |  |  |  |  | CI |
| Antib ody | Su <br> b- <br> gro <br> up | Gro up | Timi ng | N | \% | $\mathrm{LL} \underset{\mathrm{~L}}{\mathrm{U}}$ | n | \% | $\mathrm{LL} \left\lvert\, \begin{aligned} & \mathrm{U} \\ & \mathrm{~L} \end{aligned}\right.$ | n | \% | LL | $\mathrm{U}$ | n | \% | LL | $\begin{aligned} & \mathrm{U} \\ & \mathrm{~L} \end{aligned}$ | n ${ }^{\text {\% }}$ | \% | LL | $\begin{aligned} & \mathrm{U} \\ & \mathrm{~L} \end{aligned}$ | n \% | LL | $\begin{aligned} & \mathrm{U} \\ & \mathrm{~L} \end{aligned}$ | n | \% | LL | $\begin{aligned} & \mathrm{U} \\ & \mathrm{~L} \end{aligned}$ |
| VZV.g | 18- | HZ/s | PI(M | 11 | 10 | 8210 | 1 | 10 | 8210 | 1 | 10 | 82 | 10 | 1 | 10 | 82 | 10 | 18 | 89 | 66 | 98 | 189 | 66 | 98 | 1 | 89 | 66 | 98 |

 Ab.lg s G



 6) 2 |  | 2 | 0 | .5 | 0 | .0 | .8 | .5 | .3 | .7 | .8 | .0 | .1 | .9 | .3 | 9 | .1 | .3 | 9 | .1 | .0 | 5 | .2 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |

 13) | 6 | 4 | .5 | .7 | .4 | .0 | .7 | .3 | .5 | .2 | .6 | .0 | 3 | .4 | .5 | 6 | .3 | .5 | 6 | .3 | 3 | 2 | .2 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |

 ebo 1) $11 \begin{array}{lllllllllllllllllllllllllllll} & 0 & 0 & .1 & 0 & 0 & .1 & 0 & 0 & .1 & 0 & 0 & .1 & 0 & 0 & .1 & 0 & 0 & .1 & 0 & 0 & .1\end{array}$
 2) $2 \begin{array}{llllllllllllllllllllllllllll} & 0 & 0 & .4 & 0 & 0 & .4 & 0 & 0 & .4 & 0 & 0 & .4 & 0 & 0 & .4 & 0 & 0 & .4 & 0 & 0 & .4\end{array}$
 6) $\quad 0 \quad 0 \quad .6 \quad 0 \quad 0 \quad .6$

 \begin{tabular}{l|l|l|l|l|l|l|l|l|l|l|l|l|l|l|l|l|l|lll}
\hline 13$)$ \& 5 \& .3 \& 7 \& .5 \& 0 \& 0 \& .8 \& 0 \& 0 \& .8 \& 0 \& 0 \& .8 \& 0 \& 0 \& .8 \& 0 \& 0 \& .8 \& 0 <br>
\hline

 

$\geq$ \& $\mathrm{HZ} / \mathrm{s}$ \& $\mathrm{PI}(\mathrm{M}$ \& 4 \& 4 \& 10 \& 92 \& 10 \& 4 \& 91 \& 78 \& 97 \& 3 \& 86 \& 73 \& 94 \& 3 \& 86 \& 73 \& 94 \& 3 \& 82 \& 67 \& 92 \& 3 \& 75 \& 60 \& 87 <br>
3 \& 73 \& 58 \& 85 <br>
50 y \& u \& $1)$ \& 5 \& 5 \& 0 \& .1 \& 0 \& 1 \& .1 \& .8 \& .5 \& 9 \& .7 \& .2 \& .9 \& 9 \& .7 \& .2 \& .9 \& 7 \& .2 \& .9 \& .0 \& 4 \& .6 \& .5 \& .1 <br>
3 \& .3 \& .1 \& .4
\end{tabular} s








 ebo 1) 4 |  | 9 | 0 | 9 | 0 | 0 | 6 | 0 | 0 | 6 | 0 | 0 | 6 | 0 | 0 | 6 | 0 | 0 | 6 | 0 | 0 | 6 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |

 2) 4 |  | 0 | 0 | 6 | 0 | 0 | 6 | 0 | 0 | 6 | 0 | 0 | 6 | 0 | 0 | 6 |  | 0 | 0 | 6 | 0 | 0 | 6 |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| PH(M | 1 | 3 | 0 | 10 | 0 | 0 | 12 | 0 | 0 | 0 | 12 | 0 | 0 | 0 | 12 | 0 | 0 | 0 | 12 | 0 | 0 | 0 | 12 | 0 | 0 | 0 | 12 |



 13) $00 \begin{array}{lllllllllllllllllllllllllll} & 0 & 6 & .9 & 0 & 0 & 8 & 0 & 0 & 8 & 0 & 0 & 8 & 0 & 0 & 8 & 0 & 0 & 8 & 0 & 0 & 8\end{array}$

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration within the specified range
$95 \% \mathrm{CI}=95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)

PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)
Table 7.21 Adjusted geometric means and ratio of $\mathrm{HZ} /$ su over placebo for antigE antibody ELISA concentrations at Month 2 in PreChemo Groups only (Total Vaccinated Cohort)

|  |  |  | Adjusted geometric mean |  |  | Adjusted geometric mean ratio |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Timing | Group | N | Value | LL | UL | Value | LL | UL | P-value for the ratio |
| PlI(M2) | HZ/su | 75 | 24823.67 | 19853.20 | 31038.55 | 22.8 | 18.1 | 28.7 | <. 0001 |
|  | Placebo | 80 | 1089.30 | 1022.21 | 1160.80 |  | . | . | . |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval
Confidence Interval (CI) were back transformed to original units The $p$-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)
Table 7.22 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 2 in PreChemo Groups only (Total Vaccinated Cohort)


HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at Month $2 \geq 4$ fold the cut-off for Anti-gE ( $4 \times 97 \mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at Month $2 \geq 4$ fold the pre-vaccination antibody concentration
$N=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit
PII(M2) = Post-vaccination Dose II (Month 2)
Table 7.23 Adjusted geometric means and ratio of HZ/su over placebo for antigE antibody ELISA concentrations at Month 2 in all subjects (Total Vaccinated Cohort)

|  |  |  | Adjusted geometric mean |  |  | Adjusted geometric mean ratio |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Timing | Group | N | Value | LL | UL | Value | LL | UL | P-value for the ratio |
| PII(M2) | HZ/su | 99 | 15053.28 | 11569.28 | 19586.48 | 14.2 | 10.8 | 18.6 | <. 0001 |
|  | Placebo | 100 | 1062.99 | 992.91 | 1138.00 |  | . | . |  |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval
Confidence Interval (Cl) were back transformed to original units
The p-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)

Table 7.24 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 2 in all subjects (Total Vaccinated Cohort)

|  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% | \% CI |
| Test description | Group | N | n | \% | LL | UL |
| VZV.gE Ab.lgG | HZ/su | 99 | 86 | 86.9 | 78.6 | 92.8 |
|  | Placebo |  |  | 0.0 |  | 3.6 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at Month $2 \geq 4$ fold the cut-off for Anti-gE ( $4 \times 97 \mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at Month $2 \geq 4$ fold the pre-vaccination antibody
concentration
$\mathrm{N}=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
$95 \% \mathrm{Cl}=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
PII(M2) = Post-vaccination Dose II (Month 2)
Table 7.25 Seropositivity rates and geometric mean concentrations (GMCs) of anti-gE antibody at Month 0, 1, 2, 6 and 13 (Total Vaccinated Cohort)


HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
GMC = geometric mean antibody concentration calculated on all subjects
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration equal to or above specified value
95\% CI = 95\% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.26 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 in all subjects (Total Vaccinated Cohort)

|  |  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 95\% CI |  |
| Test description | Group | Timing | N | n | \% | LL | UL |
| VZV.gE Ab.lgG | HZ/su | PI(M1) | 101 | 89 | 88.1 | 80.2 | 93.7 |
|  |  | PII(M2) | 99 | 86 | 86.9 | 78.6 | 92.8 |
|  |  | PII(M6) | 50 | 37 | 74.0 | 59.7 | 85.4 |
|  |  | PII(M13) | 82 | 42 | 51.2 | 39.9 | 62.4 |
|  | Placebo | Pl(M1) | 105 | 0 | 0.0 | 0.0 | 3.5 |
|  |  | PII(M2) | 100 | 0 | 0.0 | 0.0 | 3.6 |
|  |  | PII(M6) | 55 | 2 | 3.6 | 0.4 | 12.5 |
|  |  | PII(M13) | 81 | 1 | 1.2 | 0.0 | 6.7 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination $\geq 4$ fold the cut-off for Anti-gE (4x97 $\mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at post-vaccination $\geq 4$ fold the pre-vaccination antibody concentration
$N=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
$95 \% \mathrm{Cl}=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

## Table 7.27 Mean Geometric Increase (MGI) of anti-gE antibody ELISA

 concentrations at Month 1, 2, 6 and 13 (Total Vaccinated Cohort)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ Number of subjects with available results at the two considered time points
MGI = Geometric mean of the within subject ratios of the post-vaccination reciprocal anti-gE concentration to the Month 0 reciprocal anti-gE concentration
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)
Table 7.28 Descriptive statistics of the fold increase for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 (Total Vaccinated Cohort)

| Antibody | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| VZV.gE Ab.lgG | HZ/su | Pl(M1) | 101 | 0 | 57.97 | 92.31 | 1.0 | 11.0 | 27.1 | 60.6 | 508.5 |
|  |  | PII(M2) | 99 | 0 | 32.93 | 43.87 | 0.5 | 7.0 | 19.6 | 42.7 | 286.2 |
|  |  | PII(M6) | 50 | 0 | 16.93 | 21.50 | 0.4 | 4.0 | 9.2 | 19.2 | 95.6 |
|  |  | Pll(M13) | 82 | 0 | 7.98 | 11.65 | 0.5 | 2.1 | 4.1 | 8.5 | 77.5 |
|  | Placebo | Pl(M1) | 105 | 4 | 1.02 | 0.20 | 0.6 | 0.9 | 1.0 | 1.1 | 2.1 |
|  |  | PII(M2) | 100 | 4 | 0.98 | 0.27 | 0.5 | 0.8 | 1.0 | 1.1 | 1.8 |
|  |  | PII(M6) | 55 | 2 | 1.42 | 2.99 | 0.5 | 0.7 | 0.9 | 1.0 | 22.7 |
|  |  | PlI(M13) | 81 | 1 | 1.17 | 1.90 | 0.4 | 0.8 | 0.9 | 1.1 | 17.7 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1,Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.29 Distribution of fold increase from baseline for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 (Total Vaccinated Cohort)


HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration within the specified range
$95 \% \mathrm{Cl}=95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Figure 7.16 Reverse cumulative curve for anti-gE antibody concentrations at Month $\mathbf{0}$ (Total Vaccinated Cohort)

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.17 Reverse cumulative curve for anti-gE antibody concentrations at Month 1 (Total Vaccinated Cohort)


HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.18 Reverse cumulative curve for anti-gE antibody concentrations at Month 2 (Total Vaccinated Cohort)

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.19 Reverse cumulative curve for anti-gE antibody concentrations at Month 6 (Total Vaccinated Cohort)


HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.20 Reverse cumulative curve for anti-gE antibody concentrations at Month 13 (Total Vaccinated Cohort)

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Table 7.30 Seropositivity rates and geometric mean concentrations (GMCs) of anti-gE antibody at Month 0, 1, 2, 6 and 13 by PreChemo/OnChemo groups (Total Vaccinated Cohort)


PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
GMC = geometric mean antibody concentration calculated on all subjects
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration equal to or above specified value $95 \% \mathrm{Cl}=95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.31 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | 95\% CI |  |
| Test description | Sub-group | Group | Timing | N | n | \% | LL | UL |
| VZV.gE Ab.lgG | PreChemo | HZ/su | PI(M1) | 78 | 74 | 94.9 | 87.4 | 98.6 |
|  |  |  | Pll(M2) | 75 | 70 | 93.3 | 85.1 | 97.8 |
|  |  |  | PII(M6) | 40 | 30 | 75.0 | 58.8 | 87.3 |
|  |  |  | PII(M13) | 62 | 34 | 54.8 | 41.7 | 67.5 |
|  |  | Placebo | Pl(M1) | 84 | 0 | 0.0 | 0.0 | 4.3 |
|  |  |  | PlI(M2) | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  |  |  | PlI(M6) | 46 | 1 | 2.2 | 0.1 | 11.5 |
|  |  |  | PII(M13) | 65 | 1 | 1.5 | 0.0 | 8.3 |
|  | OnChemo | HZ/su | Pl(M1) | 23 | 15 | 65.2 | 42.7 | 83.6 |
|  |  |  | PlI(M2) | 24 | 16 | 66.7 | 44.7 | 84.4 |
|  |  |  | Pll(M6) | 10 | 7 | 70.0 | 34.8 | 93.3 |
|  |  |  | PII(M13) | 20 | 8 | 40.0 | 19.1 | 63.9 |
|  |  | Placebo | Pl(M1) | 21 | 0 | 0.0 | 0.0 | 16.1 |
|  |  |  | PII(M2) | 20 | 0 | 0.0 | 0.0 | 16.8 |
|  |  |  | PII(M6) | 9 | 1 | 11.1 | 0.3 | 48.2 |
|  |  |  | PlI(M13) | 16 | 0 | 0.0 | 0.0 | 20.6 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination $\geq 4$ fold the cut-off for Anti-gE ( $4 \times 97$ $\mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at post-vaccination $\geq 4$ fold the pre-vaccination antibody concentration
$N=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
$95 \% \mathrm{CI}=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
Pl(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

## Table 7.32 Mean Geometric Increase (MGI) of anti-gE antibody ELISA

 concentrations at Month 1, 2, 6 and 13 by PreChemo/OnChemo groups (Total Vaccinated Cohort)|  |  |  |  |  |  |  | MGI |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |  |  | 95\% | \% CI |
| Sub-group | Group | N | Time point description | GMC | Time point description | GMC | Ratio order | Value | LL | UL |
| PreChemo | HZ/su | 78 | Pl(M1) | 34703.6 | PRE | 1036.5 | PI(M1) / PRE | 33.5 | 25.6 | 43.7 |
|  |  | 75 | PII(M2) | 23376.5 | PRE | 1093.2 | PII(M2) / PRE | 21.4 | 16.8 | 27.2 |
|  |  | 40 | PII(M6) | 9503.2 | PRE | 1008.0 | PII(M6) / PRE | 9.4 | 6.7 | 13.2 |
|  |  | 62 | PII(M13) | 4998.6 | PRE | 1033.5 | PII(M13) / PRE | 4.8 | 3.7 | 6.3 |
|  | Placebo | 84 | $\mathrm{Pl}(\mathrm{M} 1)$ | 1226.7 | PRE | 1246.2 | PI(M1) / PRE | 1.0 | 0.9 | 1.0 |
|  |  | 80 | PII(M2) | 1141.8 | PRE | 1208.7 | PII(M2) / PRE | 0.9 | 0.9 | 1.0 |
|  |  | 46 | PII(M6) | 1161.8 | PRE | 1216.3 | PII(M6) / PRE | 1.0 | 0.8 | 1.1 |
|  |  | 65 | PII(M13) | 1212.4 | PRE | 1274.1 | PII(M13) / PRE | 1.0 | 0.8 | 1.1 |
| OnChemo | HZ/su | 23 | $\mathrm{Pl}(\mathrm{M} 1)$ | 9966.5 | PRE | 1113.1 | PI(M1) / PRE | 9.0 | 4.6 | 17.3 |
|  |  | 24 | PII(M2) | 8842.0 | PRE | 1099.7 | PII(M2) / PRE | 8.0 | 4.1 | 15.6 |
|  |  | 10 | PII(M6) | 5645.4 | PRE | 803.2 | PII(M6) / PRE | 7.0 | 2.1 | 23.7 |
|  |  | 20 | Pl(M13) | 3492.7 | PRE | 1144.8 | PII(M13) / PRE | 3.1 | 1.8 | 5.2 |
|  | Placebo | 21 | Pl(M1) | 970.6 | PRE | 919.8 | PI(M1) / PRE | 1.1 | 1.0 | 1.1 |
|  |  | 20 | PII(M2) | 866.8 | PRE | 904.0 | PII(M2) / PRE | 1.0 | 0.8 | 1.1 |
|  |  | 9 | PII(M6) | 1818.6 | PRE | 1627.8 | PII(M6) / PRE | 1.1 | 0.7 | 1.7 |
|  |  | 16 | PlI(M13) | 741.9 | PRE | 818.4 | PII(M13) / PRE | 0.9 | 0.8 | 1.0 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ Number of subjects with available results at the two considered time points
$\mathrm{MGI}=$ Geometric mean of the within subject ratios of the post-vaccination reciprocal anti-gE concentration to the Month 0 reciprocal anti-gE concentration
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.33 Descriptive statistics of the fold increase for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by PreChemo/OnChemo groups (Total Vaccinated Cohort)

| Antibody | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| VZV.gE Ab.lgG | PreChemo | HZ/su | Pl(M1) | 78 | 0 | 67.43 | 100.24 | 2.7 | 16.5 | 33.5 | 75.6 | 508.5 |
|  |  |  | PII(M2) | 75 | 0 | 35.81 | 45.65 | 1.6 | 10.4 | 23.7 | 45.2 | 286.2 |
|  |  |  | PII(M6) | 40 | 0 | 16.29 | 20.78 | 1.2 | 4.0 | 9.5 | 18.8 | 95.6 |
|  |  |  | PII(M13) | 62 | 0 | 8.62 | 12.49 | 0.8 | 2.3 | 4.7 | 9.1 | 77.5 |
|  |  | Placebo | Pl(M1) | 84 | 2 | 1.00 | 0.21 | 0.6 | 0.9 | 1.0 | 1.1 | 2.1 |
|  |  |  | PII(M2) | 80 | 2 | 0.98 | 0.27 | 0.5 | 0.8 | 1.0 | 1.1 | 1.8 |
|  |  |  | PII(M6) | 46 | 1 | 1.43 | 3.24 | 0.5 | 0.7 | 0.9 | 1.0 | 22.7 |
|  |  |  | PII(M13) | 65 | 1 | 1.23 | 2.12 | 0.4 | 0.8 | 0.9 | 1.1 | 17.7 |
|  | OnChemo | HZ/su | Pl(M1) | 23 | 0 | 25.88 | 46.57 | 1.0 | 1.9 | 12.3 | 26.8 | 201.1 |
|  |  |  | PlI(M2) | 24 | 0 | 23.94 | 37.19 | 0.5 | 3.2 | 5.0 | 26.9 | 152.9 |
|  |  |  | Pll(M6) | 10 | 0 | 19.47 | 25.22 | 0.4 | 1.9 | 6.9 | 33.6 | 68.9 |
|  |  |  | PII(M13) | 20 | 0 | 5.99 | 8.48 | 0.5 | 1.3 | 3.0 | 5.3 | 30.1 |
|  |  | Placebo | Pl(M1) | 21 | 2 | 1.07 | 0.16 | 0.7 | 1.0 | 1.1 | 1.2 | 1.3 |
|  |  |  | PII(M2) | 20 | 2 | 0.99 | 0.24 | 0.5 | 0.9 | 1.0 | 1.1 | 1.5 |
|  |  |  | PlI(M6) | 9 | 1 | 1.35 | 1.10 | 0.6 | 0.9 | 0.9 | 1.1 | 4.1 |
|  |  |  | PII(M13) | 16 | 0 | 0.93 | 0.22 | 0.6 | 0.8 | 0.9 | 1.0 | 1.5 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1,Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.34 Distribution of fold increase from baseline for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  |  |  | $\geq 2$ fold |  |  |  |  | $\geq 4$ fold |  |  | $\geq 6$ fold |  |  |  | $\geq 8$ fold |  |  | $\geq 10$ fold |  |  |  | $\geq 12$ fold |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  |
| Antib ody | Subgroup | Grou $p$ | $\begin{aligned} & \mathrm{Timin} \\ & \mathrm{~g} \end{aligned}$ | N | n \% | \% L | LL UL | UL | n \% |  | L UL | n | \% | LL U | UL | n \% |  | L UL | n | \% | LL U | UL | \% | LL | UL |
| $\begin{aligned} & \text { VZV.g } \\ & \mathrm{E} \\ & \mathrm{Ab} . \operatorname{lgG} \end{aligned}$ | PreChe mo | $\begin{aligned} & \mathrm{HZ} / \mathrm{s} \\ & \mathrm{u} \end{aligned}$ | $\mathrm{Pl}^{\text {Pl(M1 }}$ |  | 7 10 <br> 8 0 | 10 9 <br> 0 4 | 95.10  <br> 4 0 | 10 7 <br> 0 4 | 794  <br> 4 9 | 4. 87 | 87. 98. | 7 | 92. | 84.  <br> 0 1 | 97.7 | 7  <br> 1 91 <br> 0  | 1. 82 | 82. $\begin{aligned} & 96 . \\ & 3\end{aligned}$ | 6 6 | 84. | 74.  <br> 7 8 | 91.6 | 6 78 <br> 1 2 | 4 | 86 8 |
|  |  |  | PII(M <br> 2) <br> PI |  | 7 98 <br> 4 7 |  | 92.10  <br> 8 0 | $\begin{array}{l\|l} 10 & 7 \\ 0 & 0 \\ \hline \end{array}$ | $\begin{array}{ll} 7 & 93 \\ 0 & 3 \\ \hline \end{array}$ | $\text { 3. }{ }_{1}^{85}$ | $\begin{array}{l\|l} 85 . & 97 . \\ 1 & 8 \\ \hline \end{array}$ | 6 | 88. | $. \begin{array}{l\|l} 78 \\ 4 & 4 \\ \hline \end{array}$ | $\begin{aligned} & 94 . \\ & 4 \end{aligned}$ | $\begin{array}{l\|l} \hline 6 & 82 . \\ 2 & 7 \\ \hline \end{array}$ | 2. 72 | $\begin{aligned} & 2 . \\ & 20 . \\ & 4 \\ & \hline \end{aligned}$ | 5 <br> 7 | 76. | $\begin{aligned} & 64 . \\ & 7 \end{aligned}$ | $\begin{aligned} & 85 \\ & 1 \\ & 1 \end{aligned}$ |  72 <br> 4 0 | 60 <br> 4 | 8 |
|  |  |  | PII(M <br> 6) | 4  <br> 0 3 |  | 95.  <br> 0 1 | 83. 1 1 | $\begin{array}{l\|l} 99 . & 3 \\ 4 \\ \hline \end{array}$ | $\begin{array}{l\|l} \hline 3 & 75 . \\ 0 & 0 \\ \hline \end{array}$ | - $\begin{aligned} & 58 \\ & 8\end{aligned}$ | $\begin{array}{l\|l} 58 . & 87 . \\ 3 & 3 \\ \hline \end{array}$ | 2 | ${ }^{65}$ | $\begin{array}{l\|l} 48 . & 7 \\ 3 & 4 \end{array}$ | $\begin{array}{l\|l} 79.2 \\ 4 & 2 \\ 4 \end{array}$ | 2 60 <br> 4 0 | - 43 | $\begin{aligned} & 43 . \\ & 3 \\ & 3 \\ & 1 \end{aligned}$ |  | 47. | $\begin{array}{l\|l} 31 . & 6 \\ 5 & 9 \end{array}$ | 163 | 1 45 <br> 8 0 | ${ }^{29}$ | 61 5 |
|  |  |  | $\begin{aligned} & \text { PII(M } \\ & 13) \end{aligned}$ |  |  | 80. 6 <br> 6 6 | 68.89 6 |  |  | 4. 41 | $\begin{aligned} & 41 . \\ & 7 . \\ & 7 . \\ & 5 \end{aligned}$ | 2 |  | $\begin{array}{lll} 28 & 5 \\ 1 & 6 \end{array}$ | $\begin{aligned} & 53 . \\ & 6 \end{aligned}$ | $\begin{array}{l\|l} \hline 1 & 29 . \\ 8 & 0 \\ \hline \end{array}$ |  | $\begin{aligned} & 18 . \\ & 21 . \\ & 2 \\ & \hline \end{aligned}$ |  | 24. | $\cdot \begin{array}{l\|l} 14 . & 3 \\ 2 & 7 \end{array}$ |  | 1 19 <br> 2 4 | 10 | 31 |
|  |  | Place bo | $\mathrm{PI}(\mathrm{M} 1$ <br> ) | $\begin{aligned} & 8 \\ & 4 \end{aligned}$ |  | 1.20 | 0.06 | 6.50 | 00.0 |  | 0.04 .3 | 0 | 0.0 | 0.04 | 4.3 | 00.0 |  | . 04.3 | 0 | 0.0 | 0.04 | 4.3 | 00.0 | 0.0 | 4.3 |
|  |  |  | PII(M <br> 2 ) <br> 1 | 8 | 00 | 0.0 | 0.04. | 4.50 | 00.0 |  | 0.04 .5 | 0 | 0.0 | 0.04 | 4.50 | 00.0 |  | . 4.5 | 0 | 0.0 | 0.0 | 4.50 | 00.0 | 0.0 | 4.5 |
|  |  |  | $\mathrm{PlI}(\mathrm{M}$ <br> 6$)$ | $\begin{aligned} & 4 \\ & 6 \\ & \hline \end{aligned}$ |  | 4.30 | $\begin{array}{\|c\|c} \hline 0.514 \\ & 8 \\ \hline \end{array}$ |  |  |  | $0.1 \begin{aligned} & 11 . \\ & 5 \end{aligned}$ | 1 | 2.2 | 0.11 | $11 .$ $5$ | 12.2 |  | $0.1 \begin{aligned} & 11 . \\ & 5 \\ & \hline \end{aligned}$ | 1 | 2.2 | 0.111 <br> 5 |  | 2.2 | 0.1 | 5 |
|  |  |  | $\begin{aligned} & \mathrm{PlI}(\mathrm{M} \\ & 13) \\ & \hline \end{aligned}$ | $\begin{aligned} & 6 \\ & 5 \end{aligned}$ |  | 7.72 | $2.517$ | $17.1$ | 11.5 | 50. | 0.08 .3 | 1 | 1.5 | 0.08 | 8.3 | 11.5 |  | . 08.3 | 1 | 1.5 | 0.0 | 8.3 | 1.5 | 0.0 | 8.3 |
|  | OnChe mo |  | $\mathrm{Pl}(\mathrm{M} 1$ |  |  | $\begin{array}{l\|l} 73 . & 5 \\ 9 & 6 \end{array}$ | $\begin{array}{l\|l} \text { 51. } & 89 \\ 6 & 8 \\ \hline \end{array}$ |  | $\begin{array}{ll} 1 & 65 . \\ 5 & 6 . \\ \hline \end{array}$ | $\text { 5. } 42$ | $\begin{aligned} & \text { 42. } 83 . \\ & 7 \\ & 7 \\ & \hline \end{aligned}$ | 4 |  | $. \begin{array}{l\|l} 38 . & 8 \\ 5 & 3 \end{array}$ |  | $\begin{array}{ll} 1 & 56 . \\ 3 & 5 \\ \hline \end{array}$ | $\text { 6. } 34$ | $\begin{aligned} & 34 . \\ & 5 \\ & 5 \\ & 8 \\ & 8 \end{aligned}$ |  |  |  |  | 1  <br> 2 2 | 30 6 | 2 |
|  |  |  | PlI(M <br> 2$)$ <br> 2 | 2 1 <br> 4 9 | 1 79 <br> 9 2 | 7.  <br> 2 8 | 57.92 <br> 8 | 92. 1 | $\begin{array}{l\|l} 1 & 66 . \\ 6 & 7 \\ \hline \end{array}$ | 6. 44 | $\begin{array}{l\|l} 44 . & 84 . \\ 7 & 4 \\ \hline \end{array}$ | 1 |  | $\begin{array}{l\|l} 25 . & 6 \\ 6 & 2 \\ \hline \end{array}$ | $\begin{aligned} & 67 . \\ & 2 \end{aligned}$ | $\begin{array}{l\|l} 1 & 41 . \\ 0 & 7 \\ \hline \end{array}$ |  | $\begin{aligned} & 22 . \\ & 1 \\ & 1 \\ & \hline \end{aligned}$ |  | 41. |  |  |  | 12 | 63 |
|  |  |  | $\mathrm{PlI}(\mathrm{M}$ 1 <br> 6$)$ 0 | $\begin{aligned} & 1 \\ & 0 \end{aligned}$ |  | $\begin{array}{ll} \hline 70 . & 3 \\ 0 & 8 \\ \hline \end{array}$ | $\begin{array}{l\|l} \hline 34 . & 93 \\ 8 & 3 \\ \hline \end{array}$ | $93.7$ | $\begin{array}{ll} 7 \\ 70 \\ 0 \end{array}$ | $0.34$ | $\begin{array}{ll} 34 . & 93 . \\ 8 & 3 \\ \hline \end{array}$ | 6 | $\begin{aligned} & 60 . \\ & 0 \end{aligned}$ | $\begin{array}{l\|l} 26 . & 8 \\ 2 & 8 \\ \hline \end{array}$ | $\begin{aligned} & 87 . \\ & 8 \\ & \hline \end{aligned}$ | $4 \begin{aligned} & 40 \\ & 0 \end{aligned}$ |  | $\begin{aligned} & 12 . \\ & 23 . \\ & 2 \\ & \hline \end{aligned}$ | 4 |  | $\begin{array}{ll} 12 . & 7 \\ 2 & 8 \end{array}$ | $\begin{aligned} & 73 . \\ & 8 \\ & \hline \end{aligned}$ | $4 \begin{aligned} & 40 \\ & 0\end{aligned}$ |  | 8 |
|  |  |  | PlI(M 2 <br> $13)$ 0 |  |  |  |  |  | $8 \begin{aligned} & 40 . \\ & 0 \end{aligned}$ |  | $\begin{aligned} & \text { 19. } 63 . \\ & 1 \\ & \hline \end{aligned}$ | 4 |  |  |  | $\begin{array}{l\|l} 3 & 15 . \\ 0 \end{array}$ |  | $\begin{aligned} & 3.237 . \\ & 9 \end{aligned}$ | 3 |  |  | $\begin{aligned} & 37 . \\ & 9 \\ & \hline \end{aligned}$ | 3 15 <br> 0  | 3.2 | 27 <br> 9 |
|  |  | Place bo | $\begin{aligned} & \mathrm{Pl}(\mathrm{M} 1 \\ & \mathrm{r} \\ & \hline \end{aligned}$ |  | 00 | 0.00 | 0.0 16 <br> 1  |  | 00.0 |  | $0.0 \begin{aligned} & 16 . \\ & 1 \\ & \hline \end{aligned}$ | 0 | 0.0 | 0.0 1 <br>   <br> 1  | 16. 1 | 00.0 |  | $0.0 \begin{gathered} 16 . \\ 1 \\ \hline \end{gathered}$ | 0 | 0.0 | 0.0 1 <br>  1 | 16. | 00.0 | 0.0 | 16 |
|  |  |  | $\begin{aligned} & \text { PII(M } \\ & 2) \\ & \hline \end{aligned}$ | $\begin{aligned} & 2 \\ & 0 \end{aligned}$ | 00 | 0.00 | $\begin{gathered} 0.016 \\ \\ \hline \end{gathered}$ | 16. 0 | 00.0 |  | $0.0 \begin{aligned} & 16 . \\ & 8 \\ & \hline \end{aligned}$ | 0 | 0.0 | 0.0 <br>  | $16 .$ $8$ | 00.0 |  | $0.0 \begin{aligned} & 16 . \\ & 8 \\ & \hline \end{aligned}$ | 0 | 0.0 | 0.0 1 <br>   |  | 00.0 | 0.0 | 16 8 |
|  |  |  | $\mathrm{PlI}(\mathrm{M}$ <br> 6$)$ | 9 |  |  |  | $48.1$ | $\begin{array}{ll} 111 . \\ 1 \end{array}$ |  | $0.3 \begin{aligned} & 48 . \\ & 2 \\ & \hline \end{aligned}$ | 0 | 0.0 | 0.0 <br>  | 33.0 6 | 00.0 |  | $\begin{aligned} & 0.033 . \\ & 6 \end{aligned}$ | 0 | 0.0 | 0.0 <br>  | 33. 6 | 00.0 | 0.0 | 33 <br> 6 |
|  |  |  | $\begin{aligned} & \mathrm{PII}(\mathrm{M} \\ & 13) \end{aligned}$ |  |  | 0.00 |  | $20.0$ | 00.0 | 00. | $\begin{array}{ll} 0.0 & 20 . \\ 6 \end{array}$ | 0 | 0.0 | $0.02$ | $\begin{aligned} & 20 . \\ & 6 \end{aligned}$ | 00.0 |  | $\begin{array}{ll} 0.0 & 20 . \\ 6 \end{array}$ | 0 | 0.0 | $0.02$ | $\begin{aligned} & 20 . \\ & 6 \end{aligned}$ | 00.0 | 0.0 | O20 |


|  |  |  |  |  | $\geq 14$ fold |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | 95\% CI |  |
| Antibody | Sub-group | Group | Timing | N | n | \% | LL | UL |
| VZV.gE Ab.lgG | PreChemo | HZ/su | Pl(M1) | 78 | 60 | 76.9 | 66.0 | 85.7 |
|  |  |  | Pll(M2) | 75 | 51 | 168.0 | 56.2 | 78.3 |
|  |  |  | Pll(M6) 40 | 40 | 14 | 35.0 | 20.6 | 51.7 |
|  |  |  | Pll(M13) 62 | 62 | 10 | 16.1 | 8.0 | 27.7 |
|  |  | Placebo | Pl(M1) | 84 | 0 | 0.0 | 0.0 | 4.3 |
|  |  |  | PlI(M2) | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  |  |  | Pll(M6) | 46 | 1 | 2.2 | 0.1 | 11.5 |
|  |  |  | Pll(M13) 6 | 65 | 1 | 1.5 | 0.0 | 8.3 |
|  | OnChemo | HZ/su | Pl(M1) 23 | 23 | 10 | - 43.5 | 23.2 | 65.5 |
|  |  |  | PlI(M2) | 24 | 10 | ) 41.7 | 22.1 | 63.4 |
|  |  |  | Pll(M6) | 10 | 3 | 30.0 | 6.7 | 65.2 |
|  |  |  | Pll(M13) 2 | 20 | 2 | 10.0 | 1.2 | 31.7 |
|  |  | Placebo | Pl(M1) | 21 | 0 | 0.0 | 0.0 | 16.1 |
|  |  |  | Pll(M2) 20 | 20 | 0 | 0.0 | 0.0 | 16.8 |
|  |  |  | Pll(M6) 9 | 9 | 0 | 0.0 | 0.0 | 33.6 |
|  |  |  | PII(M13) 1 | 16 | 0 | 0.0 | 0.0 | 20.6 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration within the specified range
$95 \% \mathrm{CI}=95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Figure 7.21 Reverse cumulative curve for anti-gE antibody concentrations at Month 0 by PreChemo/OnChemo groups (Total Vaccinated Cohort)


PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.22 Reverse cumulative curve for anti-gE antibody concentrations at Month 1 by PreChemo/OnChemo groups (Total Vaccinated Cohort)


PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.23 Reverse cumulative curve for anti-gE antibody concentrations at Month 2 by PreChemo/OnChemo groups (Total Vaccinated Cohort)


PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.24 Reverse cumulative curve for anti-gE antibody concentrations at Month 6 by PreChemo/OnChemo groups (Total Vaccinated Cohort)


PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.25 Reverse cumulative curve for anti-gE antibody concentrations at Month 13 by PreChemo/OnChemo groups (Total Vaccinated Cohort)


PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

## Table 7.35 Seropositivity rates and geometric mean concentrations (GMCs) of

 anti-gE antibody at Month 0, 1, 2, 6 and 13 by age strata (Total Vaccinated Cohort)|  |  |  |  |  | $\geq 97 \mathrm{mlU} / \mathrm{ml}$ |  |  |  | GMC |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | 95\% | \% Cl |  | 95\% | \% CI |  |  |
| Antibody | Sub-group | Group | Timing | N | n | \% | LL | UL | value | LL | UL | Min | Max |
| VZV.gE Ab.lgG | 18-49ys | HZ/su | PRE | 31 | 31 | 1100 | 88.8 | 100 | 1023.4 | 753.6 | 1390.0 | 302.9 | 5936.7 |
|  |  |  | Pl(M1) | 31 | 31 | 100 | 88.8 | 100 | 25949.4 | 15765.3 | 42712.2 | 495.0 | 218252.5 |
|  |  |  | Pll(M2) | 31 | 31 | 1100 | 88.8 | 100 | 16806.0 | 11513.9 | 24530.4 | 1003.8 | 69429.6 |
|  |  |  | Pll(M6) | 20 | 20 | 0100 | 83.2 | 100 | 6503.5 | 4125.7 | 10251.5 | 599.2 | 38957.3 |
|  |  |  | PII(M13) | 28 | 28 | 8100 | 87.7 | 100 | 3756.3 | 2577.6 | 5474.1 | 494.5 | 26634.9 |
|  |  | Placebo | PRE | 29 | 29 | 100 | 88.1 | 100 | 1097.2 | 827.9 | 1454.0 | 245.9 | 3801.1 |
|  |  |  | Pl(M1) | 29 | 29 | 100 | 88.1 | 100 | 1082.3 | 818.8 | 1430.5 | 242.5 | 4808.0 |
|  |  |  | PlI(M2) | 30 | 30 | 100 | 88.4 | 100 | 994.0 | 757.7 | 1304.1 | 230.8 | 3693.4 |
|  |  |  | PII(M6) | 16 | 16 | 6100 | 79.4 | 100 | 1077.9 | 759.3 | 1530.2 | 321.5 | 2818.1 |
|  |  |  | PII(M13) 2 | 24 | 24 | 100 | 85.8 | 100 | 835.1 | 609.2 | 1144.8 | 182.8 | 2333.5 |
|  | $\geq 50 y s$ | HZ/su | PRE | 86 | 85 | 98.8 | 93.7 | 100 | 1138.0 | 926.7 | 1397.6 | <97.0 | 6659.6 |
|  |  |  | Pl(M1) | 70 | 70 | 100 | 94.9 | 100 | 26197.1 | 19716.8 | 34807.2 | 383.2 | 209816.0 |
|  |  |  | PII(M2) | 68 | 68 | 100 | 94.7 | 100 | 19279.4 | 14645.9 | 25378.7 | 200.3 | 90761.1 |
|  |  |  | Pll(M6) | 30 | 30 | 100 | 88.4 | 100 | 10287.2 | 6467.4 | 16362.8 | 154.6 | 68989.4 |
|  |  |  | PlI(M13) | 54 | 54 | 4100 | 93.4 | 100 | 5076.0 | 3743.0 | 6883.7 | 234.5 | 29519.1 |
|  |  | Placebo | PRE | 82 | 81 | 198.8 | 93.4 | 100 | 1205.2 | 939.1 | 1546.5 | <97.0 | 25991.9 |
|  |  |  | Pl(M1) | 80 | 79 | 988.8 | 93.2 | 100 | 1188.3 | 952.4 | 1482.6 | <97.0 | 18838.0 |
|  |  |  | PlI(M2) | 74 | 73 | 398.6 | 92.7 | 100 | 1113.4 | 877.3 | 1413.0 | <97.0 | 25756.1 |
|  |  |  | PlI(M6) | 41 | 40 | 97.6 | 87.1 | 99.9 | 1285.1 | 928.0 | 1779.6 | <97.0 | 20172.3 |
|  |  |  | PlI(M13) | 58 | 58 | 8100 | 93.8 | 100 | 1206.4 | 930.9 | 1563.5 | 135.8 | 20722.2 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
GMC = geometric mean antibody concentration calculated on all subjects
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration equal to or above specified value
$95 \% \mathrm{Cl}=95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.36 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata (Total Vaccinated Cohort)

|  |  |  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | 95\% CI |  |
| Test description | Sub-group | Group | Timing | N | n | \% | LL | UL |
| VZV.gE Ab.lgG | 18-49ys | HZ/su | Pl(M1) | 31 | 27 | 87.1 | 70.2 | 96.4 |
|  |  |  | Pll(M2) | 31 | 27 | 87.1 | 70.2 | 96.4 |
|  |  |  | PII(M6) | 20 | 14 | 70.0 | 45.7 | 88.1 |
|  |  |  | PlI(M13) | 28 | 13 | 46.4 | 27.5 | 66.1 |
|  |  | Placebo | Pl(M1) | 28 | 0 | 0.0 | 0.0 | 12.3 |
|  |  |  | PlI(M2) | 29 | 0 | 0.0 | 0.0 | 11.9 |
|  |  |  | Pll(M6) | 15 | 1 | 6.7 | 0.2 | 31.9 |
|  |  |  | PII(M13) | 23 | 0 | 0.0 | 0.0 | 14.8 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 70 | 62 | 88.6 | 78.7 | 94.9 |
|  |  |  | PII(M2) | 68 | 59 | 86.8 | 76.4 | 93.8 |
|  |  |  | Pll(M6) | 30 | 23 | 76.7 | 57.7 | 90.1 |
|  |  |  | PlI(M13) | 54 | 29 | 53.7 | 39.6 | 67.4 |
|  |  | Placebo | Pl(M1) | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  |  |  | PlI(M2) | 71 | 0 | 0.0 | 0.0 | 5.1 |
|  |  |  | PlI(M6) | 40 | 1 | 2.5 | 0.1 | 13.2 |
|  |  |  | Pll(M13) | 58 | 1 | 1.7 | 0.0 | 9.2 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination $\geq 4$ fold the cut-off for Anti-gE ( $4 \times 97$ $\mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at post-vaccination $\geq 4$ fold the pre-vaccination antibody concentration
$\mathrm{N}=$ Number of subjects with pre- and post-vaccination results available $\mathrm{n} / \%=$ Number/percentage of responders
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.37 Mean Geometric Increase (MGI) of anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata (Total Vaccinated Cohort)

|  |  |  |  |  |  |  | MGI |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |  |  | 95\% CI |  |
| Sub-group | Group | N | Time point description | GMC | Time point description | GMC | Ratio order | Value | LL | UL |
| 18-49ys | HZ/su | 31 | Pl(M1) | 25949.4 | PRE | 1023.4 | PI(M1) / PRE | 25.4 | 15.4 | 41.8 |
|  |  | 31 | PlI(M2) | 16806.0 | PRE | 1023.4 | PlI(M2) / PRE | 16.4 | 10.9 | 24.7 |
|  |  | 20 | PII(M6) | 6503.5 | PRE | 950.4 | PII(M6) / PRE | 6.8 | 4.6 | 10.1 |
|  |  | 28 | PII(M13) | 3756.3 | PRE | 1056.8 | PII(M13) / PRE | 3.6 | 2.6 | 4.9 |
|  | Placebo | 28 | Pl(M1) | 1080.5 | PRE | 1091.2 | PI(M1) / PRE | 1.0 | 0.9 | 1.0 |
|  |  | 29 | PII(M2) | 992.2 | PRE | 1097.2 | PII(M2) / PRE | 0.9 | 0.8 | 1.0 |
|  |  | 15 | PII(M6) | 1081.2 | PRE | 1212.9 | PII(M6) / PRE | 0.9 | 0.7 | 1.2 |
|  |  | 23 | PII(M13) | 872.4 | PRE | 1014.3 | PII(M13) / PRE | 0.9 | 0.7 | 1.0 |
| $\geq 50 y s$ | HZ/su | 70 | Pl(M1) | 26197.1 | PRE | 1067.1 | PI(M1) / PRE | 24.6 | 17.6 | 34.2 |
|  |  | 68 | PII(M2) | 19279.4 | PRE | 1128.9 | PII(M2) / PRE | 17.1 | 12.4 | 23.6 |
|  |  | 30 | PII(M6) | 10287.2 | PRE | 971.8 | PII(M6) / PRE | 10.6 | 6.3 | 17.6 |
|  |  | 54 | Pl(M13) | 5076.0 | PRE | 1061.0 | PII(M13) / PRE | 4.8 | 3.5 | 6.6 |
|  | Placebo | 77 | Pl(M1) | 1205.1 | PRE | 1203.8 | PI(M1) / PRE | 1.0 | 1.0 | 1.0 |
|  |  | 71 | PII(M2) | 1118.9 | PRE | 1158.7 | PII(M2) / PRE | 1.0 | 0.9 | 1.0 |
|  |  | 40 | PlI(M6) | 1320.2 | PRE | 1300.0 | PlI(M6) / PRE | 1.0 | 0.8 | 1.2 |
|  |  | 58 | Pl(M13) | 1206.4 | PRE | 1234.3 | PII(M13) / PRE | 1.0 | 0.9 | 1.1 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group
$\mathrm{N}=$ Number of subjects with available results at the two considered time points
MGI = Geometric mean of the within subject ratios of the post-vaccination reciprocal anti-gE concentration to the Month 0 reciprocal anti-gE concentration
$95 \%$ CI $=95 \%$ confidence interval, LL $=$ Lower Limit, UL = Upper Limit
PRE = Pre-vaccination (Month 0)
$\mathrm{Pl}(\mathrm{M} 1)=$ Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.38 Descriptive statistics of the fold increase for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata (Total Vaccinated Cohort)

| Antibody | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| VZV.gE Ab.IgG | 18-49ys | HZ/su | Pl(M1) | 31 | 0 | 52.28 | 72.94 | 1.4 | 12.0 | 31.1 | 64.5 | 346.0 |
|  |  |  | PII(M2) | 31 | 0 | 26.69 | 24.06 | 1.3 | 7.7 | 17.9 | 42.7 | 96.3 |
|  |  |  | Pll(M6) | 20 | 0 | 9.03 | 6.25 | 1.1 | 3.9 | 8.1 | 12.6 | 21.9 |
|  |  |  | PII(M13) | 28 | 0 | 4.87 | 3.85 | 0.8 | 2.0 | 3.6 | 7.7 | 15.7 |
|  |  | Placebo | Pl(M1) | 28 | 1 | 1.00 | 0.14 | 0.8 | 0.9 | 1.0 | 1.1 | 1.4 |
|  |  |  | PII(M2) | 29 | 1 | 0.92 | 0.17 | 0.5 | 0.8 | 0.9 | 1.0 | 1.2 |
|  |  |  | PII(M6) | 15 | 1 | 1.04 | 0.87 | 0.6 | 0.7 | 0.9 | 0.9 | 4.1 |
|  |  |  | PlI(M13) | 23 | 1 | 0.91 | 0.40 | 0.6 | 0.7 | 0.8 | 0.9 | 2.3 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 70 | 0 | 60.49 | 100.08 | 1.0 | 10.9 | 25.8 | 54.1 | 508.5 |
|  |  |  | PII(M2) | 68 | 0 | 35.78 | 50.29 | 0.5 | 6.5 | 20.8 | 43.3 | 286.2 |
|  |  |  | Pll(M6) | 30 | 0 | 22.19 | 26.15 | 0.4 | 4.1 | 11.9 | 30.5 | 95.6 |
|  |  |  | PlI(M13) | 54 | 0 | 9.59 | 13.86 | 0.5 | 2.1 | 4.5 | 10.4 | 77.5 |
|  |  | Placebo | Pl(M1) | 77 | 3 | 1.02 | 0.22 | 0.6 | 0.9 | 1.0 | 1.1 | 2.1 |
|  |  |  | PII(M2) | 71 | 3 | 1.01 | 0.29 | 0.5 | 0.8 | 1.0 | 1.2 | 1.8 |
|  |  |  | PII(M6) | 40 | 1 | 1.56 | 3.46 | 0.5 | 0.8 | 0.9 | 1.0 | 22.7 |
|  |  |  | PII(M13) | 58 | 0 | 1.27 | 2.23 | 0.4 | 0.8 | 0.9 | 1.1 | 17.7 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1, Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.39

## Distribution of fold increase from baseline for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata (Total Vaccinated Cohort)

|  |  |  |  | $\geq 2$ fold |  |  |  |  | $\geq 4$ fold |  |  |  | $\geq 6$ fold |  |  |  |  | $\geq 8$ fold |  |  | $\geq 10$ fold |  |  |  | $\geq 12$ fold |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{CI} \end{gathered}$ |  |
| Antibo dy | Sub gro up | $\begin{aligned} & \text { Grou } \\ & \text { p } \end{aligned}$ | Timin g |  | n $\%$ | \% L | LL U | UL n |  | \% | LL U | UL | n | \% | LL | UL | n | \% | LL U | UL | n | \% | LL | UL | n | \% | LL | UL |
| $\begin{array}{\|l\|} \hline \text { VZV.g } \\ \mathrm{E} \\ \text { Ab.lgG } \end{array}$ | $\begin{aligned} & 18- \\ & 49 \mathrm{ys} \end{aligned}$ | HZ/su | $\begin{aligned} & \mathrm{Pl}(\mathrm{M} 1 \\ & ) \end{aligned}$ |  | 2 90 <br> 8 3 |  | 74. 98 <br> 2 0 | 98.  <br> 0 7 | 2 8 <br> 7 1 | 87.  <br> 1  | $\begin{array}{l\|l} 70 . & 0 \\ 2 & 4 \end{array}$ | $96 .$ | 2 | 83. 9 |  | $\begin{aligned} & 94 . \\ & 5 \end{aligned}$ | 2 | 83. 9 | 66. 3 3 | 94. | 2 | 77. 4 | 58. 9 | 40. | 2 | 74. | 45. | $88 .$ $1$ |
|  |  |  | PII(M <br> 2$)$ <br> ) | 3 3 <br> 1 0 | 3 96 <br> 0 8 |  | 83. 3 3 | 99.  <br> 9 7 | 2 8 <br> 7 1 | $87 .$ $1$ | $\begin{aligned} & 70.9 \\ & 2 \\ & 2 \end{aligned}$ | $\begin{aligned} & 96 . \\ & 4 \\ & \hline \end{aligned}$ | 2 | 80. 6 | $\begin{aligned} & 62 . \\ & 5 \end{aligned}$ | $\begin{aligned} & 92 . \\ & 5 \\ & \hline \end{aligned}$ |  | $\begin{aligned} & 74 . \\ & 2 \\ & \hline \end{aligned}$ | $\begin{array}{l\|l} 55 . & 8 \\ 4 & 1 \\ \hline \end{array}$ | 188. |  | $\begin{aligned} & 67 . \\ & 7 \\ & \hline \end{aligned}$ | $\begin{aligned} & 48 . \\ & 6 \\ & \hline \end{aligned}$ | 83. 3 | 2 | 64. 5 | 45. | $\begin{aligned} & 80 . \\ & 8 \end{aligned}$ |
|  |  |  | PII(M <br> 6) | $\begin{array}{l\|l} 2 & 1 \\ 0 & 8 \end{array}$ | $\begin{array}{ll} 1 & 90 \\ 8 & 0 \\ \hline \end{array}$ |  | $\begin{array}{l\|l\|l\|} \hline 68 & 98 \\ 3 & 8 \\ \hline \end{array}$ | $\begin{aligned} & 98 . \\ & 8 \\ & \hline \end{aligned}$ |  | $70 .$ | $\begin{array}{l\|l} \hline 45 . & 8 \\ 7 & 1 \end{array}$ | $88 .$ $1$ |  | $\begin{aligned} & 60 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 36 . \\ & 1 \end{aligned}$ | $\begin{aligned} & 80 . \\ & 9 \\ & \hline \end{aligned}$ |  | $\begin{aligned} & 50 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 27.7 \\ & 2 \\ & \hline \end{aligned}$ | $72 .$ <br> 8 |  | $\begin{aligned} & 35 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 15 . \\ & 4 \end{aligned}$ | $\begin{aligned} & 59 . \\ & 2 \end{aligned}$ | 7 |  |  | $\begin{aligned} & 59 . \\ & 2 \end{aligned}$ |
|  |  |  | $\begin{aligned} & \text { PII(M } \\ & 13) \\ & \hline \end{aligned}$ | $\begin{array}{ll} 2 & 2 \\ 8 & 1 \end{array}$ | $\begin{array}{ll} 2 & 75 \\ 1 & 0 \\ \hline \end{array}$ |  |  | $\begin{aligned} & 89 . \\ & 3 \end{aligned}$ |  | $46 .$ $4$ | $\begin{array}{l\|l} 27 . & 6 \\ 5 & 1 \\ \hline \end{array}$ | $\begin{aligned} & 66 . \\ & 1 \end{aligned}$ | 9 | $\begin{aligned} & 32 . \\ & 1 \\ & \hline \end{aligned}$ | $\begin{aligned} & 15 \\ & 9 \end{aligned}$ | $\begin{aligned} & 52 . \\ & 4 \end{aligned}$ |  | $\begin{aligned} & 17 . \\ & 9 \end{aligned}$ |  |  |  | $\begin{aligned} & 10 . \\ & 7 \end{aligned}$ | 2.3 | $\begin{aligned} & 28 . \\ & 2 \\ & \hline \end{aligned}$ | 2 | 7.1 | 0.9 | $\begin{aligned} & 23 . \\ & 5 \end{aligned}$ |
|  |  | Place bo | $\begin{aligned} & \mathrm{Pl}(\mathrm{M} 1 \\ & \mathrm{l} \\ & \hline \end{aligned}$ | $\begin{array}{l\|l} 2 & 0 \\ 8 & 0 \\ \hline \end{array}$ |  | 0.00 | 0.0 |  |  | 0.00 | $\begin{array}{r} 0.01 \\ \\ \hline \end{array}$ | $\begin{aligned} & 12 . \\ & 3 \\ & \hline \end{aligned}$ | 0 | 0.0 | 0.0 1 <br>   <br> 3  | $\begin{aligned} & 12 . \\ & 3 \\ & \hline \end{aligned}$ | 0 | 0.0 |  |  | 0 | 0.0 | 0.0 | $\begin{aligned} & 12 . \\ & 3 \end{aligned}$ | 0 | 0.0 | 0.0 | $\begin{aligned} & 12 . \\ & 3 \end{aligned}$ |
|  |  |  | PII(M <br> 2) | $\begin{array}{l\|l} 2 & 0 \\ 9 \end{array}$ |  |  | $\begin{array}{r}0.0 \\ \hline\end{array}$ | $11 .$ $9$ |  | 0.0 | $\begin{array}{r} \left.0.0 \begin{array}{l} 1 \\ 9 \end{array}\right) \end{array}$ | $\begin{aligned} & 11 . \\ & 9 \\ & \hline \end{aligned}$ | 0 | 0.0 | 0.0 11 <br>   <br> 9  | $\begin{aligned} & 11 . \\ & 9 \end{aligned}$ | 0 | 0.0 | 0.0 1 <br>   <br> 9  | $11 .$ | 0 | 0.0 | 0.0 | $11 .$ $9$ | 0 | 0.0 | 0.0 | $11$ $9$ |
|  |  |  | PII(M <br> 6) | $\begin{array}{ll} 1 & 1 \\ 5 & \\ \hline \end{array}$ |  | 6.70 | $0.2 \begin{array}{r}3 \\ 9\end{array}$ |  |  | 6.70 | $\begin{array}{r} 0.23 \\ 9 \\ \hline \end{array}$ | $\begin{aligned} & 31 . \\ & 9 \end{aligned}$ | 0 | 0.0 | 0.0  <br> 8  <br> 8  | $\begin{aligned} & 21 . \\ & 8 \\ & \hline \end{aligned}$ | 0 | 0.0 |  | $21 .$ $8$ | 0 | 0.0 | 0.0 | $\begin{aligned} & 21 . \\ & 8 \\ & \hline \end{aligned}$ | 0 | 0.0 | 0.0 | $\begin{aligned} & 21 . \\ & 8 \end{aligned}$ |
|  |  |  | $\begin{aligned} & \hline \mathrm{PI}(\mathrm{M} \\ & 13) \\ & \hline \end{aligned}$ | $\begin{array}{l\|l\|} 2 \\ 3 \end{array}$ | 28. | 8.71 | $\begin{array}{ll} 1.1 & 28 \\ & 0 \\ \hline \end{array}$ | $\begin{aligned} & 28 . \\ & 0 \end{aligned}$ | 0 | 0.0 | $\begin{array}{r} 0.0 \\ \hline \end{array}$ | $\begin{aligned} & 14 . \\ & 8 \\ & \hline \end{aligned}$ | 0 | 0.0 | 0.0 1 <br>  8 |  | 0 | 0.0 |  | $\begin{aligned} & 14 . \\ & 8 \end{aligned}$ | 0 | 0.0 | 0.0 | $14 .$ $8$ | 0 | 0.0 | 0.0 | $\begin{aligned} & 14 . \\ & 8 \end{aligned}$ |
|  | $\begin{aligned} & \geq \\ & 50 \mathrm{ys} \end{aligned}$ | HZ/su P | $\begin{aligned} & \mathrm{PI}(\mathrm{M} 1 \\ & \hline \end{aligned}$ |  | $\begin{array}{ll} 6 & 95 \\ 7 & 7 \\ \hline \end{array}$ |  | 88. 9 <br> 0 1 | 99.  <br> 1 2 | $\begin{array}{l\|l} \hline 6 & 8 \\ 2 & 6 \\ \hline \end{array}$ | $\begin{aligned} & 88 . \\ & 6 \end{aligned}$ | $\begin{array}{ll} \text { 78. } \\ 7 & 9 \\ 7 \end{array}$ | $\begin{aligned} & 94 . \\ & 9 \end{aligned}$ | 6 | 85. <br> 7 | 75.  <br> 3 9 | 92. 9 |  | 82. <br> 9 |  | 90.5 8 |  | 77. <br> 1 | 65. 6 | 86 3 | 5 | 71. 4 | 59. | 81. |
|  |  |  | $\begin{aligned} & \text { PlI(M } \\ & 2) \\ & \hline \end{aligned}$ | $\begin{array}{l\|l} 6 & 6 \\ 8 & 3 \\ \hline \end{array}$ | 6 92 <br> 3 6 |  | 83. 9 <br> 7 6 |  | $\begin{array}{lll} 5 & 8 \\ 9 & 8 \\ \hline \end{array}$ | $86 .$ | $\begin{array}{l\|l} 76 . & 0 \\ 4 & 8 \\ \hline \end{array}$ | $\begin{aligned} & 93 . \\ & 8 . \end{aligned}$ | 5 <br> 2 <br>  | $\begin{aligned} & 76 . \\ & 5 \end{aligned}$ |  |  |  |  |  |  |  |  |  |  |  |  |  | 75. <br> 9 |
|  |  |  | PII(M <br> 6) | $\begin{array}{l\|l} 3 & 2 \\ 0 & 7 \\ \hline \end{array}$ | $\begin{array}{ll} 2 & 90 \\ 7 & 0 \\ \hline \end{array}$ | 90. <br> 0 <br> 0 | 73. 9 <br> 5 9 | $\begin{aligned} & 97.2 \\ & 9 \\ & 9 \end{aligned}$ | $\begin{array}{l\|l} 2 & 7 \\ 3 & 7 \end{array}$ | $76 \text {. }$ | $\begin{aligned} & \text { 57. } \\ & 7 \\ & 7 \end{aligned}$ | $90 .$ | 2 | $\begin{aligned} & 66 . \\ & 7 \end{aligned}$ |  |  |  | $\begin{aligned} & 60 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 40 . \\ & 6 \\ & 6 \end{aligned}$ |  |  | $\begin{aligned} & 53 . \\ & 3 \end{aligned}$ |  | 71. | 1 | 50. 0 | 31. 3 | 68. 7 |
|  |  |  | $\begin{aligned} & \text { PII(M } \\ & 13) \end{aligned}$ | $\begin{array}{lll} 5 & 4 \\ 4 & 1 \end{array}$ | $\begin{array}{ll} 4 & 75 \\ 1 & 9 \end{array}$ | 75. 9 9 | $\begin{array}{ll} 62 . & 8 \\ 4 & 5 \end{array}$ | $\begin{aligned} & 86 . \\ & 5 \end{aligned}$ | $\begin{array}{l\|l} 2 & 5 \\ 9 & 7 \\ \hline \end{array}$ | $53 .$ | $\begin{array}{ll} 39 . & 6 \\ 6 & 4 \end{array}$ | $\begin{aligned} & 67 . \\ & 4 \end{aligned}$ | 2 | $\begin{aligned} & 37 . \\ & 0 \end{aligned}$ | $\begin{aligned} & 24 . \\ & 3 \end{aligned}$ |  | 1 |  |  |  |  | $\begin{aligned} & 27 . \\ & 8 \\ & \hline \end{aligned}$ |  |  | 1 | 124. | 13. 5 | 37. <br> 6 |
|  |  | Place bo | $\begin{aligned} & \mathrm{Pl}(\mathrm{M} 1 \\ & ) \end{aligned}$ | $\begin{array}{ll} \hline 7 \\ 7 \end{array}$ |  | 1.30 | 0.07 | 7.00 | 0 | 0.00 | 0.04 | 4.70 | 0 | 0.0 | 0.04 | 4.70 | 0 | 0.0 | 0.04 | 4.70 | 0 | 0.0 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 4.7 |
|  |  |  | PII(M <br> 2) | $\begin{array}{ll} 7 \\ 1 & 0 \end{array}$ | 00. | 0.0 | 0.05 | 5.10 | 0 | 0.0 | 0.05 | 5.10 | 0 | 0.0 | 0.05 | 5.10 | 0 | 0.0 | 0.05 | 5.1 | 0 | 0.0 | 0.0 | 5.1 | 0 | 0.0 | 0.0 | 5.1 |
|  |  |  | $\begin{aligned} & \text { Pll(M } \\ & 6) \\ & \hline \end{aligned}$ | $\begin{array}{l\|l} 4 \\ 0 \end{array}$ | 25. | 5.0 | 0.616 <br> 9 |  | 12 | 2.50 | $\begin{array}{r\|r\|} 0.1 \\ & 1 \\ & 2 \end{array}$ | $\begin{aligned} & 13 . \\ & 2 \\ & \hline \end{aligned}$ | 1 | 2.5 | $0.1 \begin{aligned} & 1 \\ & \\ & \\ & 2\end{aligned}$ | $\begin{aligned} & 13 . \\ & 2 \\ & \hline \end{aligned}$ | 1 | 2.5 |  |  | 1 | 2.5 | 0.1 | $\begin{aligned} & 13 . \\ & 2 \\ & \hline \end{aligned}$ | 1 | 2.5 | 0.1 | $\begin{aligned} & 13 . \\ & 2 \end{aligned}$ |
|  |  |  | $\begin{aligned} & \mathrm{PlI}(\mathrm{M} \\ & 13) \end{aligned}$ | $\begin{array}{l\|l\|} \hline 5 & 3 \\ 8 & \\ \hline \end{array}$ | 35. | 5.21 | $1.1 \begin{aligned} & 1 \\ & \\ & 4 \end{aligned}$ | $\begin{aligned} & 14 . \\ & 4 \end{aligned}$ |  | 1.70 | 0.09 | 9.2 | 1 | 1.7 | 0.0 | 9.2 | 1 | 1.7 | 0.09 | 9.2 | 1 | 1.7 | 0.0 | 9.2 | 1 | 1.7 | 0.0 | 9.2 |


|  |  |  |  |  | $\geq 14$ fold |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | 95\% CI |  |
| Antibody | Sub-group | Group | Timing | N | n | \% | LL | UL |
| VZV.gE Ab.IgG | 18-49ys | HZ/su | Pl(M1) | 31 | 23 | 74.2 | 55.4 | 88.1 |
|  |  |  | PlI(M2) | 31 | 19 | 61.3 | 42.2 | 78.2 |
|  |  |  | PII(M6) | 20 | 4 | 20.0 | 5.7 | 43.7 |
|  |  |  | PII(M13) | 28 | 1 | 3.6 | 0.1 | 18.3 |
|  |  | Placebo | Pl(M1) | 28 | 0 | 0.0 | 0.0 | 12.3 |
|  |  |  | PII(M2) | 29 | 0 | 0.0 | 0.0 | 11.9 |
|  |  |  | PII(M6) | 15 | 0 | 0.0 | 0.0 | 21.8 |
|  |  |  | PII(M13) | 23 | 0 | 0.0 | 0.0 | 14.8 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 70 | 47 | 67.1 | 54.9 | 77.9 |
|  |  |  | PlI(M2) | 68 | 42 | 61.8 | 49.2 | 73.3 |
|  |  |  | PII(M6) | 30 | 13 | 43.3 | 25.5 | 62.6 |
|  |  |  | PII(M13) | 54 | 11 | 20.4 | 10.6 | 33.5 |
|  |  | Placebo | Pl(M1) | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  |  |  | PlI(M2) | 71 | 0 | 0.0 | 0.0 | 5.1 |
|  |  |  | PII(M6) | 40 | 1 | 2.5 | 0.1 | 13.2 |
|  |  |  | PII(M13) | 58 |  | 1.7 | 0.0 | 9.2 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration within the specified range
95\% CI = 95\% confidence interval; LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Figure 7.26 Reverse cumulative curve for anti-gE antibody concentrations at Month 0 by age strata (Total Vaccinated Cohort)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.27 Reverse cumulative curve for anti-gE antibody concentrations at Month 1 by age strata (Total Vaccinated Cohort)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.28 Reverse cumulative curve for anti-gE antibody concentrations at Month 2 by age strata (Total Vaccinated Cohort)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.29 Reverse cumulative curve for anti-gE antibody concentrations at Month 6 by age strata (Total Vaccinated Cohort)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Figure 7.30 Reverse cumulative curve for anti-gE antibody concentrations at Month 13 by age strata (Total Vaccinated Cohort)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Table 7.40 Seropositivity rates and geometric mean concentrations (GMCs) of anti-gE antibody at Month 0,1,2, 6 and 13 by age strata in PreChemo Groups only (Total Vaccinated Cohort)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
GMC = geometric mean antibody concentration calculated on all subjects
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%=$ number/percentage of subjects with concentration equal to or above specified value
$95 \% \mathrm{Cl}=95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.41 Vaccine response rates for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata in PreChemo Groups only (Total Vaccinated Cohort)

|  |  |  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | 95\% CI |  |
| Test description | Sub-group | Group | Timing | N | n | \% | LL | UL |
| VZV.gE Ab.lgG | 18-49ys | HZ/su | Pl(M1) | 23 | 23 | 100 | 85.2 | 100 |
|  |  |  | PlI(M2) | 23 | 22 | 95.7 | 78.1 | 99.9 |
|  |  |  | Pll(M6) | 16 | 12 | 75.0 | 47.6 | 92.7 |
|  |  |  | PlI(M13) | 21 | 11 | 52.4 | 29.8 | 74.3 |
|  |  | Placebo | Pl(M1) | 21 | 0 | 0.0 | 0.0 | 16.1 |
|  |  |  | PII(M2) | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  |  |  | PlI(M6) | 11 | 0 | 0.0 | 0.0 | 28.5 |
|  |  |  | PlI(M13) | 17 | 0 | 0.0 | 0.0 | 19.5 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 55 | 51 | 92.7 | 82.4 | 98.0 |
|  |  |  | PII(M2) | 52 | 48 | 92.3 | 81.5 | 97.9 |
|  |  |  | Pll(M6) | 24 | 18 | 75.0 | 53.3 | 90.2 |
|  |  |  | PlI(M13) | 41 | 23 | 56.1 | 39.7 | 71.5 |
|  |  | Placebo | Pl(M1) | 63 | - | 0.0 | 0.0 | 5.7 |
|  |  |  | PlI(M2) | 58 | - | 0.0 | 0.0 | 6.2 |
|  |  |  | PlI(M6) | 35 | 1 | 2.9 | 0.1 | 14.9 |
|  |  |  | PlI(M13) | 48 | 1 | 2.1 | 0.1 | 11.1 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination $\geq 4$ fold the cut-off for Anti-gE (4x97 $\mathrm{mlU} / \mathrm{ml}$ )
For initially seropositive subjects, antibody concentration at post-vaccination $\geq 4$ fold the pre-vaccination antibody concentration
$N=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
95\% CI $=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.42 Mean Geometric Increase (MGI) of anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata in PreChemo Groups only (Total Vaccinated Cohort)

|  |  |  |  |  |  |  | MGI |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |  |  | 95\% CI |  |
| Sub-group | Group | N | Time point description | GMC | Time point description | GMC | Ratio order | Value | LL | UL |
| 18-49ys | HZ/su | 23 | PI(M1) | 41028.1 | PRE | 981.0 | Pl(M1) / PRE | 41.8 | 27.9 | 62.6 |
|  |  | 23 | PII(M2) | 21827.6 | PRE | 981.0 | PII(M2) / PRE | 22.3 | 15.1 | 32.8 |
|  |  | 16 | PII(M6) | 7025.5 | PRE | 879.0 | PII(M6) / PRE | 8.0 | 5.5 | 11.6 |
|  |  | 21 | Pl(M13) | 4316.8 | PRE | 1015.7 | PII(M13) / PRE | 4.3 | 3.0 | 6.1 |
|  | Placebo | 21 | Pl(M1) | 1039.5 | PRE | 1080.4 | PI(M1) / PRE | 1.0 | 0.9 | 1.0 |
|  |  | 22 | PII(M2) | 970.9 | PRE | 1088.7 | PII(M2) / PRE | 0.9 | 0.8 | 1.0 |
|  |  | 11 | PII(M6) | 929.0 | PRE | 1151.3 | PII(M6) / PRE | 0.8 | 0.7 | 0.9 |
|  |  | 17 | PlI(M13) | 925.8 | PRE | 1038.5 | PII(M13) / PRE | 0.9 | 0.7 | 1.1 |
| $\geq 50 y s$ | HZ/su | 55 | Pl(M1) | 32357.1 | PRE | 1060.7 | PI(M1) / PRE | 30.5 | 21.6 | 43.0 |
|  |  | 52 | PII(M2) | 24096.3 | PRE | 1146.8 | PII(M2) / PRE | 21.0 | 15.4 | 28.7 |
|  |  | 24 | PII(M6) | 11623.4 | PRE | 1104.3 | PII(M6) / PRE | 10.5 | 6.2 | 17.7 |
|  |  | 41 | PII(M13) | 5388.4 | PRE | 1042.7 | PII(M13) / PRE | 5.2 | 3.6 | 7.4 |
|  | Placebo | 63 | Pl(M1) | 1296.3 | PRE | 1306.9 | PI(M1) / PRE | 1.0 | 0.9 | 1.0 |
|  |  | 58 | PII(M2) | 1214.2 | PRE | 1257.7 | PII(M2) / PRE | 1.0 | 0.9 | 1.0 |
|  |  | 35 | Pll(M6) | 1246.4 | PRE | 1237.4 | PlI(M6) / PRE | 1.0 | 0.8 | 1.3 |
|  |  | 48 | Pl(M13) | 1334.0 | PRE | 1369.8 | PII(M13) / PRE | 1.0 | 0.8 | 1.1 |

18-49ys $=$ Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ Number of subjects with available results at the two considered time points
$\mathrm{MGI}=$ Geometric mean of the within subject ratios of the post-vaccination reciprocal anti-gE concentration to the Month 0 reciprocal anti-gE concentration
$95 \% \mathrm{CI}=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.43 Descriptive statistics of the fold increase for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata in PreChemo Groups only (Total Vaccinated Cohort)

| Antibody | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| VZV.gE Ab.lgG | 18-49ys | HZ/su | Pl(M1) | 23 | 0 | 65.80 | 80.21 | 8.2 | 25.4 | 40.3 | 75.6 | 346.0 |
|  |  |  | PlI(M2) | 23 | 0 | 30.94 | 23.84 | 2.6 | 10.4 | 24.8 | 45.2 | 96.3 |
|  |  |  | Pll(M6) | 16 | 0 | 9.87 | 6.30 | 2.7 | 4.0 | 8.8 | 14.4 | 21.9 |
|  |  |  | PII(M13) | 21 | 0 | 5.58 | 4.01 | 0.8 | 2.3 | 4.0 | 7.9 | 15.7 |
|  |  | Placebo | Pl(M1) | 21 | 1 | 0.97 | 0.13 | 0.8 | 0.9 | 0.9 | 1.0 | 1.4 |
|  |  |  | PII(M2) | 22 | 1 | 0.91 | 0.17 | 0.5 | 0.8 | 0.9 | 1.0 | 1.2 |
|  |  |  | Pll(M6) | 11 | 1 | 0.83 | 0.19 | 0.6 | 0.7 | 0.8 | 0.9 | 1.2 |
|  |  |  | PII(M13) | 17 | 1 | 0.96 | 0.46 | 0.6 | 0.7 | 0.8 | 0.9 | 2.3 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 55 | 0 | 68.11 | 108.19 | 2.7 | 11.1 | 31.3 | 81.3 | 508.5 |
|  |  |  | PII(M2) | 52 | 0 | 37.96 | 52.57 | 1.6 | 10.2 | 22.4 | 44.8 | 286.2 |
|  |  |  | Pll(M6) | 24 | 0 | 20.58 | 25.66 | 1.2 | 3.9 | 11.9 | 29.6 | 95.6 |
|  |  |  | PII(M13) | 41 | 0 | 10.18 | 14.92 | 0.9 | 2.3 | 4.9 | 10.4 | 77.5 |
|  |  | Placebo | Pl(M1) | 63 | 1 | 1.01 | 0.23 | 0.6 | 0.9 | 1.0 | 1.1 | 2.1 |
|  |  |  | PII(M2) | 58 | 1 | 1.01 | 0.30 | 0.5 | 0.8 | 1.0 | 1.2 | 1.8 |
|  |  |  | Pll(M6) | 35 | 0 | 1.62 | 3.70 | 0.5 | 0.7 | 0.9 | 1.0 | 22.7 |
|  |  |  | PII(M13) | 48 | 0 | 1.32 | 2.45 | 0.4 | 0.8 | 0.9 | 1.2 | 17.7 |

[^8]Table 7.44 Distribution of fold increase from baseline for anti-gE antibody ELISA concentrations at Month 1, 2, 6 and 13 by age strata in PreChemo Groups only (Total Vaccinated Cohort)


ebo 1) $1 \begin{array}{lllllllllllllllllllllllll} & 0 & 0 & .1 & 0 & 0 & .1 & 0 & 0 & .1 & 0 & 0 & .1 & 0 & 0 & .1 & 0 & 0 & .1 & 0 & 0 & .1\end{array}$

2) $2 \begin{array}{lllllllllllllllllllllllll} & 0 & 0 & .4 & 0 & 0 & .4 & 0 & 0 & .4 & 0 & 0 & .4 & 0 & 0 & .4 & 0 & 0 & .4 & 0 & 0 & .4\end{array}$

6) $1 \begin{array}{lllllllllllllllllllllll} & 0 & 0 & .5 & 0 & 0 & .5 & 0 & 0 & .5 & 0 & 0 & .5 & 0 & 0 & .5 & 0 & 0 & .5 & 0 & 0 & .5\end{array}$


| 13) | 7 | .8 | 5 | .4 | 0 | 0 | .5 | 0 | 0 | .5 | 0 | 0 | .5 | 0 | 0 | .5 | 0 | 0 | .5 | 0 | 0 | .5 |  |  |  |  |  |  |  |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $\mathrm{Pl}(\mathrm{M}$ | 5 | 5 | 10 | 93 | 10 | 5 | 92 | 82 | 98 | 4 | 89 | 77 | 95 | 4 | 87 | 75 | 94 | 4 | 81 | 69 | 90 | 4 | 74 | 61 | 85 | 4 | 72 | 59 | 83 |


s
PIIIM 55988910492819748471934806790375618637156823675279

2) 21 |  | 1 | .1 | .7 | 0 | 8 | 3 | .5 | .9 | 4 | .6 | .9 | .1 | 2.8 | .5 | .4 | 9 | .0 | .1 | .0 | 7 | 2 | .9 | .9 | 5 | .3 | .9 | .7 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |



PII(M) 43786289256397114126571311848129164512412409221037
13) \(1 \begin{aligned} \& 1 <br>

\& 2\end{aligned} .0 .4\)| 4 | 4 | 3 | .1 | .7 | .5 | 7 | .5 | .3 | .9 | 3 | .7 | .1 | .1 | 2 | .3 | .1 | .5 | 0 | .4 | .4 | .3 | .0 | .6 | .6 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |


ebo 1) $3 \begin{array}{lllllllllllllllllllllll} & 6 & 0 & 5 & 0 & 0 & 7 & 0 & 0 & 7 & 0 & 0 & 7 & 0 & 0 & 7 & 0 & 0 & 7 & 0 & 0 & 7\end{array}$

2) $80 \begin{array}{lllllllllllllllllllll} & 0 & 0 & 2 & 0 & 0 & 2 & 0 & 0 & 2 & 0 & 0 & 2 & 0 & 0 & 2 & 0 & 0 & 2 & 0 & 0\end{array} 2$


6) | 5 | 7 | 7 | .2 | 9 | 1 | .9 | 9 | 1 | .9 | 9 | 1 | .9 | 9 | 1 | .9 | 9 | 1 | .9 | 9 | 1 | .9 |
| ---: | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |



18-49ys $=$ Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
$\mathrm{n} / \%$ = number/percentage of subjects with concentration within the specified range
$95 \%$ CI $=95 \%$ confidence interval; LL $=$ Lower Limit, UL = Upper Limit
Pl(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M6) = Post-vaccination Dose II (Month 6)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.45 Descriptive statistics of the frequency of gE-specific CD4[2+] T-cells in PreChemo Groups only (adapted ATP cohort for CMI immunogenicity)

| Immune marker | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | HZ/su | PRE | 25 | 2 | 178.47 | 187.11 | 1.0 | 49.7 | 127.3 | 192.4 | 662.4 |
|  |  | Pl(M1) | 25 | 2 | 521.79 | 656.39 | 1.0 | 139.7 | 391.9 | 603.7 | 3276.6 |
|  |  | PlI(M2) | 22 | 5 | 1187.06 | 1292.07 | 1.0 | 393.1 | 778.8 | 1098.2 | 4835.8 |
|  |  | PII(M13) | 18 | 2 | 523.83 | 632.83 | 1.0 | 114.9 | 332.9 | 604.6 | 2416.0 |
|  | Placebo | PRE | 27 | 4 | 179.31 | 359.33 | 1.0 | 27.5 | 104.8 | 151.5 | 1894.5 |
|  |  | Pl(M1) | 30 | 1 | 119.89 | 158.66 | 1.0 | 1.0 | 50.0 | 179.4 | 567.8 |
|  |  | PlI(M2) | 29 | 2 | 140.25 | 238.68 | 1.0 | 17.4 | 61.8 | 139.5 | 1234.1 |
|  |  | PII(M13) | 19 | 0 | 125.78 | 169.65 | 1.0 | 1.0 | 51.2 | 288.6 | 497.1 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1, Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)
Table 7.46 Descriptive statistics of the fold increase of frequency of gE-specific CD4[2+] T-cells at Month 1, 2 and 13 from pre-vaccination in PreChemo Groups only (adapted ATP cohort for CMI immunogenicity)

| Immune marker | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | HZ/su | PI(M1) | 25 | 2 | 41.79 | 105.97 | 0.0 | 1.1 | 2.5 | 8.2 | 426.5 |
|  |  | Pll(M2) | 22 | 5 | 90.62 | 213.95 | 0.5 | 1.7 | 4.9 | 33.0 | 880.8 |
|  |  | PII(M13) | 17 | 3 | 14.00 | 25.51 | 0.0 | 1.3 | 2.0 | 5.2 | 94.4 |
|  | Placebo | Pl(M1) | 27 | 4 | 10.92 | 33.13 | 0.0 | 0.0 | 0.8 | 3.2 | 167.2 |
|  |  | PII(M2) | 27 | 4 | 8.00 | 18.76 | 0.0 | 0.2 | 0.9 | 1.9 | 61.8 |
|  |  | PII(M13) | 16 | 3 | 7.02 | 23.21 | 0.0 | 0.0 | 0.7 | 1.3 | 93.8 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1,Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.47 Vaccine response rates for gE-specific CD4[2+] T-cells at Month 1, 2 and 13 in PreChemo Groups only (adapted ATP cohort for CMI immunogenicity)


HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially subjects with pre-vaccination $T$ cell frequencies below the threshold, at least a 2 -fold increase as compared to the threshold ( $2 x<320>$ Events/10E6 CD4+ T cells)
For initially subjects with pre-vaccination $T$ cell frequencies above the threshold, at least a 2 -fold increase as compared to pre-vaccination T cell frequencies
$\mathrm{N}=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)
Table 7.48 Descriptive statistics of the frequency in CD4[2+] T-cells following induction with gE in PreChemo Groups only (adapted ATP cohort for CMI immunogenicity)

| Immune marker | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | HZ/su | PRE | 25 | 2 | 413.17 | 195.72 | 156.0 | 274.8 | 364.0 | 513.2 | 773.3 |
|  |  | Pl(M1) | 25 | 2 | 735.58 | 658.28 | 152.3 | 388.2 | 652.5 | 730.1 | 3427.5 |
|  |  | PlI(M2) | 22 | 5 | 1416.20 | 1259.98 | 145.8 | 745.4 | 1072.5 | 1280.9 | 4968.0 |
|  |  | PII(M13) | 18 | 2 | 797.69 | 628.43 | 90.2 | 376.9 | 569.0 | 978.1 | 2525.7 |
|  | Placebo | PRE | 27 | 4 | 449.73 | 432.31 | 94.1 | 220.2 | 340.8 | 496.9 | 2324.7 |
|  |  | Pl(M1) | 30 | 1 | 344.67 | 253.88 | 50.3 | 160.3 | 256.6 | 499.4 | 983.1 |
|  |  | PlI(M2) | 29 | 2 | 350.25 | 311.74 | 0.0 | 194.8 | 274.1 | 339.1 | 1691.1 |
|  |  | PlI(M13) | 190 | 0 | 383.00 | 246.27 | 54.9 | 222.4 | 308.1 | 477.8 | 1011.5 |

[^9]Table 7.49 Descriptive statistics of the fold increase of frequency in CD4[2+] Tcells at Month 1, 2 and 13 from pre-vaccination following induction with gE in PreChemo Groups only (adapted ATP cohort for CMI immunogenicity)

| Immune marker | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | HZ/su | Pl(M1) | 25 | 2 | 1.75 | 1.11 | 0.6 | 1.0 | 1.5 | 1.9 | 4.8 |
|  |  | Pll(M2) | 22 | 5 | 4.08 | 5.47 | 0.6 | 1.5 | 2.2 | 4.4 | 26.2 |
|  |  | PII(M13) | 17 | 3 | 2.27 | 2.96 | 0.6 | 1.0 | 1.4 | 2.3 | 13.3 |
|  | Placebo | Pl(M1) | 27 | 4 | 1.00 | 0.83 | 0.3 | 0.5 | 0.7 | 1.3 | 3.7 |
|  |  | PlI(M2) | 27 | 4 | 0.89 | 0.43 | 0.0 | 0.6 | 0.8 | 1.3 | 1.8 |
|  |  | PII(M13) | 16 | 3 | 1.13 | 0.71 | 0.3 | 0.8 | 1.0 | 1.1 | 3.0 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1,Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)
Table 7.50 Adjusted geometric means and ratio of HZ/su over placebo in frequency of CD4[2+] T-cells following induction with gE at Month 2 in PreChemo Groups only (ATP cohort for CMI immunogenicity)

|  |  |  | Adjusted geometric mean |  |  | Adjusted geometric mean ratio |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | \% Cl |  |  | \% CI |  |
| Timing | Group | N | Value | LL | UL | Value | LL | UL | P-value for the ratio |
| PII(M2) | HZ/su | 22 | 1017.88 | 699.97 | 1480.19 | 3.5 | 2.3 | 5.3 | <. 0001 |
|  | Placebo |  | 291.13 | 242.23 | 349.91 |  |  |  |  |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval
Confidence Interval (CI) were back transformed to original units
The p-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)

Table 7.51 Descriptive statistics of the frequency of gE-specific CD4[2+] T-cells in PreChemo Groups only by age strata (adapted ATP cohort for CMI immunogenicity)

| Immune marker | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | 18-49ys | HZ/su | PRE | 9 | 0 | 178.75 | 187.99 | 1.0 | 62.2 | 141.7 | 147.7 | 573.8 |
|  |  |  | Pl(M1) | 9 | 0 | 687.36 | 1018.49 | 1.0 | 55.7 | 437.6 | 644.9 | 3276.6 |
|  |  |  | PlI(M2) | 9 | 0 | 1468.65 | 1735.93 | 1.0 | 189.5 | 652.6 | 2919.3 | 4835.8 |
|  |  |  | PII(M13) | 6 | 1 | 803.28 | 977.79 | 1.0 | 150.3 | 322.7 | 1606.9 | 2416.0 |
|  |  | Placebo | PRE | 7 | 2 | 172.43 | 127.01 | 39.3 | 95.1 | 126.5 | 234.2 | 422.3 |
|  |  |  | PI(M1) | 8 | 1 | 130.24 | 117.16 | 1.0 | 21.4 | 126.6 | 204.0 | 336.9 |
|  |  |  | PII(M2) | 7 | 2 | 211.20 | 157.71 | 29.7 | 49.1 | 139.5 | 375.1 | 391.0 |
|  |  |  | PII(M13) | 5 | 0 | 258.87 | 241.81 | 1.0 | 19.6 | 288.6 | 488.0 | 497.1 |
|  | $\geq 50 y s$ | HZ/su | PRE | 16 | 2 | 178.31 | 192.79 | 1.0 | 23.1 | 127.3 | 222.4 | 662.4 |
|  |  |  | Pl(M1) | 16 | 2 | 428.66 | 332.28 | 38.2 | 198.1 | 364.0 | 572.7 | 1273.4 |
|  |  |  | PlI(M2) | 13 | 5 | 992.11 | 901.06 | 187.4 | 561.6 | 783.4 | 1014.9 | 3752.5 |
|  |  |  | PlI(M13) | 12 | 1 | 384.10 | 347.05 | 1.1 | 104.7 | 345.3 | 594.9 | 1038.2 |
|  |  | Placebo | PRE | 20 | 2 | 181.72 | 414.20 | 1.0 | 10.8 | 85.4 | 136.9 | 1894.5 |
|  |  |  | Pl(M1) | 22 | 0 | 116.13 | 173.59 | 1.0 | 1.0 | 39.5 | 167.2 | 567.8 |
|  |  |  | PII(M2) | 22 | 0 | 117.67 | 258.15 | 1.0 | 1.0 | 58.4 | 119.6 | 1234.1 |
|  |  |  | PII(M13) | 14 | 0 | 78.24 | 112.30 | 1.0 | 1.0 | 28.6 | 93.8 | 326.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1, Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.52 Descriptive statistics of the fold increase of frequency of gE-specific CD4[2+] T-cells at Month 1, 2 and 13 from pre-vaccination in PreChemo Groups only by age strata (adapted ATP cohort for CMI immunogenicity)

| Immune marker | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | 18-49ys | HZ/su | Pl(M1) | 9 | 0 | 9.35 | 17.60 | 0.0 | 2.2 | 4.6 | 5.7 | 55.7 |
|  |  |  | PlI(M2) | 9 | 0 | 15.67 | 31.31 | 0.5 | 2.4 | 4.6 | 5.1 | 97.3 |
|  |  |  | PII(M13) | 6 | 1 | 9.51 | 19.17 | 0.9 | 1.0 | 1.9 | 2.8 | 48.6 |
|  |  | Placebo | Pl(M1) | 7 | 2 | 1.09 | 1.04 | 0.0 | 0.3 | 1.0 | 1.2 | 3.2 |
|  |  |  | PII(M2) | 7 | 2 | 1.18 | 0.51 | 0.5 | 0.8 | 1.1 | 1.6 | 1.9 |
|  |  |  | PlI(M13) | 3 | 2 | 4.39 | 3.09 | 1.2 | 1.2 | 4.7 | 7.3 | 7.3 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 16 | 2 | 60.04 | 129.67 | 0.3 | 1.1 | 2.1 | 36.1 | 426.5 |
|  |  |  | PlI(M2) | 135 | 5 | 142.51 | 268.93 | 1.2 | 1.7 | 6.4 | 93.6 | 880.8 |
|  |  |  | PII(M13) | 112 | 2 | 16.44 | 28.96 | 0.0 | 1.3 | 3.0 | 31.8 | 94.4 |
|  |  | Placebo | Pl(M1) | 20 | 2 | 14.36 | 38.12 | 0.0 | 0.0 | 0.8 | 4.5 | 167.2 |
|  |  |  | PlI(M2) | 20 | 2 | 10.39 | 21.41 | 0.0 | 0.1 | 0.8 | 5.0 | 61.8 |
|  |  |  | PlI(M13) | 13 | 1 | 7.63 | 25.88 | 0.0 | 0.0 | 0.4 | 0.9 | 93.8 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1,Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.53 Vaccine response rates for the frequency of gE-specific CD4[2+] Tcells at Month 1, 2 and 13 in PreChemo Groups only by age strata (adapted ATP cohort for CMI immunogenicity)

|  |  |  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | 95\% CI |  |
| Test description | Sub-group | Group | Timing | N | n | \% | LL | UL |
| CD4[2+] | 18-49ys | HZ/su | Pl(M1) | 9 | 3 | 33.3 | 7.5 | 70.1 |
|  |  |  | PII(M2) | 9 | 5 | 55.6 | 21.2 | 86.3 |
|  |  |  | PlI(M13) | 6 | 2 | 33.3 | 4.3 | 77.7 |
|  |  | Placebo | Pl(M1) | 7 | 0 | 0.0 | 0.0 | 41.0 |
|  |  |  | PlI(M2) | 7 | 0 | 0.0 | 0.0 | 41.0 |
|  |  |  | PII(M13) | 3 | 0 | 0.0 | 0.0 | 70.8 |
|  | $\geq 50 y s$ | HZ/su | PI(M1) | 16 | 2 | 12.5 | 1.6 | 38.3 |
|  |  |  | PlI(M2) | 13 | 6 | 46.2 | 19.2 | 74.9 |
|  |  |  | PlI(M13) | 11 | 1 | 9.1 | 0.2 | 41.3 |
|  |  | Placebo | Pl(M1) | 20 | 0 | 0.0 | 0.0 | 16.8 |
|  |  |  | PlI(M2) | 20 | 0 | 0.0 | 0.0 | 16.8 |
|  |  |  | PII(M13) | 13 | 0 | 0.0 | 0.0 | 24.7 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially subjects with pre-vaccination $T$ cell frequencies below the threshold, at least a 2-fold increase as compared to the threshold ( $2 x<320>$ Events/10E6 CD4+ T cells)
For initially subjects with pre-vaccination $T$ cell frequencies above the threshold, at least a 2 -fold increase as compared to pre-vaccination T cell frequencies
$\mathrm{N}=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
95\% CI $=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.54 Adjusted geometric means and ratio of $\mathrm{HZ} / \mathrm{su}$ over placebo for gEspecific CD4[2+] T-cells frequencies at Month 2 in PreChemo Groups only by age strata (ATP cohort for CMI immunogenicity)

|  |  |  |  | Adjusted geometric mean |  |  | Adjusted geometric mean ratio |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% Cl |  |  | 95\% CI |  |  |
| Timing | Sub-Group | Group | N | Value | LL | UL | Value | LL | UL | P-value for the ratio |
| PII(M2) | 18-49ys | HZ/su | 9 | 754.2 | 333.1 | 1503.7 | 4.29 | 0.87 | 21.31 | 0.0718 |
|  |  | Placebo | 7 | 175.7 | -7.8 | 528.5 |  |  |  |  |
|  | $\geq 50 y s$ | HZ/su | 13 | 842.6 | 558.2 | 1232.8 | 17.35 | 4.34 | 69.44 | 0.0002 |
|  |  | Placebo | 20 | 48.6 | -8.5 | 122.0 | . | . | . | . |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval Confidence Interval (CI) were back transformed to original units The $p$-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)
Table 7.55 Descriptive statistics of the frequency in CD4[2+] T-cells following induction with gE in PreChemo Groups only by age strata (adapted ATP cohort for CMI immunogenicity)

| Immune marker | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | 18-49ys | HZ/su | PRE | 90 | 0 | 459.44 | 245.80 | 156.0 | 237.0 | 440.0 | 742.6 | 759.0 |
|  |  |  | Pl(M1) 9 | 90 | 0 | 868.69 | 1023.57 | 152.3 | 195.0 | 652.5 | 724.9 | 3427.5 |
|  |  |  | PII(M2) 9 | 90 | 0 | 1688.11 | 1702.25 | 145.8 | 529.6 | 1192.0 | 3031.4 | 4968.0 |
|  |  |  | PII(M13) 6 | 61 | 1 | 1020.14 | 988.63 | 90.2 | 403.3 | 555.5 | 1990.6 | 2525.7 |
|  |  | Placebo | PRE 7 | 72 | 2 | 495.30 | 339.34 | 173.4 | 257.4 | 345.4 | 708.9 | 1157.5 |
|  |  |  | Pl(M1) 8 | 81 | 1 | 388.54 | 288.30 | 50.3 | 152.2 | 355.8 | 589.3 | 863.3 |
|  |  |  | PII(M2) 7 | 72 | 2 | 441.29 | 258.35 | 223.7 | 238.0 | 290.9 | 626.6 | 877.8 |
|  |  |  | Pll(M13) 5 | 5 | 0 | 590.78 | 324.68 | 229.9 | 406.1 | 462.7 | 843.6 | 1011.5 |
|  | $\geq 50 y s$ | HZ/su | PRE | 162 | 2 | 387.15 | 164.50 | 188.6 | 276.2 | 356.7 | 452.0 | 773.3 |
|  |  |  | Pl(M1) | 162 | 2 | 660.70 | 343.45 | 223.4 | 395.8 | 636.5 | 812.5 | 1432.1 |
|  |  |  | PII(M2) | 135 | 5 | 1227.95 | 867.53 | 309.3 | 796.0 | 1058.5 | 1217.0 | 3927.5 |
|  |  |  | PlI(M13) | 121 | 1 | 686.46 | 354.37 | 277.8 | 369.6 | 569.0 | 936.2 | 1269.4 |
|  |  | Placebo | PRE 20 | 202 | 2 | 433.78 | 467.28 | 94.1 | 214.4 | 315.2 | 469.9 | 2324.7 |
|  |  |  | Pl(M1) 22 | 220 | 0 | 328.72 | 245.57 | 50.5 | 160.3 | 256.6 | 409.9 | 983.1 |
|  |  |  | Pll(M2) 22 | 220 | 0 | 321.29 | 326.90 | 0.0 | 178.5 | 258.5 | 331.5 | 1691.1 |
|  |  |  | PII(M13) 1 | 140 | 0 | 308.79 | 170.29 | 54.9 | 193.1 | 249.5 | 417.0 | 715.4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1,Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.56 Descriptive statistics of the fold increase of frequency in CD4[2+] Tcells at Month 1, 2 and 13 from pre-vaccination following induction with gE in PreChemo Groups only by age strata (adapted ATP cohort for CMI immunogenicity)

| Immune marker | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | 18-49ys | HZ/su | Pl(M1) | 9 | 0 | 1.60 | 1.19 | 0.6 | 1.0 | 1.3 | 1.7 | 4.6 |
|  |  |  | Pll(M2) | 9 | 0 | 4.97 | 8.20 | 0.6 | 1.3 | 1.6 | 4.1 | 26.2 |
|  |  |  | Plı(M13) 6 | 6 | 1 | 3.38 | 4.93 | 0.6 | 0.7 | 1.5 | 2.7 | 13.3 |
|  |  | Placebo | Pl(M1) | 7 | 2 | 0.93 | 0.37 | 0.4 | 0.7 | 0.8 | 1.3 | 1.5 |
|  |  |  | PII(M2) | 72 | 2 | 0.95 | 0.27 | 0.7 | 0.8 | 0.8 | 1.3 | 1.4 |
|  |  |  | Pll(M13) 3 | 32 | 2 | 2.28 | 0.95 | 1.2 | 1.2 | 2.7 | 3.0 | 3.0 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 162 | 2 | 1.83 | 1.10 | 0.9 | 1.1 | 1.5 | 1.9 | 4.8 |
|  |  |  | PlI(M2) | 135 | 5 | 3.47 | 2.55 | 1.1 | 1.6 | 2.5 | 4.4 | 10.1 |
|  |  |  | PII(M13) | 112 | 2 | 1.67 | 0.84 | 0.7 | 1.0 | 1.4 | 2.3 | 3.6 |
|  |  | Placebo | Pl(M1) | 202 | 2 | 1.02 | 0.95 | 0.3 | 0.5 | 0.7 | 1.2 | 3.7 |
|  |  |  | PII(M2) | 20 | 2 | 0.87 | 0.48 | 0.0 | 0.6 | 0.8 | 1.2 | 1.8 |
|  |  |  | Pll(M13) | 131 | 1 | 0.87 | 0.27 | 0.3 | 0.7 | 0.9 | 1.0 | 1.3 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1, Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)
Table 7.57 Adjusted geometric means and ratio of $\mathrm{HZ} / \mathrm{su}$ over placebo in frequency of CD4[2+] T-cells following induction with gE at Month 2 in PreChemo Groups only by age strata (ATP cohort for CMI immunogenicity)

|  |  |  |  | Adjusted geometric mean |  |  | Adjusted geometric mean ratio |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Timing | Sub-Group | Group | N | Value | LL | UL | Value | LL | UL | P-value for the ratio |
| PlI(M2) | 18-49ys | HZ/su | 9 | 975.72 | 438.06 | 2173.28 | 2.5 | 1.1 | 5.7 | 0.0282 |
|  |  | Placebo | 7 | 383.58 | 286.04 | 514.39 | . | . | . | . |
|  | $\geq 50 y s$ | HZ/su | 13 | 1078.15 | 734.52 | 1582.54 | 4.1 | 2.7 | 6.3 | <. 0001 |
|  |  | Placebo | 20 | 262.14 | 208.85 | 329.03 | . | . | . | . |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval
Confidence Interval (CI) were back transformed to original units
The $p$-value is relative to the null hypothesis Ho : Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)

Table 7.58 Vaccine response rates for gE-specific CD4[2+] T-cells frequencies at Month 2 in PreChemo Groups only (Total Vaccinated Cohort for CMI immunogenicity)

|  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | \% CI |
| Test description | Group | N | n | \% | LL | UL |
| CD4[2+] | HZ/su | 24 | 12 | 50.0 | 29.1 | 70.9 |
|  | Placebo | 29 | 0 | 0.0 | 0.0 | 11.9 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially subjects with pre-vaccination T cell frequencies below the threshold, at least a 2-fold increase as compared to the threshold ( $2 x<320>$ Events/10E6 CD4+ T cells)
For initially subjects with pre-vaccination T cell frequencies above the threshold, at least a 2 -fold increase as compared to pre-vaccination T cell frequencies
$N=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
95\% CI = 95\% confidence interval, LL = Lower Limit, UL = Upper Limit PII(M2) = Post-vaccination Dose II (Month 2)

Table 7.59 Descriptive statistics of the frequency of gE-specific CD4[2+] T-cells in PreChemo Groups only (Total Vaccinated Cohort for CMI immunogenicity)

| Immune marker | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | HZ/su | PRE | 35 | 4 | 168.18 | 171.07 | 1.0 | 46.2 | 127.2 | 203.3 | 662.4 |
|  |  | Pl(M1) | 30 | 3 | 547.69 | 653.10 | 1.0 | 104.6 | 409.2 | 652.4 | 3276.6 |
|  |  | PlI(M2) | 26 | 6 | 1180.11 | 1236.54 | 1.0 | 393.1 | 778.8 | 1508.9 | 4835.8 |
|  |  | PlI(M13) | 22 | 4 | 477.42 | 593.79 | 1.0 | 94.4 | 303.6 | 604.6 | 2416.0 |
|  | Placebo | PRE | 32 | 5 | 174.14 | 333.56 | 1.0 | 32.8 | 108.4 | 160.7 | 1894.5 |
|  |  | Pl(M1) | 36 | 1 | 128.28 | 166.44 | 1.0 | 1.0 | 55.1 | 190.4 | 567.8 |
|  |  | PlI(M2) | 32 | 2 | 132.91 | 228.67 | 1.0 | 15.2 | 60.3 | 139.4 | 1234.1 |
|  |  | PII(M13) | 24 | 1 | 114.30 | 156.68 | 1.0 | 1.0 | 42.5 | 165.0 | 497.1 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1,Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.60 Descriptive statistics of the fold increase of frequency of gE-specific CD4[2+] T-cells at Month 1, 2 and 13 from pre-vaccination in PreChemo Groups only (Total Vaccinated Cohort for CMI immunogenicity)

| Immune marker | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | HZ/su | Pl(M1) | 28 | 5 | 39.84 | 100.64 | 0.0 | 1.1 | 2.4 | 8.8 | 426.5 |
|  |  | PII(M2) | 24 | 8 | 87.87 | 205.33 | 0.5 | 1.7 | 4.9 | 63.3 | 880.8 |
|  |  | PII(M13) | 20 | 6 | 12.84 | 23.67 | 0.0 | 1.1 | 2.4 | 9.3 | 94.4 |
|  | Placebo | Pl(M1) | 32 | 5 | 9.47 | 30.53 | 0.0 | 0.3 | 1.0 | 2.9 | 167.2 |
|  |  | PlI(M2) | 295 | 5 | 9.30 | 19.73 | 0.0 | 0.2 | 1.1 | 1.9 | 61.8 |
|  |  | PII(M13) | 196 | 6 | 17.63 | 53.83 | 0.0 | 0.0 | 0.8 | 1.5 | 221.8 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1,Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
Pll(M13) = Post-vaccination Dose II (Month 13)
Table 7.61 Vaccine response rates for gE-specific CD4[2+] T-cells at Month 1, 2 and 13 in PreChemo Groups only (Total Vaccinated Cohort for CMI immunogenicity)

|  |  |  |  | Vaccine response |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 95\% CI |  |
| Test description | Group | Timing | N | n | \% | LL | UL |
| CD4[2+] | HZ/su | PI(M1) | 28 | 6 | 21.4 | 8.3 | 41.0 |
|  |  | PII(M2) 2 | 24 | 12 | 50.0 | 29.1 | 70.9 |
|  |  | PII(M13) 20 | 20 | 0 | 20.0 | 5.7 | 43.7 |
|  | Placebo | Pl(M1) | 32 | 0 | 0.0 | 0.0 | 10.9 |
|  |  | PlI(M2) 2 | 29 | 0 | 0.0 | 0.0 | 11.9 |
|  |  | PlI(M13) | 19 | 0 | 0.0 | 0.0 | 17.6 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially subjects with pre-vaccination T cell frequencies below the threshold, at least a 2-fold increase as compared to the threshold ( $2 x<320>$ Events/10E6 CD4+ T cells)
For initially subjects with pre-vaccination $T$ cell frequencies above the threshold, at least a 2 -fold increase as compared to pre-vaccination $T$ cell frequencies
$\mathrm{N}=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
$95 \% \mathrm{CI}=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.62 Descriptive statistics of the frequency in CD4[2+] T-cells following induction with gE in PreChemo Groups only (Total Vaccinated Cohort for CMI immunogenicity)

| Immune marker | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | HZ/su | PRE | 35 | 4 | 405.04 | 209.06 | 151.5 | 237.0 | 361.1 | 587.3 | 831.1 |
|  |  | Pl(M1) | 30 | 3 | 758.76 | 655.47 | 152.3 | 307.8 | 662.5 | 894.8 | 3427.5 |
|  |  | PII(M2) | 26 | 6 | 1414.89 | 1203.21 | 145.8 | 745.4 | 1072.5 | 1579.5 | 4968.0 |
|  |  | PII(M13) | 22 | 4 | 764.34 | 599.85 | 90.2 | 376.9 | 542.9 | 978.1 | 2525.7 |
|  | Placebo | PRE | 32 | 5 | 429.51 | 400.31 | 94.1 | 227.0 | 330.0 | 475.3 | 2324.7 |
|  |  | PI(M1) | 36 | 1 | 359.57 | 249.94 | 50.3 | 161.4 | 265.4 | 524.2 | 983.1 |
|  |  | PII(M2) | 32 | 2 | 348.44 | 299.44 | 0.0 | 198.5 | 265.7 | 373.1 | 1691.1 |
|  |  | PII(M13) 2 | 24 |  | 389.11 | 219.59 | 54.9 | 227.2 | 371.0 | 470.2 | 1011.5 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1, Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)
Table 7.63 Descriptive statistics of the fold increase of frequency in CD4[2+] Tcells at Month 1, 2 and 13 from pre-vaccination following induction with gE in PreChemo Groups only (Total Vaccinated Cohort for CMI immunogenicity)

| Immune marker | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | HZ/su | Pl(M1) | 28 | 5 | 1.91 | 1.54 | 0.6 | 1.0 | 1.4 | 1.9 | 7.6 |
|  |  | PII(M2) | 24 | 8 | 4.28 | 5.50 | 0.6 | 1.4 | 2.2 | 4.4 | 26.2 |
|  |  | PII(M13) | 20 | 6 | 2.15 | 2.74 | 0.6 | 0.9 | 1.5 | 2.1 | 13.3 |
|  | Placebo | Pl(M1) | 32 | 5 | 1.04 | 0.80 | 0.3 | 0.5 | 0.8 | 1.4 | 3.7 |
|  |  | PII(M2) | 29 | 5 | 0.89 | 0.42 | 0.0 | 0.6 | 0.8 | 1.1 | 1.8 |
|  |  | PlI(M13) | 19 | 6 | 1.18 | 0.66 | 0.3 | 0.9 | 1.0 | 1.3 | 3.0 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1,Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.64 Adjusted geometric means and ratio of $\mathrm{HZ} / \mathrm{su}$ over placebo in frequency of CD4[2+] T-cells following induction with gE at Month 2 in PreChemo Groups only (Total Vaccinated Cohort for CMI immunogenicity)

|  |  |  | Adjusted geometric mean Adjusted geometric mean ratio |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Timing | Group | N | Value | LL | UL | Value | LL | UL | P-value for the ratio |
| PII(M2) | HZ/su | 24 | 1000.91 | 692.93 | 1445.77 | 3.4 | 2.3 | 5.1 | <. 0001 |
|  | Placebo | 29 | 291.39 | 245.02 | 346.53 | . | . | . |  |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval
Confidence Interval (Cl) were back transformed to original units
The $p$-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)
Table 7.65 Descriptive statistics of the frequency of gE-specific CD4[2+] T-cells in PreChemo Groups only by age strata (Total Vaccinated Cohort for CMI immunogenicity)

| Immune marker | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | 18-49ys | HZ/su | PRE | 10 | 1 | 202.60 | 192.61 | 1.0 | 62.2 | 142.0 | 407.0 | 573.8 |
|  |  |  | Pl(M1) | 11 | 0 | 773.49 | 955.76 | 1.0 | 55.7 | 507.8 | 905.3 | 3276.6 |
|  |  |  | PlI(M2) | 11 | 0 | 1448.28 | 1609.47 | 1.0 | 189.5 | 652.6 | 2919.3 | 4835.8 |
|  |  |  | PII(M13) 8 | 8 | 2 | 712.43 | 864.02 | 1.0 | 119.3 | 322.7 | 1199.2 | 2416.0 |
|  |  | Placebo | PRE | 7 | 2 | 172.43 | 127.01 | 39.3 | 95.1 | 126.5 | 234.2 | 422.3 |
|  |  |  | Pl(M1) | 8 | 1 | 130.24 | 117.16 | 1.0 | 21.4 | 126.6 | 204.0 | 336.9 |
|  |  |  | PII(M2) 7 | 7 | 2 | 211.20 | 157.71 | 29.7 | 49.1 | 139.5 | 375.1 | 391.0 |
|  |  |  | PII(M13) 6 | 6 | 0 | 231.69 | 226.30 | 1.0 | 19.6 | 192.2 | 488.0 | 497.1 |
|  | $\geq 50 y s$ | HZ/su | PRE | 25 | 3 | 154.42 | 163.87 | 1.0 | 37.1 | 122.0 | 192.4 | 662.4 |
|  |  |  | Pl(M1) | 19 | 3 | 416.97 | 361.28 | 1.0 | 104.6 | 336.1 | 603.7 | 1273.4 |
|  |  |  | PlI(M2) | 15 | 6 | 983.45 | 884.41 | 152.4 | 510.7 | 783.4 | 1098.2 | 3752.5 |
|  |  |  | PlI(M13) | 14 | 2 | 343.13 | 337.91 | 1.0 | 94.4 | 253.7 | 585.3 | 1038.2 |
|  |  | Placebo | PRE | 25 | 3 | 174.62 | 373.74 | 1.0 | 15.5 | 96.7 | 142.7 | 1894.5 |
|  |  |  | Pl(M1) | 28 | 0 | 127.72 | 179.86 | 1.0 | 1.0 | 50.0 | 184.4 | 567.8 |
|  |  |  | PlI(M2) 2 | 25 | 0 | 110.99 | 242.97 | 1.0 | 1.0 | 57.8 | 119.6 | 1234.1 |
|  |  |  | PlI(M13) | 18 | 1 | 75.17 | 108.00 | 1.0 | 1.0 | 20.0 | 93.8 | 326.0 |

[^10]Table 7.66 Descriptive statistics of the fold increase of frequency of gE-specific CD4[2+] T-cells at Month 1, 2 and 13 from pre-vaccination in PreChemo Groups only by age strata (Total Vaccinated Cohort for CMI immunogenicity)

| Immune marker | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | 18-49ys | HZ/su | Pl(M1) | 10 | 1 | 8.58 | 16.77 | 0.0 | 1.6 | 3.5 | 5.7 | 55.7 |
|  |  |  | PlI(M2) | 10 | 1 | 14.20 | 29.88 | 0.5 | 1.0 | 3.8 | 5.1 | 97.3 |
|  |  |  | PII(M13) 8 | 8 | 2 | 7.85 | 16.55 | 0.2 | 0.9 | 1.9 | 4.2 | 48.6 |
|  |  | Placebo | PI(M1) | 7 |  | 1.09 | 1.04 | 0.0 | 0.3 | 1.0 | 1.2 | 3.2 |
|  |  |  | PII(M2) | 7 |  | 1.18 | 0.51 | 0.5 | 0.8 | 1.1 | 1.6 | 1.9 |
|  |  |  | PlI(M13) 4 | 4 | 2 | 3.48 | 3.11 | 0.8 | 1.0 | 2.9 | 6.0 | 7.3 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 18 | 4 | 57.20 | 122.66 | 0.0 | 1.1 | 2.1 | 62.9 | 426.5 |
|  |  |  | PII(M2) | 14 | 7 | 140.50 | 258.49 | 1.2 | 1.7 | 14.1 | 114.3 | 880.8 |
|  |  |  | PII(M13) | 124 | 4 | 16.16 | 27.63 | 0.0 | 1.4 | 3.3 | 22.4 | 94.4 |
|  |  | Placebo | Pl(M1) | 253 | 3 | 11.81 | 34.32 | 0.0 | 0.3 | 1.0 | 3.6 | 167.2 |
|  |  |  | PII(M2) | 223 | 3 | 11.88 | 22.14 | 0.0 | 0.1 | 1.0 | 8.1 | 61.8 |
|  |  |  | Pll(M13) | 154 |  | 21.40 | 60.42 | 0.0 | 0.0 | 0.4 | 1.0 | 221.8 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1, Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.67 Vaccine response rates for the frequency of gE-specific CD4[2+] Tcells at Month 1, 2 and 13 in PreChemo Groups only by age strata (Total Vaccinated Cohort for CMI immunogenicity)

| Vaccine response |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 95\% CI |  |
| Test description | Sub-group | Group | Timing | N | n \% | LL | UL |
|  | 18-49ys | HZ/su | Pl(M1) | 10 | 330.0 | 6.7 | 65.2 |
|  |  |  | PII(M2) | 10 | 550.0 | 18.7 | 81.3 |
|  |  |  | PII(M13) | 8 | 337.5 | 8.5 | 75.5 |
|  |  | Placebo | Pl(M1) | 7 | 00.0 | 0.0 | 41.0 |
|  |  |  | PlI(M2) | 7 | 00.0 | 0.0 | 41.0 |
|  |  |  | PII(M13) | 4 | 00.0 | 0.0 | 60.2 |
|  | $\geq 50 y s$ | HZ/su | PI(M1) | 18 | 316.7 | 3.6 | 41.4 |
|  |  |  | PlI(M2) | 14 | 750.0 | 23.0 | 77.0 |
|  |  |  | PlI(M13) | 12 | 18.3 | 0.2 | 38.5 |
|  |  | Placebo | Pl(M1) | 25 | 00.0 | 0.0 | 13.7 |
|  |  |  | PII(M2) | 22 | 00.0 | 0.0 | 15.4 |
|  |  |  | PlI(M13) | 15 | 00.0 | 0.0 | 21.8 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
Vaccine response defined as :
For initially subjects with pre-vaccination $T$ cell frequencies below the threshold, at least a 2-fold increase as compared to the threshold ( $2 x<320>$ Events/10E6 CD4+ T cells)
For initially subjects with pre-vaccination $T$ cell frequencies above the threshold, at least a 2 -fold increase as compared to pre-vaccination T cell frequencies
$\mathrm{N}=$ Number of subjects with pre- and post-vaccination results available
$\mathrm{n} / \%=$ Number/percentage of responders
95\% CI $=95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.68 Descriptive statistics of the frequency in CD4[2+] T-cells following induction with gE in PreChemo Groups only by age strata (Total Vaccinated Cohort for CMI immunogenicity)

| Immune marker | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | 18-49ys | HZ/su | PRE | 101 | 1 | 482.75 | 243.18 | 156.0 | 237.0 | 464.8 | 742.6 | 759.0 |
|  |  |  | Pl(M1) | 110 | 0 | 958.83 | 970.58 | 152.3 | 195.0 | 694.3 | 1266.0 | 3427.5 |
|  |  |  | PlI(M2) | 110 | 0 | 1688.37 | 1577.35 | 145.8 | 529.6 | 1192.0 | 3031.4 | 4968.0 |
|  |  |  | PlI(M13) 8 | 8 | 2 | 984.18 | 875.84 | 90.2 | 402.2 | 555.5 | 1671.1 | 2525.7 |
|  |  | Placebo | PRE | 7 | 2 | 495.30 | 339.34 | 173.4 | 257.4 | 345.4 | 708.9 | 1157.5 |
|  |  |  | Pl(M1) | 8 | 1 | 388.54 | 288.30 | 50.3 | 152.2 | 355.8 | 589.3 | 863.3 |
|  |  |  | PII(M2) | 7 | 2 | 441.29 | 258.35 | 223.7 | 238.0 | 290.9 | 626.6 | 877.8 |
|  |  |  | PII(M13) 6 | 6 | 0 | 554.00 | 304.06 | 229.9 | 370.1 | 434.4 | 843.6 | 1011.5 |
|  | $\geq 50 y s$ | HZ/su | PRE | 25 | 3 | 373.96 | 190.32 | 151.5 | 242.3 | 352.3 | 469.2 | 831.1 |
|  |  |  | Pl(M1) | 19 | 3 | 642.93 | 360.86 | 190.8 | 307.8 | 600.6 | 894.8 | 1432.1 |
|  |  |  | PlI(M2) | 156 | 6 | 1214.34 | 840.34 | 309.3 | 793.2 | 1058.5 | 1280.9 | 3927.5 |
|  |  |  | PlI(M13) | 142 | 2 | 638.71 | 348.51 | 277.8 | 362.3 | 530.8 | 894.4 | 1269.4 |
|  |  | Placebo | PRE | 25 | , | 411.09 | 420.22 | 94.1 | 221.2 | 311.1 | 442.9 | 2324.7 |
|  |  |  | Pl(M1) | 28 | 0 | 351.29 | 243.13 | 50.5 | 161.4 | 265.4 | 494.9 | 983.1 |
|  |  |  | PII(M2) | 25 | 0 | 322.44 | 309.70 | 0.0 | 184.1 | 257.3 | 331.5 | 1691.1 |
|  |  |  | PII(M13) | 18 | 1 | 334.15 | 158.91 | 54.9 | 222.4 | 336.6 | 417.0 | 715.4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1,Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PRE = Pre-vaccination (Month 0)
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)

Table 7.69 Descriptive statistics of the fold increase of frequency in CD4[2+] Tcells at Month 1, 2 and 13 from pre-vaccination following induction with gE in PreChemo Groups only by age strata (Total Vaccinated Cohort for CMI immunogenicity)

| Immune marker | Sub-group | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| CD4[2+] | 18-49ys | HZ/su | Pl(M1) | 10 | 1 | 1.55 | 1.13 | 0.6 | 1.0 | 1.2 | 1.7 | 4.6 |
|  |  |  | PlI(M2) | 10 | 1 | 4.59 | 7.83 | 0.6 | 1.1 | 1.5 | 4.1 | 26.2 |
|  |  |  | PII(M13) 8 | 8 | 2 | 2.83 | 4.30 | 0.6 | 0.6 | 1.5 | 2.2 | 13.3 |
|  |  | Placebo | Pl(M1) | 7 | 2 | 0.93 | 0.37 | 0.4 | 0.7 | 0.8 | 1.3 | 1.5 |
|  |  |  | PlI(M2) | 7 | 2 | 0.95 | 0.27 | 0.7 | 0.8 | 0.8 | 1.3 | 1.4 |
|  |  |  | PII(M13) 4 | 4 | 2 | 2.07 | 0.88 | 1.2 | 1.3 | 2.1 | 2.8 | 3.0 |
|  | $\geq 50 y s$ | HZ/su | Pl(M1) | 18 | 4 | 2.10 | 1.72 | 0.9 | 1.1 | 1.5 | 2.0 | 7.6 |
|  |  |  | PlI(M2) | 14 | 7 | 4.06 | 3.30 | 1.1 | 1.6 | 2.8 | 4.5 | 11.7 |
|  |  |  | PlI(M13) | 12 | 4 | 1.69 | 0.81 | 0.7 | 1.1 | 1.5 | 2.1 | 3.6 |
|  |  | Placebo | Pl(M1) | 25 | 3 | 1.07 | 0.88 | 0.3 | 0.5 | 0.7 | 1.4 | 3.7 |
|  |  |  | PII(M2) | 22 | 3 | 0.88 | 0.46 | 0.0 | 0.6 | 0.8 | 1.1 | 1.8 |
|  |  |  | PII(M13) | 154 |  | 0.94 | 0.31 | 0.3 | 0.7 | 1.0 | 1.1 | 1.6 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1, Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PI(M1) = Post-vaccination Dose I (Month 1)
PII(M2) = Post-vaccination Dose II (Month 2)
PII(M13) = Post-vaccination Dose II (Month 13)
Table 7.70 Adjusted geometric means and ratio of HZ/su over placebo in frequency of CD4[2+] T-cells following induction with gE at Month 2 in PreChemo Groups only by age strata (Total Vaccinated Cohort for CMI immunogenicity)

|  |  |  |  | Adjusted geometric mean |  |  | Adjusted geometric mean ratio |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% CI |  |  | 95\% Cl |  |  |
| Timing | Sub-Group | Group | N | Value | LL | UL | Value | LL | UL | P-value for the ratio |
| PlI(M2) | 18-49ys | HZ/su | 10 | 934.78 | 452.37 | 1931.64 | 2.4 | 1.1 | 5.0 | 0.0266 |
|  |  | Placebo | 7 | 395.57 | 297.85 | 525.34 | . | . | . |  |
|  | $\geq 50 y s$ | HZ/su | 14 | 1099.59 | 737.77 | 1638.87 | 4.2 | 2.7 | 6.5 | <. 0001 |
|  |  | Placebo | 22 | 263.29 | 213.42 | 324.83 |  | . | . | . |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval
Confidence Interval (CI) were back transformed to original units
The $p$-value is relative to the null hypothesis Ho : Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)

Table 7.71 Adjusted geometric means and ratio of $\mathrm{HZ} / \mathrm{su}$ over placebo for gEspecific CD4[2+] T-cells frequencies at Month 2 in PreChemo Groups only (Total Vaccinated Cohort for CMI immunogenicity)

|  |  |  | Adjusted geometric mean |  |  | Adjusted geometric mean ratio |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  | 95\% Cl |  |  |
| Timing | Group | N | Value | LL | UL | Value | LL | UL | P-value for the ratio |
| PII(M2) | HZ/su | 24 | 801.9 | 557.2 | 1124.6 | 9.39 | 3.67 | 24.00 | <. 0001 |
|  | Placebo | 29 | 85.4 | 19.6 | 169.9 | . | . | . |  |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval
Confidence Interval (Cl) were back transformed to original units
The $p$-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$
PII(M2) = Post-vaccination Dose II (Month 2)
Table 7.72 Adjusted geometric means and ratio of HZ/su over placebo for gEspecific CD4[2+] T-cells frequencies at Month 2 in PreChemo Groups only by age strata (Total Vaccinated Cohort for CMI immunogenicity)

|  |  |  |  | Adjusted geometric mean |  |  | Adjusted geometric mean ratio |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Timing | Sub-Group | Group | N | Value | LL | UL | Value | LL | UL | P-value for the ratio |
| PII(M2) | 18-49ys | HZ/su | 10 | 740.4 | 347.1 | 1411.0 | 3.90 | 0.86 | 17.64 | 0.0744 |
|  |  | Placebo | 7 | 190.0 | 1.0 | 547.6 | . |  |  | . |
|  | $\geq 50 y s$ | HZ/su | 14 | 913.6 | 613.7 | 1322.5 | 15.81 | 4.75 | 52.70 | <. 0001 |
|  |  | Placebo | 22 | 57.8 | -0.8 | 132.6 | . | . | . | . |

$18-49 y s=$ Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in a given category with available results
LL = Lower Limit, UL = Upper Limit and CI = Confidence Interval Confidence Interval (CI) were back transformed to original units The $p$-value is relative to the null hypothesis Ho: Vaccine $/$ Placebo $=1$ PII(M2) = Post-vaccination Dose II (Month 2)

Table 8.1 Number and percentage of subjects who received study vaccine doses (Total Vaccinated Cohort)

|  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=117 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=115 \end{gathered}$ |  | Total$N=232$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Total number of doses received | n | \% | n | \% | n | \% |
| 1 | 17 | 14.5 | 5 | 4.3 | 22 | 9.5 |
| 2 | 100 | 85.5 | 110 | 95.7 | 210 | 90.5 |
| Any | 117 | 100 | 115 | 100 | 232 | 100 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in each group or in total included in the considered cohort
$\mathrm{n} / \%=$ number/percentage of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least one dose
Table 8.2 Compliance in returning symptom sheets (Total Vaccinated Cohort)

| Dose | Group | Number <br> of <br> doses | Noses <br> NOT <br> according to <br> protocol | Number <br> of <br> general SS | Compliance <br> \% <br> general SS | Number <br> of <br> local SS | Compliance <br> $\%$ |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| local SS |  |  |  |  |  |  |  |$|$

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
SS = Symptom screens/sheets used for the collection of local and general solicited AEs
Compliance $\%=$ (number of doses with symptom screen/sheet return / number of administered doses) $\times 100$

Table 8.3 Incidence and nature of symptoms (solicited and unsolicited) reported during the 7 -day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated Cohort)

|  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | HZ/su | 117 | 106 | 90.6 | 83.8 | 95.2 | 117 | 84 | 71.8 | 62.7 | 79.7 | 117 | 88 | 75.2 | 66.4 | 82.7 |
|  | Placebo | 115 | 58 | 50.4 | 41.0 | 59.9 | 115 | 57 | 49.6 | 40.1 | 59.0 | 115 | 4 | 3.5 | 1.0 | 8.7 |
| Dose 2 | HZ/su | 100 | 82 | 82.0 | 73.1 | 89.0 | 100 | 76 | 76.0 | 66.4 | 84.0 | 100 | 56 | 56.0 | 45.7 | 65.9 |
|  | Placebo | 110 | 84 | 76.4 | 67.3 | 83.9 | 110 | 84 | 76.4 | 67.3 | 83.9 | 110 |  | 5.5 | 2.0 | 11.5 |
| Overall/dose | HZ/su | 217 | 188 | 86.6 | 81.4 | 90.9 | 217 | 160 | 73.7 | 67.3 | 79.5 | 217 | 144 | 66.4 | 59.7 | 72.6 |
|  | Placebo | 225 | 142 | 63.1 | 56.4 | 69.4 | 225 | 141 | 62.7 | 56.0 | 69.0 | 225 | 10 | 4.4 | 2.2 | 8.0 |
| Overall/subject | HZ/su | 117 | 109 | 93.2 | 87.0 | 97.0 | 117 | 99 | 84.6 | 76.8 | 90.6 | 117 | 94 | 80.3 | 72.0 | 87.1 |
|  | Placebo | 115 | 92 | 80.0 | 71.5 | 86.9 | 115 | 92 | 80.0 | 71.5 | 86.9 | 115 | 9 | 7.8 | 3.6 | 14.3 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$N=$ number of administered doses
$\mathrm{n} / \%$ = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, $\mathrm{LL}=$ Lower Limit, UL = Upper Limit

Table 8.4 Incidence and nature of grade 3 symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated Cohort)

|  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | HZ/su | 117 | 22 | 18.8 | 12.2 | 27.1 | 117 | 17 | 14.5 | 8.7 | 22.2 | 117 | 10 | 8.5 | 4.2 | 15.2 |
|  | Placebo | 115 | 13 | 11.3 | 6.2 | 18.6 | 115 | 13 | 11.3 | 6.2 | 18.6 | 115 | 0 | 0.0 | 0.0 | 3.2 |
| Dose 2 | HZ/su | 100 | 19 | 19.0 | 11.8 | 28.1 | 100 | 18 | 18.0 | 11.0 | 26.9 | 100 | 4 | 4.0 | 1.1 | 9.9 |
|  | Placebo | 110 | 12 | 10.9 | 5.8 | 18.3 | 110 | 12 | 10.9 | 5.8 | 18.3 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Overall/dose | HZ/su | 217 | 41 | 18.9 | 13.9 | 24.7 | 217 | 35 | 16.1 | 11.5 | 21.7 | 217 | 14 | 6.5 | 3.6 | 10.6 |
|  | Placebo | 225 | 25 | 11.1 | 7.3 | 16.0 | 225 | 25 | 11.1 | 7.3 | 16.0 | 225 | 0 | 0.0 | 0.0 | 1.6 |
| Overall/subject | HZ/su | 117 | 31 | 26.5 | 18.8 | 35.5 | 117 | 28 | 23.9 | 16.5 | 32.7 | 117 | 13 | 11.1 | 6.1 | 18.3 |
|  | Placebo | 115 | 21 | 18.3 | 11.7 | 26.5 | 115 |  | 18.3 | 11.7 | 26.5 | 115 |  | 0.0 | 0.0 | 32 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.5 Number and percentage of subjects who reported temperature by half degree measured during the 7 -day (Days $0-6$ ) post-vaccination period following each dose (no conversion) (Total Vaccinated Cohort)

|  |  | HZ/su |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95 \% Cl |  |  |  |  |  |  | 95 \% Cl |  |
| Symptom | Type | N | n \% | LL | UL | N | n $\%$ | \% L | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |
| Temperature/(*) ( ${ }^{\circ} \mathrm{C}$ ) | All | 1121 | 1311.6 | 6.3 | 19.0 | 110 | 43.6 | 3.61 | 1.0 | 9.0 |
|  | $\geq 35.5$ | 1121 | 1311.6 | 6.3 | 19.0 | 110 | 4 3.6 | 3.61 | 1.0 | 9.0 |
|  | >36.0 | 1121 | 1311.6 | 6.3 | 19.0 | 110 | 43.6 | 3.61 | 1.0 | 9.0 |
|  | >36.5 | 1121 | 1311.6 | 6.3 | 19.0 | 110 | 43.6 | 3.61 | 1.0 | 9.0 |
|  | >37.0 | 1121 | 1311.6 | 6.3 | 19.0 | 110 | 43.6 | 3.61 | 1.0 | 9.0 |
|  | >37.5 | 1128 | 87.1 | 3.1 | 13.6 | 110 | 43.6 | 3.61 | 1.0 | 9.0 |
|  | >38.0 | 1122 | 21.8 | 0.2 | 6.3 | 110 | 00. | 0.00 | 0.0 | 3.3 |
|  | >38.5 | 1121 | 10.9 | 0.0 | 4.9 | 110 | 00. | 0.00 | 0.0 | 3.3 |
|  | >39.0 | 1120 | 00.0 | 0.0 | 3.2 | 110 | 00. | 0.00 | 0.0 | 3.3 |
|  | >39.5 | 1120 | 00.0 | 0.0 | 3.2 | 110 | 00. | 0.00 | 0.0 | 3.3 |
|  | >40.0 | 1120 | 00.0 | 0.0 | 3.2 | 110 | 00. | 0.00 | 0.0 | 3.3 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |
| Temperature/(*) ( ${ }^{\circ} \mathrm{C}$ ) | All | 97 | 88.2 | 3.6 | 15.6 | 104 | 11.0 | 1.00 | 0.0 | 5.2 |
|  | $\geq 35.5$ | 978 | 88.2 | 3.6 | 15.6 | 104 | 11.0 | 1.00 | 0.0 | 5.2 |
|  | $>36.0$ | 978 | 88.2 | 3.6 | 15.6 | 104 | 11.0 | 1.00 | 0.0 | 5.2 |
|  | >36.5 | 978 | 88.2 | 3.6 | 15.6 | 104 | 411.0 | 1.00 | 0.0 | 5.2 |
|  | >37.0 | 978 | 88.2 | 3.6 | 15.6 | 104 | 411.0 | 1.00 | 0.0 | 5.2 |
|  | >37.5 | 97 | 44.1 | 1.1 | 10.2 | 104 | 11.0 | 1.00 | 0.0 | 5.2 |
|  | >38.0 | 97 | 11.0 | 0.0 | 5.6 | 104 | 11.0 | 1.00 | 0.0 | 5.2 |
|  | >38.5 | 970 | 00.0 | 0.0 | 3.7 | 104 | 00.0 | 0.00 | 0.0 | 3.5 |
|  | >39.0 | 970 | 00.0 | 0.0 | 3.7 | 104 | 00. | 0.00 | 0.0 | 3.5 |
|  | >39.5 | 970 | 00.0 | 0.0 | 3.7 | 104 | 00.0 | 0.00 | 0.0 | 3.5 |
|  | >40.0 | 970 | 00.0 | 0.0 | 3.7 | 104 | 00.0 | 0.00 | 0.0 | 3.5 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |
| Temperature/(*) ( ${ }^{\circ} \mathrm{C}$ ) | All | 209 | 2110.0 | 6.3 | 14.9 | 214 | 52. | 2.30 | 0.8 | 5.4 |
|  | $\geq 35.5$ | 2092 | 2110.0 | 6.3 | 14.9 | 214 | 52. | 2.30 | 0.8 | 5.4 |
|  | >36.0 | 2092 | 2110.0 | 6.3 | 14.9 | 214 | 52. | 2.30 | 0.8 | 5.4 |
|  | >36.5 | 2092 | 2110.0 | 6.3 | 14.9 | 214 | 52. | 2.30 | 0.8 | 5.4 |
|  | >37.0 | 2092 | 2110.0 | 6.3 | 14.9 | 214 | 52. | 2.30 | 0.8 | 5.4 |
|  | >37.5 | 209 | 125.7 | 3.0 | 9.8 | 214 | 52. | 2.30 | 0.8 | 5.4 |
|  | >38.0 | 2093 | 31.4 | 0.3 | 4.1 | 214 | 10.5 | 0.50 | 0.0 | 2.6 |
|  | >38.5 | 2091 | 10.5 | 0.0 | 2.6 | 214 | 00.0 | 0.00 | 0.0 | 1.7 |
|  | >39.0 | 2090 | 00.0 | 0.0 | 1.7 | 214 | 00.0 | 0.00 | 0.0 | 1.7 |
|  | >39.5 | 2090 | 00.0 | 0.0 | 1.7 | 214 | 00.0 | 0.00 | 0.0 | 1.7 |
|  | >40.0 | 2090 | 00.0 | 0.0 | 1.7 | 214 | 00. | 0.00 | 0.0 | 1.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |
| Temperature/(*) ( ${ }^{\circ} \mathrm{C}$ ) | All | 112 | 2017.9 | 11.3 | 26.2 | 110 | 54.5 | 4.51 | 1.5 | 10.3 |
|  | $\geq 35.5$ | 112 | 2017.9 | 11.3 | 26.2 | 110 | 54. | 4.51 | 1.5 | 10.3 |
|  | >36.0 | 112 | 2017.9 | 11.3 | 26.2 | 110 | 54. | 4.51 | 1.5 | 10.3 |
|  | >36.5 | 112 | 2017.9 | 11.3 | 26.2 | 110 | 54. | 4.51 | 1.5 | 10.3 |
|  | >37.0 | 112 | 2017.9 | 11.3 | 26.2 | 110 | 54. | 4.51 | 1.5 | 10.3 |
|  | >37.5 | 112 | 119.8 | 5.0 | 16.9 | 110 | 54. | 4.51 | 1.5 | 10.3 |
|  | >38.0 | 112 | 32.7 | 0.6 | 7.6 | 110 | 10.9 | 0.90 | 0.0 | 5.0 |
|  | >38.5 | 112 | 10.9 | 0.0 | 4.9 | 110 | 00. | 0.00 | 0.0 | 3.3 |
|  | >39.0 | 1120 | 00.0 | 0.0 | 3.2 | 110 | 00. | 0.00 | 0.0 | 3.3 |
|  | >39.5 | 1120 | 00.0 | 0.0 | 3.2 | 110 | 00.0 | 0.00 | 0.0 | 3.3 |
|  | >40.0 | 1120 | 00.0 | 0.0 | 3.2 | 110 | 00. | 0.00 | 0.0 | 3.3 |

## CONFIDENTIAL

HZ/su = Herpes Zoster sub-unit vaccine group<br>Placebo = Placebo group<br>For each dose and overall/subject:<br>$\mathrm{N}=$ number of subjects with at least one documented dose<br>$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once<br>For Overall/dose:<br>$\mathrm{N}=$ number of documented doses<br>$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom<br>95\%CI = Exact 95\% confidence interval; LL = lower limit, UL = upper limit<br>$\left(^{*}\right)=$ Temperature is measured by oral, axillary or tympanic routes<br>Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for oral, axillary or tympanic route

Table 8.6 Number and percentage of subjects who reported temperature by half degree measured via oral route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) (Total Vaccinated Cohort)

|  |  | HZ/su |  |  |  | Placebo |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95 \% Cl |  |  |  |  |  | 95 \% CI |  |
| Symptom | Type |  | n \% | \% LL | LL UL | N | n \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 112 | 43.6 | 3.61 .0 | 1.08 .9 | 110 | 10.9 | 0.0 | 5.0 |
|  | $\geq 35.5$ | 112 | 43.6 | 3.61 .0 | 1.08 .9 | 110 | 10.9 | 0.0 | 5.0 |
|  | >36.0 | 112 | 43.6 | 3.61 .0 | 1.08 .9 | 110 | 10.9 | 0.0 | 5.0 |
|  | >36.5 | 112 | 43.6 | 3.61 .0 | 1.08 .9 | 110 | 10.9 | 0.0 | 5.0 |
|  | >37.0 | 112 | 43.6 | 3.61 .0 | 1.08 .9 | 110 | 10.9 | 0.0 | 5.0 |
|  | >37.5 | 112 | 10.9 | 0.90 .0 | 0.0 4.9 | 110 | 10.9 | 0.0 | 5.0 |
|  | >38.0 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >38.5 | 1120 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >39.0 | 1120 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >39.5 | 1120 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >40.0 | 1120 | 00.0 | 0.00 .0 | 0.03 .2 | 110 |  | 0.0 | 3.3 |
| Dose 2 |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 97 | 33.1 | 3.10 .6 | 0.68 .8 | 104 | 00.0 | 0.0 | 3.5 |
|  | $\geq 35.5$ | 97 | 33.1 | 3.10 .6 | 0.68 .8 | 104 | 00.0 | 0.0 | 3.5 |
|  | >36.0 | 97 | 33.1 | 3.10 .6 | 0.68 .8 | 104 | 00.0 | 0.0 | 3.5 |
|  | >36.5 | 97 | 33.1 | 3.10 .6 | 0.68 .8 | 104 | 00.0 | 0.0 | 3.5 |
|  | >37.0 | 97 | 33.1 | 3.10 .6 | 0.68 .8 | 104 | 00.0 | 0.0 | 3.5 |
|  | >37.5 | 97 | 33.1 | 3.10 .6 | 0.68 .8 | 104 | 00.0 | 0.0 | 3.5 |
|  | >38.0 | 97 | 11.0 | 1.00 .0 | 0.05 .6 | 104 | 00.0 | 0.0 | 3.5 |
|  | >38.5 | 97 | 00.0 | 0.00 .0 | 0.03 .7 | 104 | 00.0 | 0.0 | 3.5 |
|  | >39.0 | 97 | 00.0 | 0.00 .0 | 0.03 .7 | 104 | 00.0 | 0.0 | 3.5 |
|  | >39.5 | 97 | 00.0 | 0.00 .0 | 0.03 .7 | 104 |  | 0.0 | 3.5 |
|  | >40.0 | 97 | 00.0 | 0.00 .0 | 0.03 .7 | 104 |  | 0.0 | 3.5 |
| Overall/dose |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 2097 | 73.3 | 3.31 .4 | 1.46 .8 | 214 | 10.5 | 0.0 | 2.6 |
|  | $\geq 35.5$ | 2097 | 73.3 | 3.31 .4 | 1.46 .8 | 214 | 10.5 | 0.0 | 2.6 |
|  | >36.0 | 2097 | 73.3 | 3.31 .4 | 1.46 .8 | 214 | 10.5 | 0.0 | 2.6 |
|  | >36.5 | 2097 | 73.3 | 3.31 .4 | 1.46 .8 | 214 | 10.5 | 0.0 | 2.6 |
|  | >37.0 | 2097 | 73.3 | 3.31 .4 | 1.46 .8 | 214 | 10.5 | 0.0 | 2.6 |
|  | >37.5 | 209 | 41.9 | 1.90 .5 | 0.54 .8 | 214 | 10.5 | 0.0 | 2.6 |
|  | >38.0 | 209 | 10.5 | 0.50 .0 | 0.02 .6 | 214 | 00.0 | 0.0 | 1.7 |
|  | >38.5 | 2090 | 00.0 | 0.00 .0 | 0.01 .7 | 214 |  | 0.0 | 1.7 |
|  | >39.0 | 209 | 00.0 | 0.00 .0 | 0.01 .7 | 214 |  | 0.0 | 1.7 |
|  | >39.5 | 2090 | 00.0 | 0.00 .0 | 0.01 .7 | 214 | 00.0 | 0.0 | 1.7 |
|  | >40.0 | 2090 | 00.0 | 0.00 .0 | 0.01 .7 | 214 |  | 0.0 | 1.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 112 | 65.4 | 5.42 .0 | 2.011 .3 | 110 | 10.9 | 0.0 | 5.0 |
|  | $\geq 35.5$ | 112 | 65.4 | 5.42 .0 | 2.011 .3 | 110 | 10.9 | 0.0 | 5.0 |
|  | >36.0 | 112 | 65.4 | 5.42 .0 | 2.011 .3 | 110 | 10.9 | 0.0 | 5.0 |
|  | >36.5 | 112 | 65.4 | 5.42 .0 | 2.011 .3 | 110 | 10.9 | 0.0 | 5.0 |
|  | >37.0 | 112 | 65.4 | 5.42 .0 | 2.011 .3 | 110 | 10.9 | 0.0 | 5.0 |
|  | >37.5 | 112 | 32.7 | 2.70 .6 | 0.67 .6 | 110 | 10.9 | 0.0 | 5.0 |
|  | >38.0 | 112 | 10.9 | 0.90 .0 | 0.04 .9 | 110 | 00.0 | 0.0 | 3.3 |
|  | >38.5 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >39.0 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >39.5 | 1120 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >40.0 | 1120 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |

## CONFIDENTIAL

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
95\%CI = Exact 95\% confidence interval; LL = lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for oral route

Table 8.7 Number and percentage of subjects who reported temperature by half degree measured via axillary route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) (Total Vaccinated Cohort)

|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95\% Cl |  |  |  |  |  | 95 \% Cl |  |  |  |
| Symptom | Type | N | n | \% |  | UL | N |  | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 112 | 9 | 8.0 | 3.7 | 714.7 | 110 | \| 3 | 2.7 | 0.6 | 7.8 |
|  | $\geq 35.5$ | 112 | 9 | 8.0 | 3.7 | 714.7 | 110 | 3 | 2.7 | 0.6 | 7.8 |
|  | >36.0 | 112 | 9 | 8.0 | 3.7 | 714.7 | 110 | 10 | 2.7 | 0.6 | 7.8 |
|  | >36.5 | 112 | 9 | 8.0 | 3.7 | 714.7 | 110 | 3 | 2.7 | 0.6 | 7.8 |
|  | >37.0 | 112 | 9 | 8.0 | 3.7 | 714.7 | 110 | - 3 | 2.7 | 0.6 | 7.8 |
|  | >37.5 | 112 | 7 | 6.3 | 2.5 | 512.5 | 110 | 3 | 2.7 | 0.6 | 7.8 |
|  | $>38.0$ | 112 | 2 | 1.8 | 0.2 | 26.3 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >38.5 | 112 | 1 | 0.9 | 0.0 | 04.9 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >39.0 | 112 | 0 | 0.0 | 0.0 | 03.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >39.5 | 1120 | 0 | 0.0 | 0.0 | 03.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >40.0 | 1120 | 0 | 0.0 | 0.0 | 03.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 97 | 4 | 4.1 | 1.1 | 110.2 | 104 | 41 | 1.0 | 0.0 | 5.2 |
|  | $\geq 35.5$ | 97 | 4 | 4.1 | 1.1 | 110.2 | 104 | 1 | 1.0 | 0.0 | 5.2 |
|  | $>36.0$ | 97 | 4 | 4.1 | 1.1 | 110.2 | 104 | 4 | 1.0 | 0.0 | 5.2 |
|  | >36.5 | 97 | 4 | 4.1 | 1.1 | 110.2 | 104 | 4 | 1.0 | 0.0 | 5.2 |
|  | >37.0 | 97 | 4 | 4.1 | 1.1 | 110.2 | 104 | 4 | 1.0 | 0.0 | 5.2 |
|  | $>37.5$ | 97 | 1 | 1.0 | 0.0 | 05.6 | 104 | 1 | 1.0 | 0.0 | 5.2 |
|  | >38.0 | 97 | 0 | 0.0 | 0.0 | 03.7 | 104 | 1 | 1.0 | 0.0 | 5.2 |
|  | $>38.5$ | 97 | 0 | 0.0 | 0.0 | 03.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | $>39.0$ | 97 | 0 | 0.0 | 0.0 | 03.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | >39.5 | 97 | 0 | 0.0 | 0.0 | 03.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |
|  | >40.0 | 97 | 0 | 0.0 | 0.0 | 03.7 | 104 | 0 | 0.0 | 0.0 | 3.5 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 209 | 13 | 6.2 | 3.4 | 410.4 | 214 | 4 | 1.9 | 0.5 | 4.7 |
|  | $\geq 35.5$ | 209 | 13 | 6.2 | 3.4 | 410.4 | 214 | 4 | 1.9 | 0.5 | 4.7 |
|  | $>36.0$ | 209 | 13 | 6.2 | 3.4 | 410.4 | 214 | 4 | 1.9 | 0.5 | 4.7 |
|  | >36.5 | 209 | 13 | 6.2 | 3.4 | 410.4 | 214 | 4 | 1.9 | 0.5 | 4.7 |
|  | >37.0 | 209 | 13 | 6.2 | 3.4 | 410.4 | 214 | 4 | 1.9 | 0.5 | 4.7 |
|  | >37.5 | 209 | 8 | 3.8 | 1.7 | 77.4 | 214 | 4 | 1.9 | 0.5 | 4.7 |
|  | $>38.0$ | 2092 | 2 | 1.0 |  | 13.4 | 214 | 1 | 0.5 | 0.0 | 2.6 |
|  | >38.5 | 209 | 1 | 0.5 | 0.0 | 02.6 | 214 | 0 | 0.0 | 0.0 | 1.7 |
|  | >39.0 | 2090 | 0 | 0.0 | 0.0 | 01.7 | 214 | 0 | 0.0 | 0.0 | 1.7 |
|  | $>39.5$ | 2090 | 0 | 0.0 | 0.0 | 01.7 | 214 | 0 | 0.0 | 0.0 | 1.7 |
|  | >40.0 | 209 | 0 | 0.0 |  | 01.7 | 214 | 0 | 0.0 | 0.0 | 1.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 112 | 13 | 11.6 | 6.3 | 319.0 | 110 | \| 4 | 3.6 | 1.0 | 9.0 |
|  | $\geq 35.5$ | 112 | 13 | 11.6 | 6.3 | 319.0 | 110 | 4 | 3.6 | 1.0 | 9.0 |
|  | >36.0 | 112 | 13 | 11.6 | 6.3 | 319.0 | 110 | 4 | 3.6 | 1.0 | 9.0 |
|  | >36.5 | 112 | 13 | 11.6 | 6.3 | 319.0 | 110 | 4 | 3.6 | 1.0 | 9.0 |
|  | >37.0 | 112 | 13 | 11.6 | 6.3 | 319.0 | 110 | 4 | 3.6 | 1.0 | 9.0 |
|  | >37.5 | 112 | 8 | 7.1 | 3.1 | 113.6 | 110 | 4 | 3.6 | 1.0 | 9.0 |
|  | >38.0 | 112 | 2 | 1.8 | 0.2 | 26.3 | 110 | 1 | 0.9 | 0.0 | 5.0 |
|  | >38.5 | 112 | 1 | 0.9 | 0.0 | 04.9 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >39.0 | 112 | 0 | 0.0 | 0.0 | 03.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >39.5 | 112 | 0 | 0.0 | 0.0 | 03.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |
|  | >40.0 | 1120 | 0 | 0.0 |  | 03.2 | 110 | 0 | 0.0 | 0.0 | 3.3 |

## CONFIDENTIAL

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
95\%CI = Exact 95\% confidence interval; LL = lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for axillary route

Table 8.8 Number and percentage of subjects who reported temperature by half degree measured via tympanic route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) (Total Vaccinated Cohort)

|  |  | HZ/su |  |  |  | Placebo |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95 \% Cl |  |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N | n \% | \% LL | L UL | N | n \% | LL |  |
| Dose 1 |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | $\geq 35.5$ | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >36.0 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >36.5 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >37.0 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >37.5 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >38.0 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >38.5 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >39.0 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >39.5 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >40.0 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
| Dose 2 |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 97 | 11.0 | 1.00 .0 | 0.05 .6 | 104 | 00.0 | 0.0 | 3.5 |
|  | $\geq 35.5$ | 97 | 11.0 | 1.00 .0 | 0.05 .6 | 104 | 00.0 | 0.0 | 3.5 |
|  | >36.0 | 97 | 11.0 | 1.00 .0 | 0.05 .6 | 104 | 00.0 | 0.0 | 3.5 |
|  | >36.5 | 97 | 11.0 | 1.00 .0 | 0.05 .6 | 104 | 00.0 | 0.0 | 3.5 |
|  | >37.0 | 97 | 11.0 | 1.00 .0 | 0.05 .6 | 104 | 00.0 | 0.0 | 3.5 |
|  | >37.5 | 97 | 00.0 | 0.00 .0 | 0.03 .7 | 104 | 00.0 | 0.0 | 3.5 |
|  | $>38.0$ | 97 | 00.0 | 0.00 .0 | 0.03 .7 | 104 | 00.0 | 0.0 | 3.5 |
|  | >38.5 | 97 | 00.0 | 0.00 .0 | 0.03 .7 | 104 | 00.0 | 0.0 | 3.5 |
|  | >39.0 | 97 | 00.0 | 0.00 .0 | 0.03 .7 | 104 | 00.0 | 0.0 | 3.5 |
|  | >39.5 | 97 | 00.0 | 0.00 .0 | 0.0 3.7 | 104 | 00.0 | 0.0 | 3.5 |
|  | >40.0 | 97 | 00.0 | 0.00 .0 | 0.03 .7 | 104 | 00.0 | 0.0 | 3.5 |
| Overall/dose |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 209 | 10.5 | 0.50 .0 | 0.0 2.6 | 214 | 00.0 | 0.0 | 1.7 |
|  | $\geq 35.5$ | 209 | 10.5 | 0.50 .0 | 0.02 .6 | 214 | 00.0 | 0.0 | 1.7 |
|  | >36.0 | 209 | 10.5 | 0.50 .0 | 0.02 .6 | 214 | 00.0 | 0.0 | 1.7 |
|  | $>36.5$ | 209 | 10.5 | 0.50 .0 | 0.02 .6 | 214 | 00.0 | 0.0 | 1.7 |
|  | >37.0 | 209 | 10.5 | 0.50 .0 | 0.02 .6 | 214 | 00.0 | 0.0 | 1.7 |
|  | >37.5 | 209 | 00.0 | 0.00 .0 | 0.01 .7 | 214 | 00.0 | 0.0 | 1.7 |
|  | >38.0 | 209 | 00.0 | 0.00 .0 | 0.01 .7 | 214 | 00.0 | 0.0 | 1.7 |
|  | >38.5 | 209 | 00.0 | 0.00 .0 | 0.01 .7 | 214 | 00.0 | 0.0 | 1.7 |
|  | >39.0 | 209 | 00.0 | 0.00 .0 | 0.01 .7 | 214 | 00.0 | 0.0 | 1.7 |
|  | >39.5 | 209 | 00.0 | 0.00 .0 | 0.01 .7 | 214 |  | 0.0 | 1.7 |
|  | >40.0 | 209 | 00.0 | 0.00 .0 | 0.01 .7 | 214 | 00.0 | 0.0 | 1.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) $\left({ }^{\circ} \mathrm{C}\right)$ | All | 112 | 10.9 | 0.90 .0 | 0.04 .9 | 110 | 00.0 | 0.0 | 3.3 |
|  | $\geq 35.5$ | 112 | 10.9 | 0.90 .0 | 0.04 .9 | 110 | 00.0 | 0.0 | 3.3 |
|  | >36.0 | 112 | 10.9 | 0.90 .0 | 0.04 .9 | 110 | 00.0 | 0.0 | 3.3 |
|  | >36.5 | 112 | 10.9 | 0.90 .0 | 0.04 .9 | 110 | 00.0 | 0.0 | 3.3 |
|  | >37.0 | 112 | 10.9 | 0.90 .0 | 0.04 .9 | 110 | 00.0 | 0.0 | 3.3 |
|  | >37.5 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >38.0 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >38.5 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >39.0 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >39.5 | 112 | 00.0 | 0.00 .0 | 0.03 .2 | 110 | 00.0 | 0.0 | 3.3 |
|  | >40.0 | 112 | 00.0 | 0.00 .0 | 0.0 3.2 | 110 | 00.0 | 0.0 | 3.3 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; $\mathrm{LL}=$ lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for tympanic route
Table 8.9 Number and percentage of subjects who reported temperature by half degree measured via rectal route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) (Total Vaccinated Cohort)

No records exist in this table

Table 8.10 Number of days with local symptoms during the solicited postvaccination period (Total Vaccinated Cohort)

| Solicited symptom | Dose | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Pain | Dose 1 | HZ/su | 83 | 2.8 | 1.0 | 2.0 | 2.0 | 4.0 | 7.0 |
|  |  | Placebo | 2 | 2.0 | 1.0 | 1.0 | 2.0 | 3.0 | 3.0 |
|  | Dose 2 | HZ/su | 52 | 2.7 | 1.0 | 1.0 | 2.0 | 3.5 | 7.0 |
|  |  | Placebo | 5 | 2.4 | 1.0 | 1.0 | 1.0 | 2.0 | 7.0 |
|  | Overall/dose | HZ/su | 135 | 2.8 | 1.0 | 2.0 | 2.0 | 4.0 | 7.0 |
|  |  | Placebo | 7 | 2.3 | 1.0 | 1.0 | 1.0 | 3.0 | 7.0 |
| Redness | Dose 1 | HZ/su | 33 | 3.6 | 1.0 | 2.0 | 3.0 | 5.0 | 7.0 |
|  | Dose 2 | HZ/su | 20 | 3.6 | 1.0 | 2.0 | 4.0 | 5.0 | 7.0 |
|  | Overall/dose | HZ/su | 53 | 3.6 | 1.0 | 2.0 | 4.0 | 5.0 | 7.0 |
| Swelling | Dose 1 | HZ/su | 15 | 3.7 | 2.0 | 2.0 | 4.0 | 5.0 | 7.0 |
|  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |
|  | Dose 2 | HZ/su | 8 | 3.8 | 1.0 | 2.0 | 3.5 | 5.5 | 7.0 |
|  | Overall/dose | HZ/su | 23 | 3.7 | 1.0 | 2.0 | 4.0 | 5.0 | 7.0 |
|  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.11 Number of days with grade 3 local symptoms during the solicited post-vaccination period (Total Vaccinated Cohort)

| Solicited symptom | Dose | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| Pain | Dose 1 | HZ/su | 8 | 1.1 | 1.0 | 1.0 | 1.0 | 1.0 | 2.0 |
|  | Dose 2 | $\mathrm{HZ/su}$ | 4 | 2.5 | 1.0 | 2.0 | 3.0 | 3.0 | 3.0 |
|  | Overall/dose | $\mathrm{HZ} /$ su | 12 | 1.6 | 1.0 | 1.0 | 1.0 | 2.5 | 3.0 |
| Redness | Dose 1 | $\mathrm{HZ/su}$ | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | $\mathrm{HZ/su}$ | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 = 25th percentile
Q3 $=75$ th percentile
Table 8.12 Number of days with local symptoms (Total Vaccinated Cohort)

| Solicited symptom | Dose | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Pain | Dose 1 | HZ/su | 83 | 2.9 | 1.0 | 2.0 | 2.0 | 4.0 | 15.0 |
|  |  | Placebo | 2 | 2.0 | 1.0 | 1.0 | 2.0 | 3.0 | 3.0 |
|  | Dose 2 | HZ/su | 52 | 2.8 | 1.0 | 1.0 | 2.0 | 3.5 | 11.0 |
|  |  | Placebo | 5 | 4.4 | 1.0 | 1.0 | 1.0 | 2.0 | 17.0 |
|  | Overall/dose | HZ/su | 135 | 2.9 | 1.0 | 2.0 | 2.0 | 4.0 | 15.0 |
|  |  | Placebo | 7 | 3.7 | 1.0 | 1.0 | 1.0 | 3.0 | 17.0 |
| Redness | Dose 1 | HZ/su | 33 | 4.2 | 1.0 | 2.0 | 3.0 | 5.0 | 15.0 |
|  | Dose 2 | HZ/su | 20 | 4.3 | 1.0 | 2.0 | 4.0 | 5.5 | 11.0 |
|  | Overall/dose | HZ/su | 53 | 4.2 | 1.0 | 2.0 | 4.0 | 5.0 | 15.0 |
| Swelling | Dose 1 | HZ/su | 15 | 4.9 | 2.0 | 2.0 | 4.0 | 5.0 | 14.0 |
|  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |
|  | Dose 2 | HZ/su | 8 | 4.5 | 1.0 | 2.0 | 3.5 | 7.0 | 10.0 |
|  | Overall/dose | HZ/su | 23 | 4.8 | 1.0 | 2.0 | 4.0 | 5.0 | 14.0 |
|  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of doses with the symptom (during the solicited post-vaccination period and beyond)
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.13 Solicited local symptoms ongoing beyond the 7-day (Days 0-6) postvaccination period (Total Vaccinated Cohort)

|  |  | HZ/su |  |  |  |  |  | Placebo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | Time to resolution (days) |  |  |  |  |  | Time to resolution (days) |  |  |
| Symptoms | Type | N | Ns |  | q1 | median | q3 | N | Ns |  | q1 | median | q3 |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | Any | 112 | 83 | 1 | 8 | 8 | 8 | 110 | 2 | 0 | - | - | - |
|  | Grade 3 | 112 | 8 | 0 | - | - | - | 110 | 0 | 0 | - | - | - |
| Redness | Any | 112 | 33 | 4 | 3 | 3 | 6 | 110 | 0 | 0 | - | - | - |
|  | Grade 3 | 112 | 2 | 0 | - | - | - | 110 | 0 | 0 | - | - | - |
| Swelling | Any | 112 | 15 | 3 | 3 | 6 | 9 | 110 | 1 | 0 | - | - | - |
|  | Grade 3 | 112 | 0 | 0 | - | - | - | 110 | 0 | 0 | - | - | - |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | Any | 98 | 52 | 2 | 3 | 5 | 7 | 105 | 5 |  | 10 | 10 | 10 |
|  | Grade 3 | 98 | 4 | 2 | 3 | 5 | 7 | 105 | 0 | 0 | - | - | - |
| Redness | Any | 98 | 20 | 4 | 2.5 | 3 | 5 | 105 | 0 | 0 | - | - | - |
|  | Grade 3 | 98 | 0 | 0 | - | - | - | 105 | 0 | 0 | - | - | - |
| Swelling | Any | 98 | 8 | 2 | 3 | 3 | 3 | 105 | 0 | 0 | - | - | - |
|  | Grade 3 | 98 | 0 | 0 | - | - | - | 105 | 0 | 0 | - | - | - |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | Any | 210 | 135 | 3 | 3 | 7 | 8 | 215 | 7 |  | 10 | 10 | 10 |
|  | Grade 3 | 210 | 12 | 2 | 3 | 5 | 7 | 215 | 0 | 0 | - | - | - |
| Redness | Any | 210 | 53 | 8 | 3 | 3 | 5 | 215 | 0 | 0 | - | - | - |
|  | Grade 3 | 210 | 2 | 0 | - | - | - | 215 | 0 | 0 | - | - | - |
| Swelling | Any | 210 | 23 | 5 | 3 | 3 | 6 | 215 | 1 | 0 | - | - | - |
|  | Grade 3 | 210 | 0 | 0 | - | - | - | 215 | 0 | 0 |  | - | - |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of documented doses
Ns = total number of reports for a given symptom
$\mathrm{n}=$ number of symptoms that were ongoing after the follow-up period
Time to resolution : number of days beyond the end of the follow-up period
q1 $=25$ th percentile
$q 3=75$ th percentile

Table 8.14 Number of days with general symptoms during the solicited postvaccination period (Total Vaccinated Cohort)

| Solicited symptom | Dose | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Fatigue | Dose 1 | HZ/su | 56 | 3.6 | 1.0 | 1.5 | 3.0 | 6.0 | 7.0 |
|  |  | Placebo | 44 | 4.3 | 1.0 | 2.0 | 5.0 | 6.0 | 7.0 |
|  | Dose 2 | HZ/su | 57 | 4.5 | 1.0 | 2.0 | 5.0 | 7.0 | 7.0 |
|  |  | Placebo | 57 | 4.6 | 1.0 | 3.0 | 5.0 | 7.0 | 7.0 |
|  | Overal//dose | HZ/su | 113 | 4.1 | 1.0 | 2.0 | 4.0 | 6.0 | 7.0 |
|  |  | Placebo | 101 | 4.5 | 1.0 | 2.0 | 5.0 | 6.0 | 7.0 |
| Gastrointestinal symptoms | Dose 1 | HZ/su | 32 | 3.1 | 1.0 | 1.5 | 2.5 | 4.0 | 7.0 |
|  |  | Placebo | 21 | 4.1 | 1.0 | 2.0 | 4.0 | 6.0 | 7.0 |
|  | Dose 2 | HZ/su | 41 | 4.6 | 1.0 | 3.0 | 4.0 | 7.0 | 7.0 |
|  |  | Placebo | 39 | 4.1 | 1.0 | 2.0 | 3.0 | 7.0 | 7.0 |
|  | Overall/dose | HZ/su | 73 | 3.9 | 1.0 | 2.0 | 4.0 | 6.0 | 7.0 |
|  |  | Placebo | 60 | 4.1 | 1.0 | 2.0 | 3.5 | 6.0 | 7.0 |
| Headache | Dose 1 | HZ/su | 28 | 2.9 | 1.0 | 1.0 | 2.0 | 3.5 | 7.0 |
|  |  | Placebo | 24 | 3.0 | 1.0 | 1.5 | 2.0 | 4.5 | 7.0 |
|  | Dose 2 | HZ/su | 29 | 3.4 | 1.0 | 2.0 | 2.0 | 6.0 | 7.0 |
|  |  | Placebo | 25 | 3.0 | 1.0 | 1.0 | 2.0 | 5.0 | 7.0 |
|  | Overall/dose | HZ/su | 57 | 3.1 | 1.0 | 1.0 | 2.0 | 5.0 | 7.0 |
|  |  | Placebo | 49 | 3.0 | 1.0 | 1.0 | 2.0 | 5.0 | 7.0 |
| Myalgia | Dose 1 | HZ/su | 50 | 2.9 | 1.0 | 1.0 | 2.5 | 4.0 | 7.0 |
|  |  | Placebo | 17 | 3.5 | 1.0 | 2.0 | 2.0 | 6.0 | 7.0 |
|  | Dose 2 | HZ/su | 32 | 3.7 | 1.0 | 2.0 | 3.0 | 5.5 | 7.0 |
|  |  | Placebo | 23 | 4.6 | 1.0 | 3.0 | 5.0 | 7.0 | 7.0 |
|  | Overal//dose | HZ/su | 82 | 3.2 | 1.0 | 2.0 | 3.0 | 5.0 | 7.0 |
|  |  | Placebo | 40 | 4.1 | 1.0 | 2.0 | 4.5 | 6.0 | 7.0 |
| Shivering | Dose 1 | HZ/su | 27 | 2.0 | 1.0 | 1.0 | 2.0 | 3.0 | 5.0 |
|  |  | Placebo | 13 | 2.2 | 1.0 | 1.0 | 2.0 | 2.0 | 7.0 |
|  | Dose 2 | HZ/su | 20 | 3.5 | 1.0 | 1.0 | 3.0 | 6.0 | 7.0 |
|  |  | Placebo | 17 | 2.8 | 1.0 | 1.0 | 2.0 | 4.0 | 7.0 |
|  | Overall/dose | HZ/su | 47 | 2.6 | 1.0 | 1.0 | 2.0 | 3.0 | 7.0 |
|  |  | Placebo | 30 | 2.5 | 1.0 | 1.0 | 2.0 | 4.0 | 7.0 |
| Temperature | Dose 1 | HZ/su | 13 | 2.0 | 1.0 | 1.0 | 1.0 | 2.0 | 6.0 |
|  |  | Placebo | 4 | 2.0 | 1.0 | 1.0 | 1.0 | 3.0 | 5.0 |
|  | Dose 2 | HZ/su | 8 | 1.9 | 1.0 | 1.0 | 1.5 | 2.5 | 4.0 |
|  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | HZ/su | 21 | 2.0 | 1.0 | 1.0 | 1.0 | 2.0 | 6.0 |
|  |  | Placebo | 5 | 1.8 | 1.0 | 1.0 | 1.0 | 1.0 | 5.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.15 Number of days with grade 3 general symptoms during the solicited post-vaccination period (Total Vaccinated Cohort)

| Solicited symptom | Dose | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Fatigue | Dose 1 | HZ/su | 10 | 2.1 | 1.0 | 1.0 | 2.0 | 3.0 | 4.0 |
|  |  | Placebo 3 | 3 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  | Dose 2 | HZ/su | 9 | 3.2 | 1.0 | 2.0 | 2.0 | 4.0 | 7.0 |
|  |  | Placebo 6 | 6 | 1.8 | 1.0 | 1.0 | 1.0 | 3.0 | 4.0 |
|  | Overall/dose | HZ/su | 19 | 2.6 | 1.0 | 1.0 | 2.0 | 4.0 | 7.0 |
|  |  | Placebo 9 | 9 | 1.9 | 1.0 | 1.0 | 2.0 | 2.0 | 4.0 |
| Gastrointestinal symptoms | Dose 1 | HZ/su 2 | 2 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  | Placebo 5 | 5 | 2.0 | 1.0 | 1.0 | 2.0 | 3.0 | 3.0 |
|  | Dose 2 | HZ/su | 5 | 2.2 | 1.0 | 2.0 | 2.0 | 2.0 | 4.0 |
|  |  | Placebo 3 | 3 | 2.0 | 1.0 | 1.0 | 1.0 | 4.0 | 4.0 |
|  | Overall/dose | HZ/su | 7 | 2.1 | 1.0 | 2.0 | 2.0 | 2.0 | 4.0 |
|  |  | Placebo 8 | 8 | 2.0 | 1.0 | 1.0 | 1.5 | 3.0 | 4.0 |
| Headache | Dose 1 | HZ/su | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  |  | Placebo 1 | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Dose 2 | HZ/su | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  |  | Placebo 2 | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  | Overall/dose | HZ/su | 6 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | Placebo 3 | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
| Myalgia | Dose 1 | HZ/su | 8 | 1.9 | 1.0 | 1.0 | 1.0 | 2.0 | 6.0 |
|  |  | Placebo 3 | 3 | 2.3 | 1.0 | 1.0 | 3.0 | 3.0 | 3.0 |
|  | Dose 2 | HZ/su 4 | 4 | 1.8 | 1.0 | 1.5 | 2.0 | 2.0 | 2.0 |
|  |  | Placebo 1 | 1 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 |
|  | Overall/dose | HZ/su | 12 | 1.8 | 1.0 | 1.0 | 1.5 | 2.0 | 6.0 |
|  |  | Placebo 4 | 4 | 3.0 | 1.0 | 2.0 | 3.0 | 4.0 | 5.0 |
| Shivering | Dose 1 | HZ/su | 5 | 1.6 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  |  | Placebo 2 | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  | Dose 2 | HZ/su | 3 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | Placebo 1 | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | HZ/su | 8 | 1.4 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  |  | Placebo 3 | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 = 25th percentile
Q3 $=75$ th percentile

Table 8.16 Number of days with general symptoms (Total Vaccinated Cohort)

| Solicited symptom | Dose | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Fatigue | Dose 1 | HZ/su | 56 | 8.5 | 1.0 | 1.5 | 3.0 | 6.0 | 105.0 |
|  |  | Placebo | 44 | 9.0 | 1.0 | 2.0 | 5.0 | 7.0 | 76.0 |
|  | Dose 2 | HZ/su | 57 | 8.0 | 1.0 | 2.0 | 5.0 | 7.0 | 161.0 |
|  |  | Placebo | 57 | 10.5 | 1.0 | 3.0 | 5.0 | 7.0 | 139.0 |
|  | Overall/dose | HZ/su | 113 | 8.2 | 1.0 | 2.0 | 4.0 | 7.0 | 161.0 |
|  |  | Placebo | 101 | 9.9 | 1.0 | 2.0 | 5.0 | 7.0 | 139.0 |
| Gastrointestinal symptoms | Dose 1 | HZ/su | 32 | 3.5 | 1.0 | 1.5 | 3.0 | 4.5 | 11.0 |
|  |  | Placebo | 21 | 9.8 | 1.0 | 2.0 | 5.0 | 7.0 | 60.0 |
|  | Dose 2 | HZ/su | 41 | 7.7 | 1.0 | 3.0 | 5.0 | 7.0 | 104.0 |
|  |  | Placebo | 39 | 6.5 | 1.0 | 2.0 | 4.0 | 7.0 | 55.0 |
|  | Overall/dose | HZ/su | 73 | 5.8 | 1.0 | 2.0 | 4.0 | 7.0 | 104.0 |
|  |  | Placebo | 60 | 7.6 | 1.0 | 2.0 | 4.0 | 7.0 | 60.0 |
| Headache | Dose 1 | HZ/su | 28 | 5.1 | 1.0 | 1.0 | 2.0 | 4.0 | 66.0 |
|  |  | Placebo | 24 | 8.7 | 1.0 | 1.5 | 2.0 | 4.5 | 75.0 |
|  | Dose 2 | HZ/su | 29 | 4.4 | 1.0 | 2.0 | 2.0 | 6.0 | 29.0 |
|  |  | Placebo | 25 | 4.1 | 1.0 | 1.0 | 2.0 | 5.0 | 25.0 |
|  | Overall/dose | HZ/su | 57 | 4.8 | 1.0 | 1.0 | 2.0 | 5.0 | 66.0 |
|  |  | Placebo | 49 | 6.4 | 1.0 | 1.0 | 2.0 | 5.0 | 75.0 |
| Myalgia | Dose 1 | HZ/su | 50 | 4.9 | 1.0 | 1.0 | 2.5 | 4.0 | 105.0 |
|  |  | Placebo | 17 | 4.2 | 1.0 | 2.0 | 3.0 | 6.0 | 11.0 |
|  | Dose 2 | HZ/su | 32 | 4.1 | 1.0 | 2.0 | 3.5 | 6.5 | 10.0 |
|  |  | Placebo | 23 | 11.1 | 1.0 | 3.0 | 5.0 | 7.0 | 112.0 |
|  | Overall/dose | HZ/su | 82 | 4.6 | 1.0 | 2.0 | 3.0 | 5.0 | 105.0 |
|  |  | Placebo | 40 | 8.2 | 1.0 | 2.0 | 5.0 | 6.5 | 112.0 |
| Shivering | Dose 1 | HZ/su | 27 | 2.1 | 1.0 | 1.0 | 2.0 | 3.0 | 7.0 |
|  |  | Placebo | 13 | 4.6 | 1.0 | 1.0 | 2.0 | 2.0 | 38.0 |
|  | Dose 2 | HZ/su | 20 | 4.0 | 1.0 | 1.0 | 3.0 | 6.0 | 17.0 |
|  |  | Placebo | 17 | 3.1 | 1.0 | 1.0 | 2.0 | 4.0 | 9.0 |
|  | Overall/dose | HZ/su | 47 | 2.9 | 1.0 | 1.0 | 2.0 | 3.0 | 17.0 |
|  |  | Placebo | 30 | 3.8 | 1.0 | 1.0 | 2.0 | 4.0 | 38.0 |
| Temperature | Dose 1 | HZ/su | 13 | 2.0 | 1.0 | 1.0 | 1.0 | 2.0 | 6.0 |
|  |  | Placebo | 4 | 9.8 | 1.0 | 1.0 | 7.0 | 18.5 | 24.0 |
|  | Dose 2 | HZ/su | 8 | 1.9 | 1.0 | 1.0 | 1.5 | 2.5 | 4.0 |
|  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | HZ/su | 21 | 2.0 | 1.0 | 1.0 | 1.0 | 2.0 | 6.0 |
|  |  | Placebo | 5 | 8.0 | 1.0 | 1.0 | 1.0 | 13.0 | 24.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom (during the solicited post-vaccination period and beyond)
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.17 Solicited general symptoms ongoing beyond the 7-day (Days 0-6) post-vaccination period (Total Vaccinated Cohort)

|  |  | HZ/su |  |  |  |  |  | Placebo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | Time to resolution (days) |  |  |  |  |  |  |  |  | Time to resolution (days) |  |  |
| Symptoms | Type | N | Ns | n | q1 | median | q3 | N | Ns | n | q1 | median | q3 |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | Any | 112 | 56 | 10 | 7.5 | 29.5 | 50 | 110 | 44 | 14 | 3 | 21 | 27 |
|  | Grade 3 | 112 | 10 | 2 | 2 | 2 | 2 | 110 | 3 | 0 | - | - |  |
| Gastrointestinal symptoms | Any | 112 | 32 | 5 | 1.5 | 2 | 5.5 | 110 | 21 | 7 | 8 | 12 | 31 |
|  | Grade 3 | 112 | 2 | 1 | 2 | 2 | 2 | 110 | 5 | 2 | 31 | 31 | 31 |
| Headache | Any | 112 | 28 | 4 | 2 | 32 | 62 | 110 | 24 | 3 | 10 | 57 | 69 |
|  | Grade 3 | 112 | 3 | 1 | - | - | - | 110 | 1 | 1 | 69 | 69 | 69 |
| Myalgia | Any | 112 | 50 | 4 | 2 | 50 | 98 | 110 | 17 | 4 | 2 | 2 | 9 |
|  | Grade 3 | 112 | 8 | 2 | 2 | 2 | 2 | 110 | 3 | 2 | 2 | 2 | 2 |
| Shivering | Any | 112 | 27 | 1 | 2 | 2 | 2 | 110 | 13 | 1 | 31 | 31 | 31 |
|  | Grade 3 | 112 | 5 | 1 | 2 | 2 | 2 | 110 | 2 | 0 | - | - | - |
| Temperature | Any | 112 | 13 | 0 | - | - | - | 110 | 4 | 2 | 12 | 15.5 | 19 |
|  | Grade 3 | 112 | 0 | 0 | - | - | - | 110 | 0 | 0 | - | - |  |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | Any | 97 | 57 | 9 | 2 | 6 | 17 | 104 | 57 | 18 | 5 | 8 | 36 |
|  | Grade 3 | 97 | 9 | 3 | 4 | 11 | 154 | 104 | 6 | 3 | 5 | 55 | 105 |
| Gastrointestinal symptoms | Any | 97 | 41 | 8 | 2 | 4 | 14 | 104 | 39 | 12 | 2 | 4.5 | 11 |
|  | Grade 3 | 97 | 5 | 1 | 14 | 14 | 14 | 104 | 3 | 2 | 11 | 11 | 11 |
| Headache | Any | 97 | 29 | 6 | 1.5 | 3.5 | 14 | 104 | 25 | 3 | 8 | 14 | 20 |
|  | Grade 3 | 97 | 3 | 1 | - | - | - | 104 | 2 | 0 | - | - | - |
| Myalgia | Any | 97 | 32 | 6 | 1.5 | 2.5 | 4 | 104 | 23 | 6 | 10 | 36 | 105 |
|  | Grade 3 | 97 | 4 | 1 | 1 | 1 | 1 | 104 | 1 | 0 | - | - | - |
| Shivering | Any | 97 | 20 | 2 | 1 | 5.5 | 10 | 104 | 17 | 2 | 2 | 3 | 4 |
|  | Grade 3 | 97 | 3 | 0 | - | - | - | 104 | 1 | 0 | - | - | - |
| Temperature | Any | 97 | 8 | 0 | - | - | - | 104 | 1 | 0 | - | - | - |
|  | Grade 3 | 97 | 0 | 0 | - | - | - | 104 | 0 | 0 | - | - | - |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | Any | 209 | 113 | 19 | 3 | 12 | 43 | 214 | 101 | 32 | 5 | 9 | 27 |
|  | Grade 3 | 209 | 19 | 5 | 3 | 7.5 | 82.5 | 214 | 9 | 3 | 5 | 55 | 105 |
| Gastrointestinal symptoms | Any | 209 | 73 | 13 | 3 | 2 | 9 | 214 | 60 | 19 | 2.5 | 7 | 13.5 |
|  | Grade 3 | 209 | 7 | 2 | 2 | 8 | 14 | 214 | 8 | 4 | 11 | 21 | 31 |
| Headache | Any | 209 | 57 | 10 | 2 | 3.5 | 23 | 214 | 49 | 6 | 10 | 20 | 57 |
|  | Grade 3 | 209 | 6 | 2 | - | - | - | 214 | 3 | 1 | 69 | 69 | 69 |
| Myalgia | Any | 209 | 82 | 10 | 2 | 2.5 | 5 | 214 | 40 | 10 | 2 | 9.5 | 36 |
|  | Grade 3 | 209 | 12 | 3 | 1 | 1.5 | 2 | 214 | 4 | 2 | 2 | 2 | 2 |
| Shivering | Any | 209 | 47 | 3 | 1 | 2 | 10 | 214 | 30 | 3 | 2 | 4 | 31 |
|  | Grade 3 | 209 | 8 | 1 | 2 | 2 | 2 | 214 | 3 | 0 | - | - | - |
| Temperature | Any | 209 | 21 | 0 | - | - | - | 214 | 5 | 2 | 12 | 15.5 | 19 |
|  | Grade 3 | 209 | 0 | 0 | - | - | - | 214 | 0 | 0 | - | - | - |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of documented doses
Ns = total number of reports for a given symptom
$\mathrm{n}=$ number of symptoms that were ongoing after the follow-up period
Time to resolution : number of days beyond the end of the follow-up period
q1 $=25$ th percentile
q3 $=75$ th percentile

Table 8.18 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period (Total Vaccinated Cohort)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=117 \end{aligned}$ |  |  |  | Placebo$N=115$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 100 | 85.5 | 77.8 | 91.3 | 103 | 89.6 | 82.5 | 94.5 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 5 | 4.3 | 1.4 | 9.7 | 6 | 5.2 | 1.9 | 11.0 |
|  | Febrile neutropenia (10016288) | 4 | 3.4 | 0.9 | 8.5 | 2 | 1.7 | 0.2 | 6.1 |
|  | Iron deficiency anaemia (10022972) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Leukocytosis (10024378) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Leukopenia (10024384) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Lymphopenia (10025327) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Neutropenia (10029354) | 11 | 9.4 | 4.8 | 16.2 | 15 | 13.0 | 7.5 | 20.6 |
|  | Thrombocytopenia (10043554) | 5 | 4.3 | 1.4 | 9.7 | 3 | 2.6 | 0.5 | 7.4 |
| Cardiac disorders (10007541) | Palpitations (10033557) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Tachycardia (10043071) | 2 | 1.7 | 0.2 | 6.0 | 1 | 0.9 | 0.0 | 4.7 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Tinnitus (10043882) | 1 | 0.9 | 0.0 | 4.7 | 3 | 2.6 | 0.5 | 7.4 |
| Eye disorders (10015919) | Eye discharge (10015915) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Eye irritation (10015946) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Eye swelling (10015967) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Lacrimation increased (10023644) | 3 | 2.6 | 0.5 | 7.3 | 1 | 0.9 | 0.0 | 4.7 |
|  | Myopia (10028651) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Visual acuity reduced (10047531) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 2 | 1.7 | 0.2 | 6.0 | 0 | 0.0 | 0.0 | 3.2 |
|  | Abdominal pain (10000081) | 3 | 2.6 | 0.5 | 7.3 | 1 | 0.9 | 0.0 | 4.7 |
|  | Abdominal pain upper (10000087) | 4 | 3.4 | 0.9 | 8.5 | 3 | 2.6 | 0.5 | 7.4 |
|  | Aerophagia (10052813) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Aphthous ulcer (10002959) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Constipation (10010774) | 16 | 13.7 | 8.0 | 21.3 | 12 | 10.4 | 5.5 | 17.5 |
|  | Diarrhoea (10012735) | 9 | 7.7 | 3.6 | 14.1 | 10 | 8.7 | 4.2 | 15.4 |
|  | Dry mouth (10013781) |  | 1.7 | 0.2 | 6.0 | 3 | 2.6 | 0.5 | 7.4 |
|  | Dyspepsia (10013946) | 6 | 5.1 | 1.9 | 10.8 | 13 | 11.3 | 6.2 | 18.6 |

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|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=117 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=115 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% | \% Cl |  |  |  | \% CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Dysphagia (10013950) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
|  | Epigastric discomfort (10053155) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Flatulence (10016766) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
|  | Gastrointestinal disorder (10017944) | 1 | 0.9 | 0.0 | 4.7 | 3 | 2.6 | 0.5 | 7.4 |
|  | Gastrointestinal pain (10017999) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Gastrooesophageal reflux disease (10017885) | 3 | 2.6 | 0.5 | 7.3 | 0 | 0.0 | 0.0 | 3.2 |
|  | Gingival pain (10018286) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Glossitis (10018386) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Haemorrhoidal haemorrhage (10054787) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Haemorrhoids (10019022) | 1 | 0.9 | 0.0 | 4.7 | 2 | 1.7 | 0.2 | 6.1 |
|  | Hiatus hernia (10020028) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 3.1 | 2 | 1.7 | 0.2 | 6.1 |
|  | Nausea (10028813) | 31 | 26.5 | 18.8 | 35.5 | 28 | 24.3 | 16.8 | 33.2 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 3.1 | 3 | 2.6 | 0.5 | 7.4 |
|  | Oesophagitis (10030216) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Oral pain (10031009) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Proctalgia (10036772) | 0 | 0.0 | 0.0 | 3.1 | 2 | 1.7 | 0.2 | 6.1 |
|  | Rectal tenesmus (10057071) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Stomatitis (10042128) | 4 | 3.4 | 0.9 | 8.5 | 2 | 1.7 | 0.2 | 6.1 |
|  | Swollen tongue (10042727) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Vomiting (10047700) | 10 | 8.5 | 4.2 | 15.2 | 14 | 12.2 | 6.8 | 19.6 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 30 | 25.6 | 18.0 | 34.5 | 28 | 24.3 | 16.8 | 33.2 |
|  | Axillary pain (10048750) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Catheter site pain (10052268) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Chest pain (10008479) | 2 | 1.7 | 0.2 | 6.0 | 0 | 0.0 | 0.0 | 3.2 |
|  | Chills (10008531) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Fatigue (10016256) | 4 | 3.4 | 0.9 | 8.5 | 6 | 5.2 | 1.9 | 11.0 |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.0 | 3.1 | 2 | 1.7 | 0.2 | 6.1 |
|  | Generalised oedema (10018092) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Inflammation (10061218) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Influenza like illness (10022004) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |



|  |  | $\begin{aligned} & \text { HZ/su } \\ & \mathrm{N}=117 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=115 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Influenza (10022000) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Lower respiratory tract infection (10024968) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Nasopharyngitis (10028810) | 3 | 2.6 | 0.5 | 7.3 | 1 | 0.9 | 0.0 | 4.7 |
|  | Neutropenic sepsis (10049151) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
|  | Oral fungal infection (10061324) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Oral herpes (10067152) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Oral infection (10048685) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Pneumonia (10035664) | 3 | 2.6 | 0.5 | 7.3 | 0 | 0.0 | 0.0 | 3.2 |
|  | Post procedural infection (10067268) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
|  | Respiratory tract infection (10062352) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Sepsis (10040047) | 2 | 1.7 | 0.2 | 6.0 | 0 | 0.0 | 0.0 | 3.2 |
|  | Sinusitis (10040753) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Upper respiratory tract infection (10046306) | 3 | 2.6 | 0.5 | 7.3 | 1 | 0.9 | 0.0 | 4.7 |
|  | Urinary tract infection (10046571) | 0 | 0.0 | 0.0 | 3.1 | 3 | 2.6 | 0.5 | 7.4 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Injury, poisoning and procedural complications (10022117) | Arthropod bite (10003399) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Gastrostomy failure (10050056) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Ligament sprain (10024453) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Post procedural complication (10058046) | 2 | 1.7 | 0.2 | 6.0 | 4 | 3.5 | 1.0 | 8.7 |
|  | Post procedural diarrhoea (10057585) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Radiation skin injury (10063562) | 1 | 0.9 | 0.0 | 4.7 | 2 | 1.7 | 0.2 | 6.1 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Investigations (10022891) | Blood iron decreased (10005619) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Body temperature fluctuation (10063488) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Haemoglobin decreased (10018884) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Platelet count decreased (10035528) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Weight decreased (10047895) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |



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HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)

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$\mathrm{N}=$ number of subjects with at least one administered dose n/\% = number/percentage of subjects reporting the symptom at least once $95 \% \mathrm{Cl}=$ exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.19 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period (Total Vaccinated Cohort)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=217 \end{aligned}$ |  |  |  | Placebo$N=225$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  | n |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL |  | \% | LL | UL |
| At least one symptom |  | 153 | 70.5 | 64.0 | 76.5 | 166 | 73.8 | 67.5 | 79.4 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 5 | 2.3 | 0.8 | 5.3 | 6 | 2.7 | 1.0 | 5.7 |
|  | Febrile neutropenia (10016288) | 4 | 1.8 | 0.5 | 4.7 | 3 | 1.3 | 0.3 | 3.8 |
|  | Iron deficiency anaemia (10022972) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Leukocytosis (10024378) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Leukopenia (10024384) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Lymphopenia (10025327) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Neutropenia (10029354) | 12 | 5.5 | 2.9 | 9.5 | 17 | 7.6 | 4.5 | 11.8 |
|  | Thrombocytopenia (10043554) | 6 | 2.8 | 1.0 | 5.9 | 4 | 1.8 | 0.5 | 4.5 |
| Cardiac disorders (10007541) | Palpitations (10033557) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Tachycardia (10043071) | 2 | 0.9 | 0.1 | 3.3 | 1 | 0.4 | 0.0 | 2.5 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Tinnitus (10043882) | 1 | 0.5 | 0.0 | 2.5 | 3 | 1.3 | 0.3 | 3.8 |
| Eye disorders (10015919) | Eye discharge (10015915) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Eye irritation (10015946) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Eye swelling (10015967) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Lacrimation increased (10023644) | 3 | 1.4 | 0.3 | 4.0 | 1 | 0.4 | 0.0 | 2.5 |
|  | Myopia (10028651) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Visual acuity reduced (10047531) |  | 0.5 | 0.0 | 2.5 | 1 | 0.4 | 0.0 | 2.5 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 2 | 0.9 | 0.1 | 3.3 | 0 | 0.0 | 0.0 | 1.6 |
|  | Abdominal pain (10000081) | 3 | 1.4 | 0.3 | 4.0 | 1 | 0.4 | 0.0 | 2.5 |
|  | Abdominal pain upper (10000087) | 5 | 2.3 | 0.8 | 5.3 | 3 | 1.3 | 0.3 | 3.8 |
|  | Aerophagia (10052813) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Aphthous ulcer (10002959) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Constipation (10010774) | 18 | 8.3 | 5.0 | 12.8 | 12 | 5.3 | 2.8 | 9.1 |
|  | Diarrhoea (10012735) | 11 | 5.1 | 2.6 | 8.9 | 10 | 4.4 | 2.2 | 8.0 |
|  | Dry mouth (10013781) | 2 | 0.9 | 0.1 | 3.3 | 3 | 1.3 | 0.3 | 3.8 |
|  | Dyspepsia (10013946) | 6 | 2.8 | 1.0 | 5.9 | 13 | 5.8 | 3.1 | 9.7 |

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|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=217 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=225 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.0 | 1.7 | 2 | 0.9 | 0.1 | 3.2 |
|  | Injection site pruritus (10022093) | 2 | 0.9 | 0.1 | 3.3 | 0 | 0.0 | 0.0 | 1.6 |
|  | Malaise (10025482) | 4 | 1.8 | 0.5 | 4.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Mucosal dryness (10028111) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Mucosal inflammation (10028116) | 11 | 5.1 | 2.6 | 8.9 | 8 | 3.6 | 1.5 | 6.9 |
|  | Oedema peripheral (10030124) | 3 | 1.4 | 0.3 | 4.0 | 1 | 0.4 | 0.0 | 2.5 |
|  | Pain (10033371) | 3 | 1.4 | 0.3 | 4.0 | 0 | 0.0 | 0.0 | 1.6 |
|  | Peripheral swelling (10048959) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Pyrexia (10037660) | 2 | 0.9 | 0.1 | 3.3 | 5 | 2.2 | 0.7 | 5.1 |
|  | Temperature intolerance (10057040) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Hepatic steatosis (10019708) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Hepatomegaly (10019842) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Hyperbilirubinaemia (10020578) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 1 | 0.5 | 0.0 | 2.5 | 2 | 0.9 | 0.1 | 3.2 |
|  | Hypersensitivity (10020751) | 1 | 0.5 | 0.0 | 2.5 | 1 | 0.4 | 0.0 | 2.5 |
|  | Seasonal allergy (10048908) | 0 | 0.0 | 0.0 | 1.7 | 2 | 0.9 | 0.1 | 3.2 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Bacterial infection (10060945) | 2 | 0.9 | 0.1 | 3.3 | 1 | 0.4 | 0.0 | 2.5 |
|  | Bronchitis (10006451) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Cellulitis (10007882) | 1 | 0.5 | 0.0 | 2.5 | 2 | 0.9 | 0.1 | 3.2 |
|  | Cystitis (10011781) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Erysipelas (10015145) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Folliculitis (10016936) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Gastroenteritis (10017888) | 2 | 0.9 | 0.1 | 3.3 | 1 | 0.4 | 0.0 | 2.5 |
|  | Gingivitis (10018292) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Herpes zoster (10019974) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Infection (10021789) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |





|  |  | $\begin{gathered} \begin{array}{c} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=217 \end{array} \end{gathered}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=225 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Pulmonary embolism (10037377) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 21 | 9.7 | 6.1 | 14.4 | 23 | 10.2 | 6.6 | 14.9 |
|  | Dermatitis (10012431) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Dry skin (10013786) | 1 | 0.5 | 0.0 | 2.5 | 1 | 0.4 | 0.0 | 2.5 |
|  | Erythema (10015150) | 5 | 2.3 | 0.8 | 5.3 | 1 | 0.4 | 0.0 | 2.5 |
|  | Nail dystrophy (10028698) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Onychalgia (10064251) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Palmar-plantar erythrodysaesthesia syndrome (10033553) | 2 | 0.9 | 0.1 | 3.3 | 0 | 0.0 | 0.0 | 1.6 |
|  | Pruritus (10037087) | 0 | 0.0 | 0.0 | 1.7 | 4 | 1.8 | 0.5 | 4.5 |
|  | Pruritus generalised (10052576) | 1 | 0.5 | 0.0 | 2.5 | 1 | 0.4 | 0.0 | 2.5 |
|  | Rash (10037844) | 2 | 0.9 | 0.1 | 3.3 | 4 | 1.8 | 0.5 | 4.5 |
|  | Rash macular (10037867) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 1.7 | 2 | 0.9 | 0.1 | 3.2 |
|  | Scar pain (10049002) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Skin disorder (10040831) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Swelling face (10042682) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Urticaria (10046735) | 2 | 0.9 | 0.1 | 3.3 | 1 | 0.4 | 0.0 | 2.5 |
| Social circumstances (10041244) | Menopause (10027308) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Haematoma (10018852) | 1 | 0.5 | 0.0 | 2.5 | 1 | 0.4 | 0.0 | 2.5 |
|  | Hot flush (10060800) | 0 | 0.0 | 0.0 | 1.7 | 2 | 0.9 | 0.1 | 3.2 |
|  | Hypotension (10021097) | 1 | 0.5 | 0.0 | 2.5 | 1 | 0.4 | 0.0 | 2.5 |
|  | Lymphocele (10048642) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Phlebitis (10034879) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Thrombosis (10043607) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Vascular pain (10047095) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)

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$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.20 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the $\mathbf{3 0 - d a y}$ (Days 0-29) post-vaccination period (Total Vaccinated Cohort)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=117 \end{aligned}$ |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=115 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL UL | n | \% |  | UL |
| At least one symptom |  | 18 | 15.4 | 9.423 .2 | 15 | 13.0 | 7.5 | 20.6 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 0 | 0.0 | 0.03 .1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Febrile neutropenia (10016288) | 4 | 3.4 | 0.98 .5 | 2 | 1.7 | 0.2 | 6.1 |
|  | Neutropenia (10029354) | 3 | 2.6 | 0.57 .3 | 3 | 2.6 | 0.5 | 7.4 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.03 .1 | 1 | 0.9 | 0.0 | 4.7 |
| Gastrointestinal disorders (10017947) | Abdominal pain (10000081) | 1 | 0.9 | 0.04 .7 | - | 0.0 | 0.0 | 3.2 |
|  | Constipation (10010774) | 0 | 0.0 | 0.03 .1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.03 .1 | 1 | 0.9 | 0.0 | 4.7 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 0 | 0.0 | 0.03 .1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Malaise (10025482) | 0 | 0.0 | 0.03 .1 | 1 | 0.9 | 0.0 | 4.7 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 1 | 0.9 | 0.04 .7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.03 .1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Lower respiratory tract infection (10024968) | 1 | 0.9 | 0.04 .7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Nasopharyngitis (10028810) | 1 | 0.9 | 0.04 .7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Sepsis (10040047) | 1 | 0.9 | 0.04 .7 | 0 | 0.0 | 0.0 | 3.2 |
| Injury, poisoning and procedural complications (10022117) | Post procedural diarrhoea (10057585) | 1 | 0.9 | 0.04 .7 | 0 | 0.0 | 0.0 | 3.2 |
| Investigations (10022891) | Platelet count decreased (10035528) | 1 | 0.9 | 0.04 .7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Weight increased (10047899) | 0 | 0.0 | 0.03 .1 | 1 | 0.9 | 0.0 | 4.7 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 0.9 | 0.04 .7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Prostate cancer (10060862) | 0 | 0.0 | 0.03 .1 | 1 | 0.9 | 0.0 | 4.7 |
| Nervous system disorders (10029205) | Hepatic encephalopathy (10019660) | 1 | 0.9 | 0.04 .7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Seizure (10039906) | 1 | 0.9 | 0.04.7 | 0 | 0.0 | 0.0 | 3.2 |
| Psychiatric disorders (10037175) | Insomnia (10022437) | 0 | 0.0 | 0.03 .1 | 1 | 0.9 | 0.0 | 4.7 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.03 .1 | 2 | 1.7 | 0.2 | 6.1 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.03 .1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Renal impairment (10062237) | 1 | 0.9 | 0.04.7 | 0 | 0.0 | 0.0 | 3.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Pleural effusion (10035598) | 0 | 0.0 | 0.03 .1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Pulmonary embolism (10037377) | 1 | 0.9 | 0.04 .7 | 0 | 0.0 | 0.0 | 3.2 |



HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.21 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period (Total Vaccinated Cohort)



HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of administered doses
n/\% = number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.22 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) postvaccination period (Total Vaccinated Cohort)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=117 \end{aligned}$ |  |  |  | Placebo$N=115$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL |  | \% |  | UL |
| At least one symptom |  | 10 | 8.5 | 4.2 | 15.2 | 9 | 7.8 | 3.6 | 14.3 |
| Blood and lymphatic system disorders (10005329) | Neutropenia (10029354) | 0 | 0.0 | 0.0 | 3.1 |  | 0.9 | 0.0 | 4.7 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 0.9 | 0.0 | 4.7 |  | 0.9 | 0.0 | 4.7 |
| Gastrointestinal disorders (10017947) | Swollen tongue (10042727) | 1 | 0.9 | 0.0 | 4.7 |  | 0.0 | 0.0 | 3.2 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 2 | 1.7 | 0.2 | 6.0 |  | 0.9 | 0.0 | 4.7 |
|  | Axillary pain (10048750) | 0 | 0.0 | 0.0 | 3.1 |  | 0.9 | 0.0 | 4.7 |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.0 | 3.1 |  | 0.9 | 0.0 | 4.7 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 3.1 |  | 0.9 | 0.0 | 4.7 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.0 | 3.1 |  | 0.9 | 0.0 | 4.7 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 3.1 |  | 0.9 | 0.0 | 4.7 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.0 | 3.1 | 2 | 1.7 | 0.2 | 6.1 |
|  | Injection site pruritus (10022093) | 2 | 1.7 | 0.2 | 6.0 | 0 | 0.0 | 0.0 | 3.2 |
|  | Malaise (10025482) | 1 | 0.9 | 0.0 | 4.7 |  | 0.0 | 0.0 | 3.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 3.1 |  | 0.9 | 0.0 | 4.7 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 1 | 0.9 | 0.0 | 4.7 |  | 0.0 | 0.0 | 3.2 |
|  | Oral herpes (10067152) | 1 | 0.9 | 0.0 | 4.7 |  | 0.0 | 0.0 | 3.2 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 3.1 |  | 0.9 | 0.0 | 4.7 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 1 | 0.9 | 0.0 | 4.7 |  | 0.9 | 0.0 | 4.7 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 0 | 0.0 | 0.0 | 3.1 |  | 0.9 | 0.0 | 4.7 |
|  | Muscle contractions involuntary (10028293) | 1 | 0.9 | 0.0 | 4.7 |  | 0.0 | 0.0 | 3.2 |
| Skin and subcutaneous tissue disorders (10040785) | Erythema (10015150) | 1 | 0.9 | 0.0 | 4.7 |  | 0.0 | 0.0 | 3.2 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 3.1 |  | 0.9 | 0.0 | 4.7 |
|  | Urticaria (10046735) | 0 | 0.0 | 0.0 | 3.1 |  | 0.9 |  |  |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
n/\% = number/percentage of subjects reporting the symptom at least once
$95 \%$ CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.23 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (Total Vaccinated Cohort)


HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.24 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the $\mathbf{3 0 - d a y}$ (Days $0-29$ ) post-vaccination period (Total Vaccinated Cohort)

|  |  |  | $\begin{aligned} & \text { Z/su } \\ & =117 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% Cl |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL UL | n \% | LL |  |
| At least one symptom |  | 10.9 | 0.04 .7 | 00.0 | 0.0 | 3.2 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 10.9 | 0.04 .7 | 00.0 |  | 3.2 |
| $\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group Placebo = Placebo group |  |  |  |  |  |  |
| At least one symptom $=$ at least one symptom experienced (regardless of the MedDRA Preferred Term) |  |  |  |  |  |  |
| $\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once |  |  |  |  |  |  |

Table 8.25 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (Total Vaccinated Cohort)

|  |  | $\begin{aligned} & \begin{array}{l} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=217 \end{array} \end{aligned}$ | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=225 \end{aligned}$ |
| :---: | :---: | :---: | :---: |
|  |  | 95\% Cl | 95\% CI |
| Primary System Organ Class (CODE) P | Preferred Term (CODE) | n \% LL UL n | \% LL UL |
| At least one symptom |  | 10.50 .02 .50 | 0.00 .01 .6 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 10.50 .02 .50 | 0.00 .01 .6 |
| $\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group <br> Placebo $=$ Placebo group |  |  |  |
|  |  |  |  |
| At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term) $\mathrm{N}=$ number of administered doses |  |  |  |
| n/\% = number/percentage of doses with the | the symptom |  |  |
| 95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit |  |  |  |

Table 8.26 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 30 -day (Days 0-29) post-vaccination period (Total Vaccinated Cohort)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=117 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=115 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 31 | 26.5 | 18.8 | 35.5 | 33 | 28.7 | 20.6 | 37.9 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 2 | 1.7 | 0.2 | 6.0 | 3 | 2.6 | 0.5 | 7.4 |
|  | Febrile neutropenia (10016288) | 4 | 3.4 | 0.9 | 8.5 | 2 | 1.7 | 0.2 | 6.1 |
|  | Neutropenia (10029354) | 2 | 1.7 | 0.2 | 6.0 | 3 | 2.6 | 0.5 | 7.4 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Abdominal pain (10000081) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Abdominal pain upper (10000087) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
|  | Constipation (10010774) | 0 | 0.0 | 0.0 | 3.1 | 3 | 2.6 | 0.5 | 7.4 |
|  | Diarrhoea (10012735) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Dyspepsia (10013946) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Dysphagia (10013950) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Gastrooesophageal reflux disease (10017885) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Nausea (10028813) | 3 | 2.6 | 0.5 | 7.3 | 0 | 0.0 | 0.0 | 3.2 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Stomatitis (10042128) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Swollen tongue (10042727) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Vomiting (10047700) | 1 | 0.9 | 0.0 | 4.7 | 4 | 3.5 | 1.0 | 8.7 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 3 | 2.6 | 0.5 | 7.3 | 0 | 0.0 | 0.0 | 3.2 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Mucosal inflammation (10028116) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
|  | Pyrexia (10037660) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |



|  |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =117 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { aceb } \\ & =11 \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | CI |  |  |  | Cl |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
| Nervous system disorders (10029205) | Dizziness (10013573) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Headache (10019211) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Hepatic encephalopathy (10019660) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Motor dysfunction (10061296) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Neuropathy peripheral (10029331) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Paraesthesia (10033775) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Seizure (10039906) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
|  | Syncope (10042772) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
| Psychiatric disorders (10037175) | Anxiety (10002855) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.0 | 3.1 | 2 | 1.7 | 0.2 | 6.1 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Cough (10011224) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Epistaxis (10015090) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Hiccups (10020039) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Pulmonary embolism (10037377) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
| Skin and subcutaneous tissue disorders (10040785) | Erythema (10015150) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Rash (10037844) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Scar pain (10049002) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Urticaria (10046735) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Thrombosis (10043607) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.27 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 30-day (Days 0-29) post-vaccination period (Total Vaccinated Cohort)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=217 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=225 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 36 | 16.6 | 11.9 | 22.2 | 43 | 19.1 | 14.2 | 24.9 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 2 | 0.9 | 0.1 | 3.3 | 3 | 1.3 | 0.3 | 3.8 |
|  | Febrile neutropenia (10016288) | 4 | 1.8 | 0.5 | 4.7 | 3 | 1.3 | 0.3 | 3.8 |
|  | Neutropenia (10029354) | 3 | 1.4 | 0.3 | 4.0 | 3 | 1.3 | 0.3 | 3.8 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 0.5 | 0.0 | 2.5 | 1 | 0.4 | 0.0 | 2.5 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Abdominal pain (10000081) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Abdominal pain upper (10000087) | 1 | 0.5 | 0.0 | 2.5 | 1 | 0.4 | 0.0 | 2.5 |
|  | Constipation (10010774) | 0 | 0.0 | 0.0 | 1.7 | 3 | 1.3 | 0.3 | 3.8 |
|  | Diarrhoea (10012735) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Dyspepsia (10013946) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Dysphagia (10013950) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Gastrooesophageal reflux disease (10017885) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Nausea (10028813) | 3 | 1.4 | 0.3 | 4.0 | 0 | 0.0 | 0.0 | 1.6 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Stomatitis (10042128) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Swollen tongue (10042727) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Vomiting (10047700) | 1 | 0.5 | 0.0 | 2.5 | 4 | 1.8 | 0.5 | 4.5 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 3 | 1.4 | 0.3 | 4.0 | 0 | 0.0 | 0.0 | 1.6 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Mucosal inflammation (10028116) | 1 | 0.5 | 0.0 | 2.5 | 1 | 0.4 | 0.0 | 2.5 |
|  | Pyrexia (10037660) | 1 | 0.5 | 0.0 | 2.5 | 1 | 0.4 | 0.0 | 2.5 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |



|  |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =21 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { ceeb } \\ & =22 \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | Cl |  |  |  | CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
| Nervous system disorders (10029205) | Dizziness (10013573) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Headache (10019211) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Hepatic encephalopathy (10019660) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Motor dysfunction (10061296) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Neuropathy peripheral (10029331) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Paraesthesia (10033775) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Seizure (10039906) | 1 | 0.5 | 0.0 | 2.5 | 1 | 0.4 | 0.0 | 2.5 |
|  | Syncope (10042772) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
| Psychiatric disorders (10037175) | Anxiety (10002855) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.0 | 1.7 | 2 | 0.9 | 0.1 | 3.2 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Cough (10011224) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Epistaxis (10015090) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Hiccups (10020039) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Pulmonary embolism (10037377) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
| Skin and subcutaneous tissue disorders (10040785) | Erythema (10015150) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Rash (10037844) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Scar pain (10049002) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Urticaria (10046735) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |
| Vascular disorders (10047065) | Embolism (10061169) |  | 0.0 | 0.0 | 1.7 | 1 | 0.4 | 0.0 | 2.5 |
|  | Thrombosis (10043607) | 1 | 0.5 | 0.0 | 2.5 | 0 | 0.0 | 0.0 | 1.6 |

$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.28 Global Summary of unsolicited signs and symptoms reported with medically attended visit, within the 30 -day (Days $0-29$ ) postvaccination period (Total Vaccinated Cohort)

|  | Group |  |  |
| :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | Total |
| Number of subjects with at least one unsolicited symptom reported | 31 | 33 | 64 |
| Number of doses followed by at least one unsolicited symptom | 36 | 43 | 79 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term | 60 | 62 | 122 |
| Number of unsolicited symptoms reported** | 60 | 62 | 122 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.29 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to 30 days post last vaccination (Total Vaccinated Cohort)

No records exist in this table

Table 8.30 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from 30 days post last vaccination up to the study end (Total Vaccinated Cohort)

|  |  | $\begin{aligned} & \text { HZ/su } \\ & \mathrm{N}=117 \end{aligned}$ |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=115 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95\% CI |  |  |  | 95\% Cl |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL | UL |  | \% | LL | UL |
| At least one symptom |  | 00.0 | 0.0 | 3.1 |  | 0.9 | 0.0 | 4.7 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 00.0 | 0.0 | 3.1 |  | 0.9 | 0.0 | 4.7 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.31 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to the study end (Total Vaccinated Cohort)

|  |  |  | $\begin{aligned} & \text { Z/su } \\ & =117 \end{aligned}$ |  | $\begin{aligned} & \text { acebo } \\ & =115 \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% Cl |  | 95\% Cl |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL UL | n \% | LL UL |
| At least one symptom |  | 00.0 | 0.03 .1 | 10.9 | 0.04 .7 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) 0 | 00.0 | 0.03 .1 | 10.9 | 0.04 .7 |
| $\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine groupPlacebo = Placebo group |  |  |  |  |  |
|  |  |  |  |  |  |
| At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term) |  |  |  |  |  |
| $\mathrm{N}=$ number of subjects with at least one administered dose |  |  |  |  |  |
| $\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once |  |  |  |  |  |
| 95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit |  |  |  |  |  |

Table 8.32 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to 30 days post last vaccination (Total Vaccinated Cohort)



HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.33 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relation to vaccination from first vaccination up to 30 days post last vaccination (Total Vaccinated Cohort)

No records exist in this table

Table 8.34 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from 30 days post last vaccination up to the study end (Total Vaccinated Cohort)


|  |  | $\begin{gathered} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=117 \end{gathered}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=115 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Device related sepsis (10069802) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Diverticulitis (10013538) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Epiglottitis (10015030) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Gastroenteritis (10017888) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Lung infection (10061229) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Neutropenic sepsis (10049151) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Oral candidiasis (10030963) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Pleural infection (10061351) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Pneumonia (10035664) | 1 | 0.9 | 0.0 | 4.7 | 2 | 1.7 | 0.2 | 6.1 |
|  | Respiratory tract infection (10062352) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
|  | Sepsis (10040047) | 1 | 0.9 | 0.0 | 4.7 | 2 | 1.7 | 0.2 | 6.1 |
|  | Staphylococcal infection (10058080) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Upper respiratory tract infection (10046306) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Injury, poisoning and procedural complications (10022117) | Lumbar vertebral fracture (10049947) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Metabolism and nutrition disorders (10027433) | Diabetic ketoacidosis (10012671) | 2 | 1.7 | 0.2 | 6.0 | 0 | 0.0 | 0.0 | 3.2 |
|  | Hypokalaemia (10021015) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Hyponatraemia (10021036) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Malnutrition (10061273) | 2 | 1.7 | 0.2 | 6.0 | 0 | 0.0 | 0.0 | 3.2 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Musculoskeletal chest pain (10050819) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Bladder cancer (10005003) | 2 | 1.7 | 0.2 | 6.0 | 0 | 0.0 | 0.0 | 3.2 |
|  | Breast cancer recurrent (10006198) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Cholangiocarcinoma (10008593) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Colon cancer (10009944) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Colorectal cancer (10061451) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Colorectal cancer metastatic (10052358) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Head and neck cancer (10067821) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Liposarcoma (10024627) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Lung neoplasm malignant (10058467) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
|  | Malignant melanoma (10025650) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Metastases to central nervous system (10059282) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Metastases to liver (10027457) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |


|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=117 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=115 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Non-small cell lung cancer (10061873) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Ovarian cancer (10033128) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Prostate cancer (10060862) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Rectal cancer metastatic (10055097) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Squamous cell carcinoma of lung (10041826) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Tongue neoplasm malignant stage unspecified (10043966) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Tumour haemorrhage (10049750) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Uterine leiomyosarcoma (10046799) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Bronchial obstruction (10006440) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Pleural effusion (10035598) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
|  | Pulmonary embolism (10037377) | 0 | 0.0 | 0.0 | 3.1 | 2 | 1.7 | 0.2 | 6.1 |
|  | Respiratory failure (10038695) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
| Surgical and medical procedures (10042613) | Abdominal hernia repair (10060802) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Vascular disorders (10047065) | Superior vena cava occlusion (10058988) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.35 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and
Preferred Term with causal relation to vaccination from 30 days post last vaccination up to the study end (Total Vaccinated Cohort)

No records exist in this table

Table 8.36 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to the study end (Total Vaccinated Cohort)


|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=117 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=115 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Device related sepsis (10069802) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Diverticulitis (10013538) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Epiglottitis (10015030) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Gastroenteritis (10017888) | 2 | 1.7 | 0.2 | 6.0 | 0 | 0.0 | 0.0 | 3.2 |
|  | Hepatitis c (10019744) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Lower respiratory tract infection (10024968) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Lung infection (10061229) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Nasopharyngitis (10028810) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Neutropenic sepsis (10049151) | 1 | 0.9 | 0.0 | 4.7 | 2 | 1.7 | 0.2 | 6.1 |
|  | Oral candidiasis (10030963) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Pleural infection (10061351) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Pneumonia (10035664) | 1 | 0.9 | 0.0 | 4.7 | 2 | 1.7 | 0.2 | 6.1 |
|  | Respiratory tract infection (10062352) | 2 | 1.7 | 0.2 | 6.0 | 1 | 0.9 | 0.0 | 4.7 |
|  | Sepsis (10040047) | 3 | 2.6 | 0.5 | 7.3 | 2 | 1.7 | 0.2 | 6.1 |
|  | Staphylococcal infection (10058080) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Upper respiratory tract infection (10046306) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Urinary tract infection (10046571) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Lumbar vertebral fracture (10049947) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Metabolism and nutrition disorders (10027433) | Diabetic ketoacidosis (10012671) | 2 | 1.7 | 0.2 | 6.0 | 0 | 0.0 | 0.0 | 3.2 |
|  | Hypokalaemia (10021015) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Hyponatraemia (10021036) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Malnutrition (10061273) | 2 | 1.7 | 0.2 | 6.0 | 0 | 0.0 | 0.0 | 3.2 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Musculoskeletal chest pain (10050819) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Bladder cancer (10005003) | 2 | 1.7 | 0.2 | 6.0 | 0 | 0.0 | 0.0 | 3.2 |
|  | Breast cancer recurrent (10006198) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Cholangiocarcinoma (10008593) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |


|  |  | $\begin{aligned} & \text { HZ/su } \\ & \mathrm{N}=117 \end{aligned}$ |  |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=115 \end{aligned}$ |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Colon cancer (10009944) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Colorectal cancer (10061451) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Colorectal cancer metastatic (10052358) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Head and neck cancer (10067821) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Liposarcoma (10024627) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Lung neoplasm malignant (10058467) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
|  | Malignant melanoma (10025650) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Metastases to central nervous system (10059282) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Metastases to liver (10027457) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Non-small cell lung cancer (10061873) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Ovarian cancer (10033128) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Prostate cancer (10060862) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
|  | Rectal cancer metastatic (10055097) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Squamous cell carcinoma of lung (10041826) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Tongue neoplasm malignant stage unspecified (10043966) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Tumour haemorrhage (10049750) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Uterine leiomyosarcoma (10046799) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Nervous system disorders (10029205) | Hepatic encephalopathy (10019660) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
|  | Seizure (10039906) | 1 | 0.9 | 0.0 | 4.7 | 1 | 0.9 | 0.0 | 4.7 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 1 | 0.9 | 0.0 | 4.7 | 2 | 1.7 | 0.2 | 6.1 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Bronchial obstruction (10006440) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Pleural effusion (10035598) | 1 | 0.9 | 0.0 | 4.7 | 2 | 1.7 | 0.2 | 6.1 |
|  | Pulmonary embolism (10037377) | 1 | 0.9 | 0.0 | 4.7 | 2 | 1.7 | 0.2 | 6.1 |
|  | Respiratory failure (10038695) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |
| Skin and subcutaneous tissue disorders (10040785) | Rash (10037844) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Surgical and medical procedures (10042613) | Abdominal hernia repair (10060802) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
| Vascular disorders (10047065) | Superior vena cava occlusion (10058988) | 0 | 0.0 | 0.0 | 3.1 | 1 | 0.9 | 0.0 | 4.7 |
|  | Thrombosis (10043607) | 1 | 0.9 | 0.0 | 4.7 | 0 | 0.0 | 0.0 | 3.2 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

## CONFIDENTIAL

116427 (ZOSTER-028)
Report Final
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.37 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relation to vaccination from first vaccination up to the study end (Total Vaccinated Cohort)

No records exist in this table
Table 8.38 Number and percentage of subjects with fatal outcome reported up to the study end (Total Vaccinated Cohort)

|  | HZ/su <br> $\mathrm{N}=117$ |  | Placebo <br> $\mathrm{N}=115$ |
| :--- | :--- | :--- | :--- |
| Characteristics | n | $\%$ | n |
| Fatalities | 12 | 10.3 | 11 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
Table 8.39 Percentage of subjects with concomitant medication during the 30day (Days 0-29) post-vaccination period (Total Vaccinated Cohort)

|  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | 95\% CI |  |  |  |  |  |  |  | 95\% CI |  |
|  | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |
| Any | 117 | 109 | 93.2 | 87.0 | 97.0 | 115 | 109 | 94.8 | 89.0 | 98.1 |
| Steroids to prevent chemotherapy nausea and vomiting | 117 | 99 | 84.6 | 76.8 | 90.6 | 115 | 98 | 85.2 | 77.4 | 91.1 |
| Any in anticipation of study vaccine reaction | 117 | 0 | 0.0 | 0.0 | 3.1 | 115 | 0 | 0.0 | 0.0 | 3.2 |
| Any chronic use | 117 | 4 | 3.4 | 0.9 | 8.5 | 115 | 8 | 7.0 | 3.1 | 13.2 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |
| Any | 100 | 90 | 90.0 | 82.4 | 95.1 | 110 | 94 | 85.5 | 77.5 | 91.5 |
| Steroids to prevent chemotherapy nausea and vomiting | 100 | 82 | 82.0 | 73.1 | 89.0 | 110 | 82 | 74.5 | 65.4 | 82.4 |
| Any in anticipation of study vaccine reaction | 100 | 0 | 0.0 | 0.0 | 3.6 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Any chronic use | 100 | 2 | 2.0 | 0.2 | 7.0 | 110 | 7 | 6.4 | 2.6 | 12.7 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |
| Any | 217 | 199 | 91.7 | 87.2 | 95.0 | 225 | 203 | 90.2 | 85.6 | 93.8 |
| Steroids to prevent chemotherapy nausea and vomiting | 217 | 181 | 83.4 | 77.8 | 88.1 | 225 | 180 | 80.0 | 74.2 | 85.0 |
| Any in anticipation of study vaccine reaction | 217 | 0 | 0.0 | 0.0 | 1.7 | 225 | 0 | 0.0 | 0.0 | 1.6 |
| Any chronic use | 217 | 6 | 2.8 | 1.0 | 5.9 | 225 | 15 | 6.7 | 3.8 | 10.8 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |
| Any | 117 | 113 | 96.6 | 91.5 | 99.1 | 115 | 113 | 98.3 | 93.9 | 99.8 |
| Steroids to prevent chemotherapy nausea and vomiting | 117 | 104 | 88.9 | 81.7 | 93.9 | 115 | 101 | 87.8 | 80.4 | 93.2 |
| Any in anticipation of study vaccine reaction | 117 | 0 | 0.0 | 0.0 | 3.1 | 115 | 0 | 0.0 | 0.0 | 3.2 |
| Any chronic use | 117 | 6 | 5.1 | 1.9 | 10.8 | 115 | 13 | 11.3 | 6.2 | 18.6 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with the administered dose
$\mathrm{n} / \%=$ number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.40 Number and percentage of subjects who received study vaccine doses (ATP cohort for safety up to 30 days post last vaccination)

|  | $\begin{array}{\|l\|} \hline \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=113 \end{array}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=112 \end{aligned}$ |  | $\begin{gathered} \hline \text { Total } \\ \mathrm{N}=225 \end{gathered}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Total number of doses received | n | \% | n | \% | n | \% |
| 1 | 17 | 15.0 | 5 | 4.5 | 22 | 9.8 |
| 2 | 96 | 85.0 | 107 | 95.5 | 203 | 90.2 |
| Any | 113 | 100 | 112 | 100 | 225 | 100 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in each group or in total included in the considered cohort
$\mathrm{n} / \%=$ number/percentage of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least one dose
Table 8.41 Compliance in returning symptom sheets (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

| Dose | Group | Number of doses | Doses NOT according to protocol | Number of general SS | Compliance \% general SS | Number of local SS | ```Compliance % local SS``` |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 1 | HZ/su | 113 | 3 | 108 | 95.6 | 108 | 95.6 |
|  | Placebo | 112 | 6 | 107 | 95.5 | 107 | 95.5 |
| 2 | HZ/su | 96 | 4 | 93 | 96.9 | 94 | 97.9 |
|  | Placebo | 107 | 7 | 103 | 96.3 | 103 | 96.3 |
| Total | HZ/su | 209 | 7 | 201 | 96.2 | 202 | 96.7 |
|  | Placebo | 219 | 13 | 210 | 95.9 | 210 | 95.9 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
SS = Symptom screens/sheets used for the collection of local and general solicited AEs
Compliance \% = (number of doses with symptom screen/sheet return / number of administered doses) X 100

Table 8.42 Incidence and nature of symptoms (solicited and unsolicited) reported during the 7 -day (Days $0-6$ ) post-vaccination period following each dose and overall (ATP cohort for safety up to 30 days post last vaccination)

|  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | HZ/su | 113 | 102 | 90.3 | 83.2 | 95.0 | 113 | 81 | 71.7 | 62.4 | 79.8 | 113 | 84 | 74.3 | 65.3 | 82.1 |
|  | Placebo | 112 | 56 | 50.0 | 40.4 | 59.6 | 112 | 55 | 49.1 | 39.5 | 58.7 | 112 | 4 | 3.6 | 1.0 | 8.9 |
| Dose 2 | HZ/su | 96 | 78 | 81.3 | 72.0 | 88.5 | 96 | 72 | 75.0 | 65.1 | 83.3 | 96 | 53 | 55.2 | 44.7 | 65.4 |
|  | Placebo | 107 | 82 | 76.6 | 67.5 | 84.3 | 107 | 82 | 76.6 | 67.5 | 84.3 | 107 | 6 | 5.6 | 2.1 | 11.8 |
| Overall/dose | HZ/su | 209 | 180 | 86.1 | 80.7 | 90.5 | 209 | 153 | 73.2 | 66.7 | 79.1 | 209 | 137 | 65.6 | 58.7 | 72.0 |
|  | Placebo | 219 | 138 | 63.0 | 56.2 | 69.4 | 219 | 137 | 62.6 | 55.8 | 69.0 | 219 | 10 | 4.6 | 2.2 | 8.2 |
| Overall/subject | HZ/su | 113 | 105 | 92.9 | 86.5 | 96.9 | 113 | 95 | 84.1 | 76.0 | 90.3 | 113 | 90 | 79.6 | 71.0 | 86.6 |
|  | Placebo | 112 |  | 80.4 | 71.8 | 87.3 | 112 |  | 80.4 | 71.8 | 87 | 112 |  | 8.0 | 3.7 | 14.7 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine
administered
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.43 Incidence and nature of grade 3 symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (ATP cohort for safety up to 30 days post last vaccination)

|  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | HZ/su | 113 | 21 | 18.6 | 11.9 | 27.0 | 113 | 17 | 15.0 | 9.0 | 23.0 | 113 | 9 | 8.0 | 3.7 | 4.6 |
|  | Placebo | 112 | 13 | 11.6 | 6.3 | 19.0 | 112 | 13 | 11.6 | 6.3 | 19.0 | 112 | 0 | 0.0 | 0.0 | 3.2 |
| Dose 2 | HZ/su | 96 | 18 | 18.8 | 11.5 | 28.0 | 96 | 17 | 17.7 | 10.7 | 26.8 | 96 | 4 | 4.2 | 1.1 | 10.3 |
|  | Placebo | 107 | 12 | 11.2 | 5.9 | 18.8 | 107 | 12 | 11.2 | 5.9 | 18.8 | 107 | 0 | 0.0 | 0.0 | 3.4 |
| Overall/dose | HZ/su | 209 | 39 | 18.7 | 13.6 | 24.6 | 209 | 34 | 16.3 | 11.5 | 22.0 | 209 | 13 | 6.2 | 3.4 | 10.4 |
|  | Placebo | 219 | 25 | 11.4 | 7.5 | 16.4 | 219 | 25 | 11.4 | 7.5 | 16.4 | 219 | 0 | 0.0 | 0.0 | 1.7 |
| Overall/subject | HZ/su | 113 | 29 | 25.7 | 17.9 | 34.7 | 113 | 27 | 23.9 | 16.4 | 32.8 | 113 | 12 | 10.6 | 5.6 | 17.8 |
|  | Placebo | 11 | 21 | 18.8 | 12.0 | 27.2 | 112 |  | 18.8 | 12.0 | 27 | 112 |  | 0.0 |  |  |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine
administered
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.44 Incidence and nature of symptoms (solicited only) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (ATP cohort for safety up to 30 days post last vaccination)

|  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | HZ/su | 108 | 100 | 92.6 | 85.9 | 96.7 | 108 | 77 | 71.3 | 61.8 | 79.6 | 108 | 84 | 77.8 | 68.8 | 85.2 |
|  | Placebo | 107 | 51 | 47.7 | 37.9 | 57.5 | 107 | 50 | 46.7 | 37.0 | 56.6 | 107 | 3 | 2.8 | 0.6 | 8.0 |
| Dose 2 | HZ/su | 94 | 71 | 75.5 | 65.6 | 83.8 | 93 | 63 | 67.7 | 57.3 | 77.1 | 94 | 53 | 56.4 | 45.8 | 66.6 |
|  | Placebo | 103 | 59 | 57.3 | 47.2 | 67.0 | 103 | 59 | 57.3 | 47.2 | 67.0 | 103 | 5 | 4.9 | 1.6 | 11.0 |
| Overall/dose | HZ/su | 202 | 171 | 84.7 | 78.9 | 89.3 | 201 | 140 | 69.7 | 62.8 | 75.9 | 202 | 137 | 67.8 | 60.9 | 74.2 |
|  | Placebo | 210 | 110 | 52.4 | 45.4 | 59.3 | 210 | 109 | 51.9 | 44.9 | 58.8 | 210 | 8 | 3.8 | 1.7 | 7.4 |
| Overall/subject | HZ/su | 108 | 103 | 95.4 | 89.5 | 98.5 | 108 | 87 | 80.6 | 71.8 | 87.5 | 108 | 90 | 83.3 | 74.9 | 89.8 |
|  | Placebo | 107 | 71 | 66.4 | 56.6 | 75.2 | 107 | 71 | 66.4 | 56.6 | 75.2 | 107 | , | 6.5 | 2.7 | 13.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered 95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.45 Incidence and nature of grade 3 symptoms (solicited only) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (ATP cohort for safety up to 30 days post last vaccination)

|  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | L |
| Dose 1 | HZ/su | 108 | 19 | 17.6 | 10.9 | 26.1 | 108 | 15 | 13.9 | 8.0 | 21.9 | 108 | 9 | 8.3 | 3.9 | 5.2 |
|  | Placebo | 107 | 11 | 10.3 | 5.2 | 17.7 | 107 | 11 | 10.3 | 5.2 | 17.7 | 107 | 0 | 0.0 | 0.0 | 3.4 |
| Dose 2 | HZ/su | 94 | 16 | 17.0 | 10.1 | 26.2 | 93 | 15 | 16.1 | 9.3 | 25.2 | 94 | 4 | 4.3 | 1.2 | 10.5 |
|  | Placebo | 103 | 10 | 9.7 | 4.8 | 17.1 | 103 | 10 | 9.7 | 4.8 | 17.1 | 103 | 0 | 0.0 | 0.0 | 3.5 |
| Overall/dose | HZ/su | 202 | 35 | 17.3 | 12.4 | 23.3 | 201 | 30 | 14.9 | 10.3 | 20.6 | 202 | 13 | 6.4 | 3.5 | 10.8 |
|  | Placebo | 210 | 21 | 10.0 | 6.3 | 14.9 | 210 | 21 | 10.0 | 6.3 | 14.9 | 210 | 0 | 0.0 | 0.0 | 1.7 |
| Overall/subject | HZ/su | 108 | 26 | 24.1 | 16.4 | 33.3 | 108 | 24 | 22.2 | 14.8 | 31.2 | 108 | 12 | 11.1 | 5.9 | 18.6 |
|  | Placebo | 10 |  | 15.9 | 9.5 | 24.2 | 107 | 17 | 15.9 | 9.5 | 24. | 107 |  | 0.0 |  | 3.4 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered 95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.46 Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (ATP cohort for safety up to 30 days post last vaccination)

|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95 \% CI |  |  |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N | n | \% | LL | UL | N | n \% |  | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 108 | 79 | 73.1 | 63.8 | 81.2 | 107 | 21.9 | 0.2 | 26.6 |
|  | Grade 2 or 3 | 108 | 25 | 23.1 | 15.6 | 32.2 | 107 | 00.0 | 0.0 | 3.4 |
|  | Grade 3 | 108 | 7 | 6.5 | 2.6 | 12.9 | 107 | 00.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 1 | 0.9 | 0.0 | 5.1 | 107 | 00.0 | 0.0 | 3.4 |
| Redness (mm) | All | 108 | 30 | 27.8 | 19.6 | 37.2 | 107 | 00.0 | 0.0 | 3.4 |
|  | $>50$ | 108 | 17 | 15.7 | 9.4 | 24.0 | 107 | 00.0 | 0.0 | 3.4 |
|  | >100 | 108 | 2 | 1.9 | 0.2 | 6.5 | 107 | 00.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
| Swelling (mm) | All | 108 | 14 | 13.0 | 7.3 | 20.8 | 107 | 10.9 | 0.0 | 5.1 |
|  | $>50$ | 108 | 8 | 7.4 | 3.3 | 14.1 | 107 | 00.0 | 0.0 | 3.4 |
|  | >100 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 94 | 49 | 52.1 | 41.6 | 62.5 | 103 | 54.9 | 1.6 | 11.0 |
|  | Grade 2 or 3 | 94 | 18 | 19.1 | 11.8 | 28.6 | 103 | 11.0 | 0.0 | 5.3 |
|  | Grade 3 | 94 | 4 | 4.3 | 1.2 | 10.5 | 103 | 00.0 | 0.0 | 3.5 |
|  | Medical advice | 94 | 0 | 0.0 | 0.0 | 3.8 | 103 | 00.0 | 0.0 | 3.5 |
| Redness (mm) | All | 94 | 18 | 19.1 | 11.8 | 28.6 | 103 | 00.0 | 0.0 | 3.5 |
|  | $>50$ | 94 | 7 | 7.4 | 3.0 | 14.7 | 103 | 00.0 | 0.0 | 3.5 |
|  | >100 | 94 | 0 | 0.0 | 0.0 | 3.8 | 103 | 00.0 | 0.0 | 3.5 |
|  | Medical advice | 94 | 0 | 0.0 | 0.0 | 3.8 | 103 | 00.0 | 0.0 | 3.5 |
| Swelling (mm) | All | 94 | 8 | 8.5 | 3.7 | 16.1 | 103 | 00.0 | 0.0 | 3.5 |
|  | $>50$ | 94 | 4 | 4.3 | 1.2 | 10.5 | 103 | 00.0 | 0.0 | 3.5 |
|  | >100 | 94 | 0 | 0.0 | 0.0 | 3.8 | 103 | 00.0 | 0.0 | 3.5 |
|  | Medical advice | 94 | 0 | 0.0 | 0.0 | 3.8 | 103 | 00.0 | 0.0 | 3.5 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 202 | 128 | 63.4 | 56.3 | 70.0 | 210 | 73.3 | 1.4 | 6.7 |
|  | Grade 2 or 3 | 202 | 43 | 21.3 | 15.9 | 27.6 | 210 | 10.5 | 0.0 | 2.6 |
|  | Grade 3 | 202 | 11 | 5.4 | 2.7 | 9.5 | 210 | 00.0 | 0.0 | 1.7 |
|  | Medical advice | 202 | 1 | 0.5 | 0.0 | 2.7 | 210 | 00.0 | 0.0 | 1.7 |
| Redness (mm) | All | 202 | 48 | 23.8 | 18.1 | 30.2 | 210 | 00.0 | 0.0 | 1.7 |
|  | $>50$ | 202 | 24 | 11.9 | 7.8 | 17.2 | 210 | 00.0 | 0.0 | 1.7 |
|  | >100 | 202 | 2 | 1.0 | 0.1 | 3.5 | 210 | 00.0 | 0.0 | 1.7 |
|  | Medical advice | 202 | 0 | 0.0 | 0.0 | 1.8 | 210 | 00.0 | 0.0 | 1.7 |
| Swelling (mm) | All | 202 | 22 | 10.9 | 7.0 | 16.0 | 210 | 10.5 | 0.0 | 2.6 |
|  | $>50$ | 202 | 12 | 5.9 | 3.1 | 10.1 | 210 | 00.0 | 0.0 | 0 1.7 |
|  | >100 | 202 | 0 | 0.0 | 0.0 | 1.8 | 210 | 00.0 | 0.0 | 1.7 |
|  | Medical advice | 202 | 0 | 0.0 | 0.0 | 1.8 | 210 | 00.0 | 0.0 | 1.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 108 | 86 | 79.6 | 70.8 | 86.8 | 107 | 76.5 | 2.7 | 13.0 |
|  | Grade 2 or 3 | 108 | 32 | 29.6 | 21.2 | 39.2 | 107 | 10.9 | 0.0 | 5.1 |
|  | Grade 3 | 108 | 10 | 9.3 | 4.5 | 16.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 1 | 0.9 | 0.0 | 5.1 | 107 | 00.0 | 0.0 | 3.4 |
| Redness (mm) | All | 108 | 37 | 34.3 | 25.4 | 44.0 | 107 | 00.0 | 0.0 | 3.4 |
|  | $>50$ | 108 | 18 | 16.7 | 10.2 | 25.1 | 107 | 00.0 | 0.0 | . 3.4 |
|  | >100 | 108 | 2 | 1.9 | 0.2 | 6.5 | 107 | 00.0 | 0.0 | 3 3.4 |
|  | Medical advice | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3 3.4 |
| Swelling (mm) | All | 108 | 17 | 15.7 | 9.4 | 24.0 | 107 | 10.9 | 0.0 | 5.1 |


|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | \% CI |  |  |  | \% Cl |
| Symptom | Type | N | n | \% | LL | UL | N | n \% | LL | UL |
|  | >50 | 108 | 10 | 9.3 | 4.5 | 16.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >100 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; $\mathrm{LL}=$ lower limit, UL = upper limit

Table 8.47 Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (ATP cohort for safety up to 30 days post last vaccination)

|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95 \% CI |  |  |  |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 108 | 53 | 49.1 | 39.3 | 58.9 | 107 | 42 | 39.3 | 30.0 | 49.2 |
|  | Grade 2 or 3 | 108 | 29 | 26.9 | 18.8 | 36.2 | 107 | 15 | 14.0 | 8.1 | 22.1 |
|  | Grade 3 | 108 | 10 | 9.3 | 4.5 | 16.4 | 107 | 3 | 2.8 | 0.6 | 8.0 |
|  | Related | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 10 | 9.3 | 4.6 | 16.5 |
|  | Grade 2 or 3 Related | 108 | 8 | 7.4 | 3.3 | 14.1 | 107 | 4 | 3.7 | 1.0 | 9.3 |
|  | Grade 3 Related | 108 | 3 | 2.8 | 0.6 | 7.9 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 0 | 0.0 | 0.0 | 3.4 |
| Gastrointestinal symptoms | All | 108 | 32 | 29.6 | 21.2 | 39.2 | 107 | 21 | 19.6 | 12.6 | 28.4 |
|  | Grade 2 or 3 | 108 | 14 | 13.0 | 7.3 | 20.8 | 107 | 11 | 10.3 | 5.2 | 17.7 |
|  | Grade 3 | 108 | 2 | 1.9 | 0.2 | 6.5 | 107 | 5 | 4.7 | 1.5 | 10.6 |
|  | Related | 108 | 9 | 8.3 | 3.9 | 15.2 | 107 | 2 | 1.9 | 0.2 | 6.6 |
|  | Grade 2 or 3 Related | 108 | 2 | 1.9 | 0.2 | 6.5 | 107 | 1 | 0.9 | 0.0 | 5.1 |
|  | Grade 3 Related | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 1 | 0.9 | 0.0 | 5.1 |
|  | Medical advice | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 2 | 1.9 | 0.2 | 6.6 |
| Headache | All | 108 | 26 | 24.1 | 16.4 | 33.3 | 107 | 23 | 21.5 | 14.1 | 30.5 |
|  | Grade 2 or 3 | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 7 | 6.5 | 2.7 | 13.0 |
|  | Grade 3 | 108 | 3 | 2.8 | 0.6 | 7.9 | 107 | 1 | 0.9 | 0.0 | 5.1 |
|  | Related | 108 | 9 | 8.3 | 3.9 | 15.2 | 107 | 4 | 3.7 | 1.0 | 9.3 |
|  | Grade 2 or 3 Related | 108 | 5 | 4.6 | 1.5 | 10.5 | 107 | 1 | 0.9 | 0.0 | 5.1 |
|  | Grade 3 Related | 108 | 2 | 1.9 | 0.2 | 6.5 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 0 | 0.0 | 0.0 | 3.4 |
| Myalgia | All | 108 | 49 | 45.4 | 35.8 | 55.2 | 107 | 17 | 15.9 | 9.5 | 24.2 |
|  | Grade 2 or 3 | 108 | 20 | 18.5 | 11.7 | 27.1 | 107 | 9 | 8.4 | 3.9 | 15.4 |
|  | Grade 3 | 108 | 8 | 7.4 | 3.3 | 14.1 | 107 | 3 | 2.8 | 0.6 | 8.0 |
|  | Related | 108 | 24 | 22.2 | 14.8 | 31.2 | 107 | 3 | 2.8 | 0.6 | 8.0 |
|  | Grade 2 or 3 Related | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | - | 1.9 | 0.2 | 6.6 |
|  | Grade 3 Related | 108 | 7 | 6.5 | 2.6 | 12.9 | 107 | - | 0.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 0 | 0.0 | 0.0 | 3.4 |
| Shivering | All | 108 | 26 | 24.1 | 16.4 | 33.3 | 107 | 13 | 12.1 | 6.6 | 19.9 |
|  | Grade 2 or 3 | 108 | 8 | 7.4 | 3.3 | 14.1 | 107 | 6 | 5.6 | 2.1 | 11.8 |
|  | Grade 3 | 108 | 5 | 4.6 | 1.5 | 10.5 | 107 | 2 | 1.9 | 0.2 | 6.6 |
|  | Related | 108 | 11 | 10.2 | 5.2 | 17.5 | 107 | 4 | 3.7 | 1.0 | 9.3 |
|  | Grade 2 or 3 Related | 108 | 6 | 5.6 | 2.1 | 11.7 | 107 | 2 | 1.9 | 0.2 | 6.6 |
|  | Grade 3 Related | 108 | 4 | 3.7 | 1.0 | 9.2 | 107 | - | 0.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 0 | 0.0 | 0.0 | 3.4 |
| Temperature/(*) ( ${ }^{\text {C }}$ ) | All | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 |  | 3.7 | 1.0 | 9.3 |
|  | $\geq 37.5$ | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 4 | 3.7 | 1.0 | 9.3 |
|  | >38.0 | 108 | 2 | 1.9 | 0.2 | 6.5 | 107 | - | 0.0 | 0.0 | 3.4 |
|  | >38.5 | 108 | 1 | 0.9 | 0.0 | 5.1 | 107 |  | 0.0 | 0.0 | 3.4 |
|  | >39.0 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 |  | 0.0 | 0.0 | 3.4 |
|  | >39.5 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | >40.0 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | - | 0.0 | 0.0 | 3.4 |
|  | Related | 108 | 11 | 10.2 | 5.2 | 17.5 | 107 | 1 | 0.9 | 0.0 | 5.1 |
|  | >38.0 Related | 108 | 2 | 1.9 | 0.2 | 6.5 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | >39.0 Related | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 1 | 0.9 | 0.0 | 5.1 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 93 | 54 | 58.1 | 47.4 | 68.2 | 103 | 56 | 54.4 | 44.3 | 64.2 |


|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95 \% Cl |  |  |  |  |  |  |  | $95 \% \mathrm{Cl}$ |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 2 or 3 | 93 | 27 | 29.0 | 20.1 | 39.4 | 103 | 29 | 28.2 | 19.7 | 37.9 |
|  | Grade 3 | 93 | 9 | 9.7 | 4.5 | 17.6 | 103 | 6 | 5.8 | 2.2 | 12.2 |
|  | Related | 93 | 6 | 6.5 | 2.4 | 13.5 | 103 | 8 | 7.8 | 3.4 | 14.7 |
|  | Grade 2 or 3 Related | 93 | 2 | 2.2 | 0.3 | 7.6 | 103 |  | 3.9 | 1.1 | 9.6 |
|  | Grade 3 Related | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | 1 | 1.0 | 0.0 | 5.3 |
|  | Medical advice | 93 | 1 | 1.1 | 0.0 | 5.8 | 103 | 1 | 1.0 | 0.0 | 5.3 |
| Gastrointestinal symptoms | All | 93 | 38 | 40.9 | 30.8 | 51.5 | 103 | 38 | 36.9 | 27.6 | 47.0 |
|  | Grade 2 or 3 | 93 | 19 | 20.4 | 12.8 | 30.1 | 103 | 15 | 14.6 | 8.4 | 22.9 |
|  | Grade 3 | 93 | 5 | 5.4 | 1.8 | 12.1 | 103 | 3 | 2.9 | 0.6 | 8.3 |
|  | Related | 93 | 6 | 6.5 | 2.4 | 13.5 | 103 | 2 | 1.9 | 0.2 | 6.8 |
|  | Grade 2 or 3 Related | 93 | 2 | 2.2 | 0.3 | 7.6 | 103 | 2 | 1.9 | 0.2 | 6.8 |
|  | Grade 3 Related | 93 | 1 | 1.1 | 0.0 | 5.8 | 103 | 0 | 0.0 | 0.0 | 3.5 |
|  | Medical advice | 93 | 1 | 1.1 | 0.0 | 5.8 | 103 | - | 0.0 | 0.0 | 3.5 |
| Headache | All | 93 | 29 | 31.2 | 22.0 | 41.6 | 103 | 24 | 23.3 | 15.5 | 32.7 |
|  | Grade 2 or 3 | 93 | 14 | 15.1 | 8.5 | 24.0 | 103 | 7 | 6.8 | 2.8 | 13.5 |
|  | Grade 3 | 93 | 3 | 3.2 | 0.7 | 9.1 | 103 | 2 | 1.9 | 0.2 | 6.8 |
|  | Related | 93 | 7 | 7.5 | 3.1 | 14.9 | 103 | 2 | 1.9 | 0.2 | 6.8 |
|  | Grade 2 or 3 Related | 93 | 4 | 4.3 | 1.2 | 10.6 | 103 | 1 | 1.0 | 0.0 | 5.3 |
|  | Grade 3 Related | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | 0 | 0.0 | 0.0 | 3.5 |
|  | Medical advice | 93 | 1 | 1.1 | 0.0 | 5.8 | 103 | 0 | 0.0 | 0.0 | 3.5 |
| Myalgia | All | 93 | 30 | 32.3 | 22.9 | 42.7 | 103 | 22 | 21.4 | 13.9 | 30.5 |
|  | Grade 2 or 3 | 93 | 14 | 15.1 | 8.5 | 24.0 | 103 | 12 | 11.7 | 6.2 | 19.5 |
|  | Grade 3 | 93 | 3 | 3.2 | 0.7 | 9.1 | 103 | 1 | 1.0 | 0.0 | 5.3 |
|  | Related | 93 | 13 | 14.0 | 7.7 | 22.7 | 103 | 4 | 3.9 | 1.1 | 9.6 |
|  | Grade 2 or 3 Related | 93 | 6 | 6.5 | 2.4 | 13.5 | 103 | 2 | 1.9 | 0.2 | 6.8 |
|  | Grade 3 Related | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | - | 0.0 | 0.0 | 3.5 |
|  | Medical advice | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | - | 0.0 | 0.0 | 3.5 |
| Shivering | All | 93 | 18 | 19.4 | 11.9 | 28.9 | 103 | 17 | 16.5 | 9.9 | 25.1 |
|  | Grade 2 or 3 | 93 | 9 | 9.7 | 4.5 | 17.6 | 103 | 1 | 1.0 | 0.0 | 5.3 |
|  | Grade 3 | 93 | 2 | 2.2 | 0.3 | 7.6 | 103 | 1 | 1.0 | 0.0 | 5.3 |
|  | Related | 93 | 6 | 6.5 | 2.4 | 13.5 | 103 | 4 | 3.9 | 1.1 | 9.6 |
|  | Grade 2 or 3 Related | 93 | 3 | 3.2 | 0.7 | 9.1 | 103 | 0 | 0.0 | 0.0 | 3.5 |
|  | Grade 3 Related | 93 | 1 | 1.1 | 0.0 | 5.8 | 103 | 0 | 0.0 | 0.0 | 3.5 |
|  | Medical advice | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | - | 0.0 | 0.0 | 3.5 |
| Temperature/(*) ( ${ }^{\text {C }}$ ) | All | 93 | 8 | 8.6 | 3.8 | 16.2 | 103 | 1 | 1.0 | 0.0 | 5.3 |
|  | $\geq 37.5$ | 93 | 8 | 8.6 | 3.8 | 16.2 | 103 | 1 | 1.0 | 0.0 | 5.3 |
|  | >38.0 | 93 | 1 | 1.1 | 0.0 | 5.8 | 103 | 1 | 1.0 | 0.0 | 5.3 |
|  | >38.5 | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | 0 | 0.0 | 0.0 | 3.5 |
|  | >39.0 | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | - | 0.0 | 0.0 | 3.5 |
|  | >39.5 | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | - | 0.0 | 0.0 | 3.5 |
|  | >40.0 | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | - | 0.0 | 0.0 | 3.5 |
|  | Related | 93 | 4 | 4.3 | 1.2 | 10.6 | 103 | - | 0.0 | 0.0 | 3.5 |
|  | >38.0 Related | 93 | 1 | 1.1 | 0.0 | 5.8 | 103 | 0 | 0.0 | 0.0 | 3.5 |
|  | >39.0 Related | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | - | 0.0 | 0.0 | 3.5 |
|  | Medical advice | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | 0 | 0.0 | 0.0 | 3.5 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 201 | 107 | 53.2 | 46.1 | 60.3 | 210 | 98 | 46.7 | 39.8 | 53.7 |
|  | Grade 2 or 3 | 201 | 56 | 27.9 | 21.8 | 34.6 | 210 | 44 | 21.0 | 15.7 | 27.1 |
|  | Grade 3 | 201 | 19 | 9.5 | 5.8 | 14.4 | 210 | - | 4.3 | 2.0 | 8.0 |
|  | Related | 201 | 19 | 9.5 | 5.8 | 14.4 | 210 | 18 | 8.6 | 5.2 | 13.2 |
|  | Grade 2 or 3 Related | 201 | 10 | 5.0 | 2.4 | 9.0 | 210 | 8 | 3.8 | 1.7 | 7.4 |
|  | Grade 3 Related | 201 | 3 | 1.5 | 0.3 | 4.3 | 210 | 1 | 0.5 | 0.0 | 2.6 |
|  | Medical advice | 201 | 1 | 0.5 | 0.0 | 2.7 | 210 | 1 | 0.5 | 0.0 | 2.6 |


|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95 \% CI |  | N | n |  | 95 \% CI |  |
| Symptom | Type | N | n | \% | LL | UL |  |  | \% | LL | UL |
| Gastrointestinal symptoms | All | 201 | 70 | 34.8 | 28.3 | 41.8 | 210 | 59 | 28.1 | 22.1 | 34.7 |
|  | Grade 2 or 3 | 201 | 33 | 16.4 | 11.6 | 22.3 | 210 | 26 | 12.4 | 8.2 | 17.6 |
|  | Grade 3 | 201 | 7 | 3.5 | 1.4 | 7.0 | 210 | 8 | 3.8 | 1.7 | 7.4 |
|  | Related | 201 | 15 | 7.5 | 4.2 | 12.0 | 210 | - | 1.9 | 0.5 | 4.8 |
|  | Grade 2 or 3 Related | 201 | 4 | 2.0 | 0.5 | 5.0 | 210 | , | 1.4 | 0.3 | 4.1 |
|  | Grade 3 Related | 201 | 1 | 0.5 | 0.0 | 2.7 | 210 |  | 0.5 | 0.0 | 2.6 |
|  | Medical advice | 201 | 1 | 0.5 | 0.0 | 2.7 | 210 | 2 | 1.0 | 0.1 | 3.4 |
| Headache | All | 201 | 55 | 27.4 | 21.3 | 34.1 | 210 | 47 | 22.4 | 16.9 | 28.6 |
|  | Grade 2 or 3 | 201 | 27 | 13.4 | 9.0 | 18.9 | 210 | 14 | 6.7 | 3.7 | 10.9 |
|  | Grade 3 | 201 | 6 | 3.0 | 1.1 | 6.4 | 210 | 3 | 1.4 | 0.3 | 4.1 |
|  | Related | 201 | 16 | 8.0 | 4.6 | 12.6 | 210 | 6 | 2.9 | 1.1 | 6.1 |
|  | Grade 2 or 3 Related | 201 | 9 | 4.5 | 2.1 | 8.3 | 210 | 2 | 1.0 | 0.1 | 3.4 |
|  | Grade 3 Related | 201 | 2 | 1.0 | 0.1 | 3.5 | 210 | - | 0.0 | 0.0 | 1.7 |
|  | Medical advice | 201 | 1 | 0.5 | 0.0 | 2.7 | 210 | 0 | 0.0 | 0.0 | 1.7 |
| Myalgia | All | 201 | 79 | 39.3 | 32.5 | 46.4 | 210 | 39 | 18.6 | 13.6 | 24.5 |
|  | Grade 2 or 3 | 201 | 34 | 16.9 | 12.0 | 22.8 | 210 | 21 | 10.0 | 6.3 | 14.9 |
|  | Grade 3 | 201 | 11 | 5.5 | 2.8 | 9.6 | 210 | 4 | 1.9 | 0.5 | 4.8 |
|  | Related | 201 | 37 | 18.4 | 13.3 | 24.5 | 210 | 7 | 3.3 | 1.4 | 6.7 |
|  | Grade 2 or 3 Related | 201 | 19 | 9.5 | 5.8 | 14.4 | 210 | 4 | 1.9 | 0.5 | 4.8 |
|  | Grade 3 Related | 201 | 7 | 3.5 | 1.4 | 7.0 | 210 | 0 | 0.0 | 0.0 | 1.7 |
|  | Medical advice | 201 | 0 | 0.0 | 0.0 | 1.8 | 210 | - | 0.0 | 0.0 | 1.7 |
| Shivering | All | 201 | 44 | 21.9 | 16.4 | 28.3 | 210 | 30 | 14.3 | 9.9 | 19.8 |
|  | Grade 2 or 3 | 201 | 17 | 8.5 | 5.0 | 13.2 | 210 | 7 | 3.3 | 1.4 | 6.7 |
|  | Grade 3 | 201 | 7 | 3.5 | 1.4 | 7.0 | 210 | 3 | 1.4 | 0.3 | 4.1 |
|  | Related | 201 | 17 | 8.5 | 5.0 | 13.2 | 210 |  | 3.8 | 1.7 | 7.4 |
|  | Grade 2 or 3 Related | 201 | 9 | 4.5 | 2.1 | 8.3 | 210 | 2 | 1.0 | 0.1 | 3.4 |
|  | Grade 3 Related | 201 | 5 | 2.5 | 0.8 | 5.7 | 210 | - | 0.0 | 0.0 | 1.7 |
|  | Medical advice | 201 | 0 | 0.0 | 0.0 | 1.8 | 210 | - | 0.0 | 0.0 | 1.7 |
| Temperature/(*) ( ${ }^{\text {C }}$ ) | All | 201 | 21 | 10.4 | 6.6 | 15.5 | 210 | 5 | 2.4 | 0.8 | 5.5 |
|  | $\geq 37.5$ | 201 | 21 | 10.4 | 6.6 | 15.5 | 210 | 5 | 2.4 | 0.8 | 5.5 |
|  | $>38.0$ | 201 | 3 | 1.5 | 0.3 | 4.3 | 210 | 1 | 0.5 | 0.0 | 2.6 |
|  | >38.5 | 201 | 1 | 0.5 | 0.0 | 2.7 | 210 | 0 | 0.0 | 0.0 | 1.7 |
|  | $>39.0$ | 201 | 0 | 0.0 | 0.0 | 1.8 | 210 | - | 0.0 | 0.0 | 1.7 |
|  | >39.5 | 201 | 0 | 0.0 | 0.0 | 1.8 | 210 | 0 | 0.0 | 0.0 | 1.7 |
|  | >40.0 | 201 | 0 | 0.0 | 0.0 | 1.8 | 210 | 0 | 0.0 | 0.0 | 1.7 |
|  | Related | 201 | 15 | 7.5 | 4.2 | 12.0 | 210 | 1 | 0.5 | 0.0 | 2.6 |
|  | >38.0 Related | 201 | 3 | 1.5 | 0.3 | 4.3 | 210 | 0 | 0.0 | 0.0 | 1.7 |
|  | >39.0 Related | 201 | 0 | 0.0 | 0.0 | 1.8 | 210 | 0 | 0.0 | 0.0 | 1.7 |
|  | Medical advice | 201 | 0 | 0.0 | 0.0 | 1.8 | 210 | 1 | 0.5 | 0.0 | 2.6 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 108 | 74 | 68.5 | 58.9 | 77.1 | 107 | 66 | 61.7 | 51.8 | 70.9 |
|  | Grade 2 or 3 | 108 | 43 | 39.8 | 30.5 | 49.7 | 107 | 36 | 33.6 | 24.8 | 43.4 |
|  | Grade 3 | 108 | 16 | 14.8 | 8.7 | 22.9 | 107 | - | 7.5 | 3.3 | 14.2 |
|  | Related | 108 | 17 | 15.7 | 9.4 | 24.0 | 107 | 14 | 13.1 | 7.3 | 21.0 |
|  | Grade 2 or 3 Related | 108 | 10 | 9.3 | 4.5 | 16.4 | 107 | 8 | 7.5 | 3.3 | 14.2 |
|  | Grade 3 Related | 108 | 3 | 2.8 | 0.6 | 7.9 | 107 | 1 | 0.9 | 0.0 | 5.1 |
|  | Medical advice | 108 | 1 | 0.9 | 0.0 | 5.1 | 107 | 1 | 0.9 | 0.0 | 5.1 |
| Gastrointestinal symptoms | All | 108 | 48 | 44.4 | 34.9 | 54.3 | 107 | 48 | 44.9 | 35.2 | 54.8 |
|  | Grade 2 or 3 | 108 | 24 | 22.2 | 14.8 | 31.2 | 107 | 21 | 19.6 | 12.6 | 28.4 |
|  | Grade 3 | 108 | 6 | 5.6 | 2.1 | 11.7 | 107 | 7 | 6.5 | 2.7 | 13.0 |
|  | Related | 108 | 11 | 10.2 | 5.2 | 17.5 | 107 | 3 | 2.8 | 0.6 | 8.0 |
|  | Grade 2 or 3 Related | 108 | 3 | 2.8 | 0.6 | 7.9 | 107 | 3 | 2.8 | 0.6 | 8.0 |
|  | Grade 3 Related | 108 | 1 | 0.9 | 0.0 | 5.1 | 107 | 1 | 0.9 | 0.0 | 5.1 |


|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95 \% CI |  |  |  |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Medical advice | 108 | 1 | 0.9 | 0.0 | 5.1 | 107 | 2 | 1.9 | 0.2 | 6.6 |
| Headache | All | 108 | 41 | 38.0 | 28.8 | 47.8 | 107 | 38 | 35.5 | 26.5 | 45.4 |
|  | Grade 2 or 3 | 108 | 21 | 19.4 | 12.5 | 28.2 | 107 | 13 | 12.1 | 6.6 | 19.9 |
|  | Grade 3 | 108 | 6 | 5.6 | 2.1 | 11.7 | 107 | 3 | 2.8 | 0.6 | 8.0 |
|  | Related | 108 | 15 | 13.9 | 8.0 | 21.9 | 107 | 6 | 5.6 | 2.1 | 11.8 |
|  | Grade 2 or 3 Related | 108 | 8 | 7.4 | 3.3 | 14.1 | 107 | 2 | 1.9 | 0.2 | 6.6 |
|  | Grade 3 Related | 108 | 2 | 1.9 | 0.2 | 6.5 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 1 | 0.9 | 0.0 | 5.1 | 107 | 0 | 0.0 | 0.0 | 3.4 |
| Myalgia | All | 108 | 58 | 53.7 | 43.8 | 63.3 | 107 | 30 | 28.0 | 19.8 | 37.5 |
|  | Grade 2 or 3 | 108 | 29 | 26.9 | 18.8 | 36.2 | 107 | 18 | 16.8 | 10.3 | 25.3 |
|  | Grade 3 | 108 | 11 | 10.2 | 5.2 | 17.5 | 107 | 4 | 3.7 | 1.0 | 9.3 |
|  | Related | 108 | 29 | 26.9 | 18.8 | 36.2 | 107 | 5 | 4.7 | 1.5 | 10.6 |
|  | Grade 2 or 3 Related | 108 | 16 | 14.8 | 8.7 | 22.9 | 107 | 4 | 3.7 | 1.0 | 9.3 |
|  | Grade 3 Related | 108 | 7 | 6.5 | 2.6 | 12.9 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 0 | 0.0 | 0.0 | 3.4 |
| Shivering | All | 108 | 37 | 34.3 | 25.4 | 44.0 | 107 | 25 | 23.4 | 15.7 | 32.5 |
|  | Grade 2 or 3 | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 7 | 6.5 | 2.7 | 13.0 |
|  | Grade 3 | 108 | 5 | 4.6 | 1.5 | 10.5 | 107 | 3 | 2.8 | 0.6 | 8.0 |
|  | Related | 108 | 15 | 13.9 | 8.0 | 21.9 | 107 | 5 | 4.7 | 1.5 | 10.6 |
|  | Grade 2 or 3 Related | 108 | 7 | 6.5 | 2.6 | 12.9 | 107 | 2 | 1.9 | 0.2 | 6.6 |
|  | Grade 3 Related | 108 | 4 | 3.7 | 1.0 | 9.2 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 0 | 0.0 | 0.0 | 3.4 |
| Temperature/(*) ( ${ }^{( } \mathrm{C}$ ) | All | 108 | 20 | 18.5 | 11.7 | 27.1 | 107 | 5 | 4.7 | 1.5 | 10.6 |
|  | $\geq 37.5$ | 108 | 20 | 18.5 | 11.7 | 27.1 | 107 | 5 | 4.7 | 1.5 | 10.6 |
|  | >38.0 | 108 | 3 | 2.8 | 0.6 | 7.9 | 107 | 1 | 0.9 | 0.0 | 5.1 |
|  | $>38.5$ | 108 | 1 | 0.9 | 0.0 | 5.1 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | >39.0 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | >39.5 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | >40.0 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | Related | 108 | 14 | 13.0 | 7.3 | 20.8 | 107 | 1 | 0.9 | 0.0 | 5.1 |
|  | >38.0 Related | 108 | 3 | 2.8 | 0.6 | 7.9 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | >39.0 Related | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 0 | 0.0 | 0.0 | 3.4 |
|  | Medical advice | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 1 | 0.9 | 0.0 | 5.1 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit
$\left(^{*}\right)=$ Temperature is measured by oral, axillary or tympanic routes
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for oral, axillary or tympanic route

Table 8.48 Number and percentage of subjects who reported temperature by half degree measured during the 7 -day (Days $0-6$ ) post-vaccination period following each dose (no conversion) (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95\% Cl |  |  |  |  |  |  | 95 \% CI |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n $\%$ | LL |  |  |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(*) ( ${ }^{\circ} \mathrm{C}$ ) | All | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 43.7 | 1.0 | 09 | 9.3 |
|  | $\geq 35.5$ | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 43.7 | 1.0 | 09 | 9.3 |
|  | >36.0 | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 43.7 | 1.0 | 09 | 9.3 |
|  | >36.5 | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 43.7 | 1.0 | 09 | 9.3 |
|  | >37.0 | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 43.7 | 1.0 | 09 | 9.3 |
|  | >37.5 | 108 | 8 | 7.4 | 3.3 | 14.1 | 107 | 43.7 | 1.0 | 09 | 9.3 |
|  | $>38.0$ | 108 | 2 | 1.9 | 0.2 | 6.5 | 107 | 00.0 | 0.0 | 03 | 3.4 |
|  | >38.5 | 108 | 1 | 0.9 | 0.0 | 5.1 | 107 | 00.0 | 0.0 | 03 | 3.4 |
|  | >39.0 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 03 | 3.4 |
|  | >39.5 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 |  | 3.4 |
|  | >40.0 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 |  | 3.4 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(*) ( ${ }^{\circ} \mathrm{C}$ ) | All | 93 | 8 | 8.6 | 3.8 | 16.2 | 103 | 11.0 | 0.0 | 0 | . 3 |
|  | $\geq 35.5$ | 93 | 8 | 8.6 | 3.8 | 16.2 | 103 | 11.0 | 0.0 | 05 | 5.3 |
|  | >36.0 | 93 | 8 | 8.6 | 3.8 | 16.2 | 103 | 11.0 | 0.0 | 05 | 5.3 |
|  | >36.5 | 93 | 8 | 8.6 | 3.8 | 16.2 | 103 | 11.0 | 0.0 | 05 | 5.3 |
|  | >37.0 | 93 | 8 | 8.6 | 3.8 | 16.2 | 103 | 11.0 | 0.0 | 05 | 5.3 |
|  | >37.5 | 93 | 4 | 4.3 | 1.2 | 10.6 | 103 | 11.0 | 0.0 | 05 | 5.3 |
|  | >38.0 | 93 | 1 | 1.1 | 0.0 | 5.8 | 103 | 11.0 | 0.0 | 05 | 5.3 |
|  | >38.5 | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | 00.0 | 0.0 |  | 3.5 |
|  | $>39.0$ | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | 00.0 | 0.0 |  | 3.5 |
|  | >39.5 | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | 00.0 | 0.0 |  | 3.5 |
|  | >40.0 | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | 00.0 | 0.0 |  | . 5 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(*) ( ${ }^{\circ} \mathrm{C}$ ) | All | 201 | 21 | 10.4 | 6.6 | 15.5 | 210 | 52.4 | 0.8 | 85 | 5.5 |
|  | $\geq 35.5$ | 201 | 21 | 10.4 | 6.6 | 15.5 | 210 | 52.4 | 0.8 | 85 | 5.5 |
|  | >36.0 | 201 | 21 | 10.4 | 6.6 | 15.5 | 210 | 52.4 | 0.8 | 85 | 5.5 |
|  | >36.5 | 201 | 21 | 10.4 | 6.6 | 15.5 | 210 | 52.4 | 0.8 | 85 | 5.5 |
|  | >37.0 | 201 | 21 | 10.4 | 6.6 | 15.5 | 210 | 52.4 | 0.8 | 85 | 5.5 |
|  | >37.5 | 201 | 12 | 6.0 | 3.1 | 10.2 | 210 | 52.4 | 0.8 | 85 | 5.5 |
|  | $>38.0$ | 201 | 3 | 1.5 | 0.3 | 4.3 | 210 | 10.5 | 0.0 | 02 | 2.6 |
|  | >38.5 | 201 | 1 | 0.5 | 0.0 | 2.7 | 210 | 00.0 | 0.0 | 0 | 1.7 |
|  | >39.0 | 201 | 0 | 0.0 | 0.0 | 1.8 | 210 | 00.0 | 0.0 | 0 | 1.7 |
|  | >39.5 | 201 | 0 | 0.0 | 0.0 | 1.8 | 210 | 00.0 | 0.0 | 01 | 1.7 |
|  | >40.0 | 201 | 0 | 0.0 | 0.0 | 1.8 | 210 | 00.0 | 0.0 |  | 1.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(*) ( ${ }^{\circ} \mathrm{C}$ ) | All | 108 | 20 | 18.5 | 11.7 | 27.1 | 107 | 54.7 | 1.5 |  | 10.6 |
|  | $\geq 35.5$ | 108 | 20 | 18.5 | 11.7 | 27.1 | 107 | 54.7 | 1.5 | 510 | 10.6 |
|  | >36.0 | 108 | 20 | 18.5 | 11.7 | 27.1 | 107 | 54.7 | 1.5 | 510 | 10.6 |
|  | >36.5 | 108 | 20 | 18.5 | 11.7 | 27.1 | 107 | 54.7 | 1.5 |  | 10.6 |
|  | >37.0 | 108 | 20 | 18.5 | 11.7 | 27.1 | 107 | 54.7 | 1.5 |  | 10.6 |
|  | >37.5 | 108 | 11 | 10.2 | 5.2 | 17.5 | 107 | 54.7 | 1.5 |  | 10.6 |
|  | >38.0 | 108 | 3 | 2.8 | 0.6 | 7.9 | 107 | 10.9 | 0.0 | 05 | 5.1 |
|  | >38.5 | 108 | 1 | 0.9 | 0.0 | 5.1 | 107 | 00.0 | 0.0 | 03 | 3.4 |
|  | >39.0 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 03 | 3.4 |
|  | >39.5 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 03 | 3.4 |
|  | >40.0 | 108 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 03 | 3.4 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
95\%CI = Exact 95\% confidence interval; LL = lower limit, UL = upper limit
$\left(^{*}\right)=$ Temperature is measured by oral, axillary or tympanic routes
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for oral, axillary or tympanic route
Table 8.49 Number and percentage of subjects who reported temperature by half degree measured via oral route during the 7-day (Days 0-6) post-vaccination period following each dose (no conversion) (ATP cohort for safety up to 30 days post last vaccination)



Table 8.50 Number and percentage of subjects who reported temperature by half degree measured via axillary route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) (ATP cohort for safety up to 30 days post last vaccination)

|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95 \% Cl |  |  |  |  |  |  |  | 95 \% Cl |  |
| Symptom | Type | N | n | \% | LL | UL | N | n \% |  | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 108 | 9 | 8.3 | 3.9 | 115.2 | 107 | 32.8 | 2.8 | 0.6 | 8.0 |
|  | $\geq 35.5$ | 108 | 9 | 8.3 | 3.9 | 15.2 | 107 | 32.8 | 2.8 | 0.6 | 8.0 |
|  | >36.0 | 108 | 9 | 8.3 | 3.9 | 15.2 | 107 | 32.8 | 2.8 | 0.6 | 8.0 |
|  | >36.5 | 108 | 9 | 8.3 | 3.9 | 15.2 | 107 | 32.8 | 2.8 | 0.6 | 8.0 |
|  | >37.0 | 108 | 9 | 8.3 | 3.9 | 15.2 | 107 | 32.8 | 2.8 | 0.6 | 8.0 |
|  | >37.5 | 108 | 7 | 6.5 | 2.6 | 12.9 | 107 | 32.8 | 2.8 | 0.6 | 8.0 |
|  | >38.0 | 108 | 2 | 1.9 | 0.2 | 6.5 | 107 | 00.0 | 0.0 | 0.0 | 3.4 |
|  | >38.5 | 108 | 1 | 0.9 | 0.0 | 5.1 | 107 | 00.0 | 0.0 | 0.0 | 3.4 |
|  | $>39.0$ | 108 | 0 | 0.0 | 0.0 | O 3.4 | 107 | 00.0 | 0.0 | 0.0 | 3.4 |
|  | >39.5 | 1080 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 0.0 | 3.4 |
|  | >40.0 | 1080 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 0.0 | 3.4 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 93 | 4 | 4.3 | 1.2 | 10.6 | 103 | 11.0 | 1.0 | 0.0 | 5.3 |
|  | $\geq 35.5$ | 93 | 4 | 4.3 | 1.2 | 10.6 | 103 | 11.0 | 1.0 | 0.0 | 5.3 |
|  | >36.0 | 93 | 4 | 4.3 | 1.2 | 10.6 | 103 | 11.0 | 1.0 | 0.0 | 5.3 |
|  | $>36.5$ | 93 | 4 | 4.3 | 1.2 | 10.6 | 103 | 11.0 | 1.0 | 0.0 | 5.3 |
|  | >37.0 | 93 | 4 | 4.3 | 1.2 | 10.6 | 103 | 11.0 | 1.0 | 0.0 | 5.3 |
|  | $>37.5$ | 93 | 1 | 1.1 | 0.0 | 5.8 | 103 | 11.0 | 1.0 | 0.0 | 5.3 |
|  | $>38.0$ | 93 | 0 | 0.0 | 0.0 | O 3.9 | 103 | 11.0 | 1.0 | 0.0 | 5.3 |
|  | >38.5 | 93 | 0 | 0.0 | 0.0 | . 3.9 | 103 | 00.0 | 0.0 | 0.0 | 3.5 |
|  | >39.0 | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | 00.0 | 0.0 | 0.0 | 3.5 |


|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n \% | \% | LL |  | JL |
|  | >39.5 | 93 | 0 | 0.0 | 0.0 | 3.9 | 103 | 00 | 0.0 | 0.0 | 3 | 3.5 |
|  | >40.0 | 930 | 0 | 0.0 | 0.0 | 3.9 | 103 | 00 | 0.0 | 0.0 |  | 3.5 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 201 | 136 | 6.5 | 3.5 | 10.8 | 210 | 41 | 1.9 | 0.5 |  | 4.8 |
|  | $\geq 35.5$ | 201 | 136 | 6.5 | 3.5 | 510.8 | 210 | 41 | 1.9 | 0.5 |  | 4.8 |
|  | >36.0 | 201 | 136 | 6.5 | 3.5 | 510.8 | 210 | 41 | 1.9 | 0.5 | 4 | 4.8 |
|  | >36.5 | 201 | 136 | 6.5 | 3.5 | 10.8 | 210 | 41 | 1.9 | 0.5 | 4 | 4.8 |
|  | >37.0 | 201 | 136 | 6.5 | 3.5 | 10.8 | 210 | 41 | 1.9 | 0.5 | 4 | 4.8 |
|  | >37.5 | 2018 | 8 | 4.0 | 1.7 | 7.7 | 210 | 41 | 1.9 | 0.5 | . 4 | 4.8 |
|  | >38.0 | 2012 | 2 | 1.0 | 0.1 | 13.5 | 210 | 10 | 0.5 | 0.0 | 2 | 2.6 |
|  | >38.5 | 201 | 1 | 0.5 | 0.0 | 2.7 | 210 | 00 | 0.0 | 0.0 |  | 1.7 |
|  | >39.0 | 2010 | 0 | 0.0 | 0.0 | 1.8 | 210 | 00 | 0.0 | 0.0 |  | 1.7 |
|  | >39.5 | 2010 | 0 | 0.0 | 0.0 | 1.8 | 210 | 00 | 0.0 | 0.0 | 1. | 1.7 |
|  | >40.0 | 2010 | 0 | 0.0 | 0.0 | 1.8 | 210 | 00 | 0.0 | 0.0 |  | 1.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 413 | 3.7 | 1.0 |  | 9.3 |
|  | $\geq 35.5$ | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 43 | 3.7 | 1.0 |  | 9.3 |
|  | >36.0 | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 43 | 3.7 | 1.0 |  | 9 3 |
|  | >36.5 | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 43 | 3.7 | 1.0 |  | 9 3 |
|  | >37.0 | 108 | 13 | 12.0 | 6.6 | 19.7 | 107 | 43 | 3.7 | 1.0 |  | 9 3 |
|  | >37.5 | 108 | 8 | 7.4 | 3.3 | 14.1 | 107 | 43 | 3.7 | 1.0 | 9 | 9.3 |
|  | >38.0 | 108 | 2 | 1.9 | 0.2 | 26.5 | 107 | 10 | 0.9 | 0.0 |  | . 1 |
|  | >38.5 | 108 | 1 | 0.9 | 0.0 | 5.1 | 107 | 00 | 0.0 | 0.0 |  | 3.4 |
|  | >39.0 | 1080 | 0 | 0.0 | 0.0 | - 3.4 | 107 | 00 | 0.0 | 0.0 |  | 3.4 |
|  | >39.5 | 1080 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00 | 0.0 | 0.0 |  | 3.4 |
|  | >40.0 | 1080 | 0 | 0.0 | 0.0 | 3.4 | 107 | 00 | 0.0 | 0.0 |  | 3.4 |
| HZ/su = Herpes Zoster sub-unit vaccine group |  |  |  |  |  |  |  |  |  |  |  |  |
| Placebo = Placebo group |  |  |  |  |  |  |  |  |  |  |  |  |
| For each dose and overall/subject: |  |  |  |  |  |  |  |  |  |  |  |  |
| $\mathrm{N}=$ number of subjects with at least one documented dose |  |  |  |  |  |  |  |  |  |  |  |  |
| $\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once |  |  |  |  |  |  |  |  |  |  |  |  |
| For Overall/dose: |  |  |  |  |  |  |  |  |  |  |  |  |
| $\mathrm{N}=$ number of documented doses |  |  |  |  |  |  |  |  |  |  |  |  |
| $\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of sympto |  |  |  |  |  |  |  |  |  |  |  |  |
| 95\%CI = Exact 95\% confidence interval; LL = lower limit, UL = upper limit |  |  |  |  |  |  |  |  |  |  |  |  |
| Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for axillary route |  |  |  |  |  |  |  |  |  |  |  |  |

Table 8.51 Number and percentage of subjects who reported temperature by half degree measured via tympanic route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) (ATP cohort for safety up to 30 days post last vaccination)

|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95 \% Cl |  |  |  |  |  |  | 95 \% Cl |  |
| Symptom | Type | N | n \% | \% LL | LL | UL | N | n $\%$ | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 108 | 00. | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | $\geq 35.5$ | 108 | 00.0 | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >36.0 | 108 | 00. | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >36.5 | 108 | 00. | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >37.0 | 108 | 00. | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >37.5 | 108 | 00.0 | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >38.0 | 108 | 00.0 | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >38.5 | 108 | 00.0 | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >39.0 | 108 | 00. | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >39.5 | 108 | 00. | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >40.0 | 108 | 00.0 | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 93 | 11. | 1.10. | 0.0 | 5.8 | 103 | 00.0 | 0.0 | 3.5 |
|  | $\geq 35.5$ | 93 | 11. | 1.10. | 0.0 | 5.8 | 103 | 00.0 | 0.0 | 3.5 |
|  | >36.0 | 93 | 11. | 1.10. | 0.0 | 5.8 | 103 | 00.0 | 0.0 | 3.5 |
|  | >36.5 | 93 | 11. | 1.10. | 0.0 | 5.8 | 103 | 00.0 | 0.0 | 3.5 |
|  | >37.0 | 93 | 11. | 1.10. | 0.0 | 5.8 | 103 | 00.0 | 0.0 | 3.5 |
|  | >37.5 | 93 | 00.0 | 0.00. | 0.0 | 3.9 | 103 | 00.0 | 0.0 | 3.5 |
|  | >38.0 | 93 | 00. | 0.00. | 0.0 | 3.9 | 103 | 00.0 | 0.0 | 3.5 |
|  | >38.5 | 93 | 00. | 0.00. | 0.0 | 3.9 | 103 | 00.0 | 0.0 | 3.5 |
|  | >39.0 | 93 | 00.0 | 0.00. | 0.0 | 3.9 | 103 | 00.0 | 0.0 | 3.5 |
|  | >39.5 | 93 | 00. | 0.00. | 0.0 | 3.9 | 103 | 00.0 | 0.0 | 3.5 |
|  | >40.0 | 93 | 00.0 | 0.00. | 0.0 | 3.9 | 103 |  | 0.0 | 3.5 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 201 | 10.5 | 0.50. | 0.0 | 2.7 | 210 | 010.0 | 0.0 | 1.7 |
|  | $\geq 35.5$ | 201 | 10.5 | 0.50. | 0.0 | 2.7 | 210 | 00.0 | 0.0 | 1.7 |
|  | >36.0 | 201 | 10.5 | 0.50. | 0.0 | 2.7 | 210 | 00.0 | 0.0 | 1.7 |
|  | >36.5 | 201 | 10.5 | 0.50. | 0.0 | 2.7 | 210 | 00.0 | 0.0 | 1.7 |
|  | >37.0 | 201 | 10.5 | 0.50. | 0.0 | 2.7 | 210 | 00.0 | 0.0 | 1.7 |
|  | >37.5 | 201 | 00.0 | 0.00. | 0.0 | 1.8 | 210 | 00.0 | 0.0 | 1.7 |
|  | >38.0 | 201 | 00. | 0.00. | 0.0 | 1.8 | 210 | 00.0 | 0.0 | 1.7 |
|  | >38.5 | 201 | 00. | 0.00. | 0.0 | 1.8 | 210 | 00.0 | 0.0 | 1.7 |
|  | >39.0 | 201 | 00.0 | 0.00. | 0.0 | 1.8 | 210 | 00.0 | 0.0 | 1.7 |
|  | >39.5 | 201 | 00. | 0.00. | 0.0 | 1.8 | 210 | 00.0 | 0.0 | 1.7 |
|  | >40.0 | 201 | 00.0 | 0.00. | 0.0 | 1.8 | 210 | 00.0 | 0.0 | 1.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 108 | 10.9 | 0.90. | 0.0 | 5.1 | 107 | 00.0 | 0.0 | 3.4 |
|  | $\geq 35.5$ | 108 | 10.9 | 0.90. | 0.0 | 5.1 | 107 | 00.0 | 0.0 | 3.4 |
|  | >36.0 | 108 | 10.9 | 0.90. | 0.0 | 5.1 | 107 | 00.0 | 0.0 | 3.4 |
|  | >36.5 | 108 | 10.9 | 0.90. | 0.0 | 5.1 | 107 | 00.0 | 0.0 | 3.4 |
|  | >37.0 | 108 | 10. | 0.90. | 0.0 | 5.1 | 107 | 00.0 | 0.0 | 3.4 |
|  | >37.5 | 108 | 00.0 | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >38.0 | 108 | 00.0 | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >38.5 | 108 | 00.0 | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >39.0 | 108 | 00.0 | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >39.5 | 108 | 00.0 | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |
|  | >40.0 | 108 | 00.0 | 0.00. | 0.0 | 3.4 | 107 | 00.0 | 0.0 | 3.4 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; $\mathrm{LL}=$ lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for tympanic route
Table 8.52 Number and percentage of subjects who reported temperature by half degree measured via rectal route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) (ATP cohort for safety up to 30 days post last vaccination)

No records exist in this table

Table 8.53 Number of days with local symptoms during the solicited postvaccination period (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

| Solicited symptom | Dose | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Pain | Dose 1 | HZ/su | 79 | 2.8 | 1.0 | 2.0 | 2.0 | 4.0 | 7.0 |
|  |  | Placebo | 2 | 2.0 | 1.0 | 1.0 | 2.0 | 3.0 | 3.0 |
|  | Dose 2 | HZ/su | 49 | 2.7 | 1.0 | 1.0 | 2.0 | 3.0 | 7.0 |
|  |  | Placebo | 5 | 2.4 | 1.0 | 1.0 | 1.0 | 2.0 | 7.0 |
|  | Overall/dose | HZ/su | 128 | 2.8 | 1.0 | 2.0 | 2.0 | 4.0 | 7.0 |
|  |  | Placebo | 7 | 2.3 | 1.0 | 1.0 | 1.0 | 3.0 | 7.0 |
| Redness | Dose 1 | HZ/su | 30 | 3.7 | 1.0 | 2.0 | 3.5 | 5.0 | 7.0 |
|  | Dose 2 | HZ/su | 18 | 3.6 | 1.0 | 2.0 | 4.0 | 5.0 | 7.0 |
|  | Overall/dose | HZ/su | 48 | 3.7 | 1.0 | 2.0 | 4.0 | 5.0 | 7.0 |
| Swelling | Dose 1 | HZ/su | 14 | 3.9 | 2.0 | 2.0 | 4.0 | 5.0 | 7.0 |
|  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |
|  | Dose 2 | HZ/su | 8 | 3.8 | 1.0 | 2.0 | 3.5 | 5.5 | 7.0 |
|  | Overall/dose | HZ/su | 22 | 3.8 | 1.0 | 2.0 | 4.0 | 5.0 | 7.0 |
|  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of doses with the symptom
Q1 $=$ 25th percentile
Q3 $=75$ th percentile

Table 8.54 Number of days with grade 3 local symptoms during the solicited post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)

| Solicited symptom | Dose | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| Pain | Dose 1 | HZ/su | 7 | 1.1 | 1.0 | 1.0 | 1.0 | 1.0 | 2.0 |
|  | Dose 2 | $\mathrm{HZ/su}$ | 4 | 2.5 | 1.0 | 2.0 | 3.0 | 3.0 | 3.0 |
|  | Overall/dose | $\mathrm{HZ/su}$ | 11 | 1.6 | 1.0 | 1.0 | 1.0 | 3.0 | 3.0 |
| Redness | Dose 1 | $\mathrm{HZ/su}$ | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | $\mathrm{HZ} /$ su | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=25$ th percentile
Q3 $=75$ th percentile
Table 8.55 Number of days with local symptoms (ATP cohort for safety up to 30 days post last vaccination)

| Solicited symptom | Dose | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Pain | Dose 1 | HZ/su | 79 | 2.9 | 1.0 | 2.0 | 2.0 | 4.0 | 15.0 |
|  |  | Placebo | 2 | 2.0 | 1.0 | 1.0 | 2.0 | 3.0 | 3.0 |
|  | Dose 2 | HZ/su | 49 | 2.9 | 1.0 | 1.0 | 2.0 | 3.0 | 11.0 |
|  |  | Placebo | 5 | 4.4 | 1.0 | 1.0 | 1.0 | 2.0 | 17.0 |
|  | Overall/dose | HZ/su | 128 | 2.9 | 1.0 | 2.0 | 2.0 | 4.0 | 15.0 |
|  |  | Placebo | 7 | 3.7 | 1.0 | 1.0 | 1.0 | 3.0 | 17.0 |
| Redness | Dose 1 | HZ/su | 30 | 4.3 | 1.0 | 2.0 | 3.5 | 5.0 | 15.0 |
|  | Dose 2 | HZ/su | 18 | 4.4 | 1.0 | 2.0 | 4.0 | 6.0 | 11.0 |
|  | Overall/dose | HZ/su | 48 | 4.4 | 1.0 | 2.0 | 4.0 | 5.5 | 15.0 |
| Swelling | Dose 1 | HZ/su | 14 | 5.1 | 2.0 | 2.0 | 4.0 | 5.0 | 14.0 |
|  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |
|  | Dose 2 | HZ/su | 8 | 4.5 | 1.0 | 2.0 | 3.5 | 7.0 | 10.0 |
|  | Overall/dose | HZ/su | 22 | 4.9 | 1.0 | 2.0 | 4.0 | 5.0 | 14.0 |
|  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom (during the solicited post-vaccination period and beyond)
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.56 Solicited local symptoms ongoing beyond the 7-day (Days 0-6) postvaccination period (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

|  |  | HZ/su |  |  |  |  |  | Placebo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | Time to resolution (days) |  |  |  |  |  | Time to resolution (days) |  |  |  |  |  |
| Symptoms | Type | N | Ns |  | q1 | median | q3 | N |  | Ns n | q 1 | median | q3 |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | Any | 108 | 879 | 1 | 8 | 8 | 8 | 107 | 72 | 0 | 0- | - | - |
|  | Grade 3 | 108 | 7 | 0 | - | - | - | 107 | 70 | 0 | 0- | - | - |
| Redness | Any | 108 | 830 | 4 | 3 | 3 | 6 | 107 | 70 | 0 | 0 | - | - |
|  | Grade 3 | 108 | 2 | 0 | - | - | - | 107 | 70 | 0 | 0- | - | - |
| Swelling | Any | 108 | 814 | 3 | 3 | 6 | 9 | 107 | 71 | 0 | 0- | - | - |
|  | Grade 3 | 108 | 0 | 0 | - | - | - | 107 | 70 | 0 | 0- | - | - |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | Any | 94 | 49 | 2 | 3 | 5 | 7 | 103 | 35 | 1 | 110 | 10 | 10 |
|  | Grade 3 | 94 | 4 | 2 | 3 | 5 | 7 | 103 | 30 | 0 | 0- | - | - |
| Redness | Any | 94 | 18 | 4 | 2.5 | 3 | 5 | 103 | 30 | 0 | 0- | - | - |
|  | Grade 3 | 94 | 0 | 0 | - | - | - | 103 | 30 | 0 | 0- | - | - |
| Swelling | Any | 94 | 8 | 2 | 3 | 3 | 3 | 103 | 30 | 0 | 0- | - | - |
|  | Grade 3 | 94 | 0 | 0 | - | - | - | 103 | 30 | 0 | 0- | - | - |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | Any | 202 | 2128 | 3 | 3 | 7 | 8 | 210 | 07 |  | 110 | 10 | 10 |
|  | Grade 3 | 202 | 211 | 2 | 3 | 5 | 7 | 210 | 00 | 0 | 0- | - | - |
| Redness | Any | 202 | 248 | 8 | 3 | 3 | 5 | 210 | 00 |  | 0- | - | - |
|  | Grade 3 | 202 | 2 | 0 | - | - | - | 210 | 00 | 0 | 0 | - | - |
| Swelling | Any | 202 | 22 | 5 | 3 | 3 | 6 | 210 | 01 | 0 | 0- | - | - |
|  | Grade 3 | 202 | 0 | 0 | - | - | - | 210 | 00 | 0 | -- | - | - |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of documented doses
Ns = total number of reports for a given symptom
$\mathrm{n}=$ number of symptoms that were ongoing after the follow-up period
Time to resolution : number of days beyond the end of the follow-up period
q1 $=25$ th percentile
$q 3=75$ th percentile

Table 8.57 Number of days with general symptoms during the solicited postvaccination period (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

| Solicited symptom | Dose | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Fatigue | Dose 1 | HZ/su | 53 | 3.5 | 1.0 | 1.0 | 3.0 | 6.0 | 7.0 |
|  |  | Placebo | 42 | 4.3 | 1.0 | 2.0 | 5.0 | 6.0 | 7.0 |
|  | Dose 2 | HZ/su | 54 | 4.4 | 1.0 | 2.0 | 5.0 | 7.0 | 7.0 |
|  |  | Placebo | 56 | 4.6 | 1.0 | 3.0 | 5.0 | 7.0 | 7.0 |
|  | Overall/dose | HZ/su | 107 | 4.0 | 1.0 | 2.0 | 4.0 | 6.0 | 7.0 |
|  |  | Placebo | 98 | 4.5 | 1.0 | 2.0 | 5.0 | 6.0 | 7.0 |
| Gastrointestinal symptoms | Dose 1 | HZ/su | 32 | 3.1 | 1.0 | 1.5 | 2.5 | 4.0 | 7.0 |
|  |  | Placebo | 21 | 4.1 | 1.0 | 2.0 | 4.0 | 6.0 | 7.0 |
|  | Dose 2 | HZ/su | 38 | 4.6 | 1.0 | 3.0 | 4.0 | 7.0 | 7.0 |
|  |  | Placebo | 38 | 4.1 | 1.0 | 2.0 | 3.0 | 7.0 | 7.0 |
|  | Overall/dose | HZ/su | 70 | 3.9 | 1.0 | 2.0 | 3.5 | 6.0 | 7.0 |
|  |  | Placebo | 59 | 4.1 | 1.0 | 2.0 | 4.0 | 6.0 | 7.0 |
| Headache | Dose 1 | HZ/su | 26 | 2.9 | 1.0 | 1.0 | 2.0 | 4.0 | 7.0 |
|  |  | Placebo | 23 | 3.1 | 1.0 | 1.0 | 2.0 | 5.0 | 7.0 |
|  | Dose 2 | HZ/su | 29 | 3.4 | 1.0 | 2.0 | 2.0 | 6.0 | 7.0 |
|  |  | Placebo | 24 | 3.0 | 1.0 | 1.0 | 2.0 | 5.0 | 7.0 |
|  | Overall/dose | HZ/su | 55 | 3.2 | 1.0 | 1.0 | 2.0 | 5.0 | 7.0 |
|  |  | Placebo | 47 | 3.1 | 1.0 | 1.0 | 2.0 | 5.0 | 7.0 |
| Myalgia | Dose 1 | HZ/su | 49 | 2.9 | 1.0 | 1.0 | 2.0 | 4.0 | 7.0 |
|  |  | Placebo | 17 | 3.5 | 1.0 | 2.0 | 2.0 | 6.0 | 7.0 |
|  | Dose 2 | HZ/su | 30 | 3.7 | 1.0 | 2.0 | 3.0 | 6.0 | 7.0 |
|  |  | Placebo | 22 | 4.5 | 1.0 | 3.0 | 5.0 | 6.0 | 7.0 |
|  | Overall/dose | HZ/su | 79 | 3.2 | 1.0 | 1.0 | 3.0 | 5.0 | 7.0 |
|  |  | Placebo | 39 | 4.0 | 1.0 | 2.0 | 4.0 | 6.0 | 7.0 |
| Shivering | Dose 1 | HZ/su | 26 | 2.0 | 1.0 | 1.0 | 1.5 | 3.0 | 5.0 |
|  |  | Placebo | 13 | 2.2 | 1.0 | 1.0 | 2.0 | 2.0 | 7.0 |
|  | Dose 2 | HZ/su | 18 | 3.5 | 1.0 | 1.0 | 3.0 | 7.0 | 7.0 |
|  |  | Placebo | 17 | 2.8 | 1.0 | 1.0 | 2.0 | 4.0 | 7.0 |
|  | Overall/dose | HZ/su | 44 | 2.6 | 1.0 | 1.0 | 2.0 | 3.0 | 7.0 |
|  |  | Placebo | 30 | 2.5 | 1.0 | 1.0 | 2.0 | 4.0 | 7.0 |
| Temperature | Dose 1 | HZ/su | 13 | 2.0 | 1.0 | 1.0 | 1.0 | 2.0 | 6.0 |
|  |  | Placebo | 4 | 2.0 | 1.0 | 1.0 | 1.0 | 3.0 | 5.0 |
|  | Dose 2 | HZ/su | 8 | 1.9 | 1.0 | 1.0 | 1.5 | 2.5 | 4.0 |
|  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | HZ/su | 21 | 2.0 | 1.0 | 1.0 | 1.0 | 2.0 | 6.0 |
|  |  | Placebo | 5 | 1.8 | 1.0 | 1.0 | 1.0 | 1.0 | 5.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=$ 25th percentile
Q3 $=75$ th percentile

Table 8.58 Number of days with grade 3 general symptoms during the solicited post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)

| Solicited symptom | Dose | Group N | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Fatigue | Dose 1 | HZ/su | 10 | 2.1 | 1.0 | 1.0 | 2.0 | 3.0 | 4.0 |
|  |  | Placebo 3 | 32 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  | Dose 2 | HZ/su 9 | 9 | 3.2 | 1.0 | 2.0 | 2.0 | 4.0 | 7.0 |
|  |  | Placebo 6 | 6 | 1.8 | 1.0 | 1.0 | 1.0 | 3.0 | 4.0 |
|  | Overall/dose | HZ/su 1 | 192 | 2.6 | 1.0 | 1.0 | 2.0 | 4.0 | 7.0 |
|  |  | Placebo 9 | 9 | 1.9 | 1.0 | 1.0 | 2.0 | 2.0 | 4.0 |
| Gastrointestinal symptoms | Dose 1 | HZ/su 2 | 2 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  | Placebo 5 | 5 | 2.0 | 1.0 | 1.0 | 2.0 | 3.0 | 3.0 |
|  | Dose 2 | HZ/su 5 | 52 | 2.2 | 1.0 | 2.0 | 2.0 | 2.0 | 4.0 |
|  |  | Placebo 3 | 32 | 2.0 | 1.0 | 1.0 | 1.0 | 4.0 | 4.0 |
|  | Overall/dose | HZ/su 7 | 7 | 2.1 | 1.0 | 2.0 | 2.0 | 2.0 | 4.0 |
|  |  | Placebo 8 | 8 | 2.0 | 1.0 | 1.0 | 1.5 | 3.0 | 4.0 |
| Headache | Dose 1 | HZ/su 3 | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  |  | Placebo 1 | 11 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Dose 2 | HZ/su 3 | 31 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  |  | Placebo 2 | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  | Overall/dose | HZ/su 6 | 6 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | Placebo 3 | 31 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
| Myalgia | Dose 1 | HZ/su 8 | 81 | 1.9 | 1.0 | 1.0 | 1.0 | 2.0 | 6.0 |
|  |  | Placebo 3 | 32 | 2.3 | 1.0 | 1.0 | 3.0 | 3.0 | 3.0 |
|  | Dose 2 | HZ/su 3 | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  |  | Placebo 1 | 15 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 |
|  | Overall/dose | HZ/su 1 | 111 | 1.8 | 1.0 | 1.0 | 1.0 | 2.0 | 6.0 |
|  |  | Placebo 4 | 4 | 3.0 | 1.0 | 2.0 | 3.0 | 4.0 | 5.0 |
| Shivering | Dose 1 | HZ/su 5 | 5 | 1.6 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  |  | Placebo 2 | 21 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  | Dose 2 | HZ/su 2 | 21 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | Placebo 1 | 11 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | HZ/su 7 | 7 | 1.4 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  |  | Placebo 3 | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=$ 25th percentile
Q3 $=75$ th percentile

Table 8.59 Number of days with general symptoms (ATP cohort for safety up to 30 days post last vaccination)

| Solicited symptom | Dose | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Fatigue | Dose 1 | HZ/su | 53 | 8.7 | 1.0 | 1.0 | 3.0 | 6.0 | 105.0 |
|  |  | Placebo | 42 | 8.5 | 1.0 | 2.0 | 5.0 | 7.0 | 76.0 |
|  | Dose 2 | HZ/su | 54 | 8.1 | 1.0 | 2.0 | 5.0 | 7.0 | 161.0 |
|  |  | Placebo | 56 | 10.6 | 1.0 | 3.0 | 5.5 | 7.0 | 139.0 |
|  | Overall/dose | HZ/su | 107 | 8.4 | 1.0 | 2.0 | 4.0 | 7.0 | 161.0 |
|  |  | Placebo | 98 | 9.7 | 1.0 | 2.0 | 5.0 | 7.0 | 139.0 |
| Gastrointestinal symptoms | Dose 1 | HZ/su | 32 | 3.5 | 1.0 | 1.5 | 3.0 | 4.5 | 11.0 |
|  |  | Placebo | 21 | 9.8 | 1.0 | 2.0 | 5.0 | 7.0 | 60.0 |
|  | Dose 2 | HZ/su | 38 | 7.9 | 1.0 | 3.0 | 4.5 | 7.0 | 104.0 |
|  |  | Placebo | 38 | 6.6 | 1.0 | 3.0 | 4.0 | 7.0 | 55.0 |
|  | Overall/dose | HZ/su | 70 | 5.9 | 1.0 | 2.0 | 4.0 | 7.0 | 104.0 |
|  |  | Placebo | 59 | 7.7 | 1.0 | 2.0 | 4.0 | 7.0 | 60.0 |
| Headache | Dose 1 | HZ/su | 26 | 5.4 | 1.0 | 1.0 | 2.0 | 5.0 | 66.0 |
|  |  | Placebo | 23 | 9.0 | 1.0 | 1.0 | 2.0 | 5.0 | 75.0 |
|  | Dose 2 | HZ/su | 29 | 4.4 | 1.0 | 2.0 | 2.0 | 6.0 | 29.0 |
|  |  | Placebo | 24 | 4.2 | 1.0 | 1.0 | 2.0 | 5.5 | 25.0 |
|  | Overall/dose | HZ/su | 55 | 4.9 | 1.0 | 1.0 | 2.0 | 6.0 | 66.0 |
|  |  | Placebo | 47 | 6.6 | 1.0 | 1.0 | 2.0 | 5.0 | 75.0 |
| Myalgia | Dose 1 | HZ/su | 49 | 4.9 | 1.0 | 1.0 | 2.0 | 4.0 | 105.0 |
|  |  | Placebo | 17 | 4.2 | 1.0 | 2.0 | 3.0 | 6.0 | 11.0 |
|  | Dose 2 | HZ/su | 30 | 4.1 | 1.0 | 2.0 | 3.5 | 7.0 | 10.0 |
|  |  | Placebo | 22 | 11.3 | 1.0 | 3.0 | 5.0 | 6.0 | 112.0 |
|  | Overall/dose | HZ/su | 79 | 4.6 | 1.0 | 1.0 | 3.0 | 5.0 | 105.0 |
|  |  | Placebo | 39 | 8.2 | 1.0 | 2.0 | 5.0 | 6.0 | 112.0 |
| Shivering | Dose 1 | HZ/su | 26 | 2.0 | 1.0 | 1.0 | 1.5 | 3.0 | 7.0 |
|  |  | Placebo | 13 | 4.6 | 1.0 | 1.0 | 2.0 | 2.0 | 38.0 |
|  | Dose 2 | HZ/su | 18 | 4.1 | 1.0 | 1.0 | 3.0 | 7.0 | 17.0 |
|  |  | Placebo | 17 | 3.1 | 1.0 | 1.0 | 2.0 | 4.0 | 9.0 |
|  | Overall/dose | HZ/su | 44 | 2.9 | 1.0 | 1.0 | 2.0 | 3.0 | 17.0 |
|  |  | Placebo | 30 | 3.8 | 1.0 | 1.0 | 2.0 | 4.0 | 38.0 |
| Temperature | Dose 1 | HZ/su | 13 | 2.0 | 1.0 | 1.0 | 1.0 | 2.0 | 6.0 |
|  |  | Placebo | 4 | 9.8 | 1.0 | 1.0 | 7.0 | 18.5 | 24.0 |
|  | Dose 2 | HZ/su | 8 | 1.9 | 1.0 | 1.0 | 1.5 | 2.5 | 4.0 |
|  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | HZ/su | 21 | 2.0 | 1.0 | 1.0 | 1.0 | 2.0 | 6.0 |
|  |  | Placebo | 5 | 8.0 | 1.0 | 1.0 | 1.0 | 13.0 | 24.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of doses with the symptom (during the solicited post-vaccination period and beyond)
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.60 Solicited general symptoms ongoing beyond the 7-day (Days 0-6) post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)

|  |  | HZ/su |  |  |  |  |  | Placebo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | Time to resolution (days) |  |  |  |  |  |  |  |  | Time to resolution (days) |  |  |
| Symptoms | Type | N | Ns | n | q1 | median | q3 | N | Ns | n | $q 1$ | median | q3 |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | Any | 108 | 53 | 10 | 7.5 | 29.5 | 50 | 107 | 42 | 13 | 3 | 19 | 23 |
|  | Grade 3 | 108 | 10 | 2 | 2 | 2 | 2 | 107 | 3 | 0 | - |  |  |
| Gastrointestinal symptoms | Any | 108 | 32 | 5 | 1.5 | 2 | 5.5 | 107 | 21 | 7 | 8 | 12 | 31 |
|  | Grade 3 | 108 | 2 | 1 | 2 | 2 | 2 | 107 | 5 | 2 | 31 | 31 | 31 |
| Headache | Any | 108 | 26 | 4 | 2 | 32 | 62 | 107 | 23 | 3 | 10 | 57 | 69 |
|  | Grade 3 | 108 | 3 | 1 | - | - | - | 107 | 1 | 1 | 69 | 69 | 69 |
| Myalgia | Any | 108 | 49 | 4 | 2 | 50 | 98 | 107 | 17 | 4 | 2 | 2 | 9 |
|  | Grade 3 | 108 | 8 | 2 | 2 | 2 | 2 | 107 | 3 | 2 | 2 | 2 | 2 |
| Shivering | Any | 108 | 26 | 1 | 2 | 2 | 2 | 107 | 13 | 1 | 31 | 31 | 31 |
|  | Grade 3 | 108 | 5 | 1 | 2 | 2 | 2 | 107 | 2 | 0 | - | - | - |
| Temperature | Any | 108 | 13 | 0 | - | - | - | 107 | 4 | 2 | 12 | 15.5 | 19 |
|  | Grade 3 | 108 | 0 | 0 | - | - | - | 107 | 0 | 0 | - | - | - |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | Any | 93 | 54 | 9 | 2 | 6 | 17 | 103 | 56 | 18 | 5 | 8 | 36 |
|  | Grade 3 | 93 | 9 | 3 | 4 | 11 | 154 | 103 | 6 | 3 | 5 | 55 | 105 |
| Gastrointestinal symptoms | Any | 93 | 38 | 8 | 2 | 4 | 14 | 103 | 38 | 12 | 2 | 4.5 | 11 |
|  | Grade 3 | 93 | 5 | 1 | 14 | 14 | 14 | 103 | 3 | 2 | 11 | 11 | 11 |
| Headache | Any | 93 | 29 | 6 | 1.5 | 3.5 | 14 | 103 | 24 | 3 | 8 | 14 | 20 |
|  | Grade 3 | 93 | 3 | 1 | - | - | - | 103 | 2 | 0 | - | - | - |
| Myalgia | Any | 93 | 30 | 6 | 1.5 | 2.5 | 4 | 103 | 22 | 6 | 10 | 36 | 105 |
|  | Grade 3 | 93 | 3 | 1 | 1 | 1 | 1 | 103 | 1 | 0 | - | - | - |
| Shivering | Any | 93 | 18 | 2 | 1 | 5.5 | 10 | 103 | 17 | 2 | 2 | 3 | 4 |
|  | Grade 3 | 93 | 2 | 0 | - |  |  | 103 | 1 | 0 | - | - | - |
| Temperature | Any | 93 | 8 | 0 | - | - | - | 103 | 1 | 0 | - | - | - |
|  | Grade 3 | 93 | 0 | 0 | - | - | - | 103 | 0 | 0 | - | - | - |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | Any | 201 | 107 | 19 | 3 | 12 | 43 | 210 | 98 | 31 | 5 | 8.5 | 25 |
|  | Grade 3 | 201 | 19 | 5 | 3 | 7.5 | 82.5 | 210 | 9 | 3 | 5 | 55 | 105 |
| Gastrointestinal symptoms | Any | 201 | 70 | 13 | 2 | 2 | 9 | 210 | 59 | 19 | 2.5 | 7 | 13.5 |
|  | Grade 3 | 201 | 7 | 2 | 2 | 8 | 14 | 210 | 8 | 4 | 11 | 21 | 31 |
| Headache | Any | 201 | 55 | 10 | 2 | 3.5 | 23 | 210 | 47 | 6 | 10 | 20 | 57 |
|  | Grade 3 | 201 | 6 | 2 | - | - | - | 210 | 3 | 1 | 69 | 69 | 69 |
| Myalgia | Any | 201 | 79 | 10 | 2 | 2.5 | 5 | 210 | 39 | 10 | 2 | 9.5 | 36 |
|  | Grade 3 | 201 | 11 | 3 | 1 | 1.5 | 2 | 210 | 4 | 2 | 2 | 2 | 2 |
| Shivering | Any | 201 | 44 | 3 | 1 | 2 | 10 | 210 | 30 | 3 | 2 | 4 | 31 |
|  | Grade 3 | 201 | 7 | 1 | 2 | 2 | 2 | 210 | 3 | 0 | - | - | - |
| Temperature | Any | 201 | 21 | 0 | - | - | - | 210 | 5 | 2 | 12 | 15.5 | 19 |
|  | Grade 3 | 2010 | 0 | 0 | - | - | - | 210 | 0 | 0 | - | - | - |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of documented doses
Ns = total number of reports for a given symptom
$\mathrm{n}=$ number of symptoms that were ongoing after the follow-up period
Time to resolution : number of days beyond the end of the follow-up period
q1 $=25$ th percentile
$q 3=75$ th percentile

Table 8.61 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)


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|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=113 \end{aligned}$ |  |  |  | Placebo$N=112$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% | CI |  |  |  | \% CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Dyspepsia (10013946) | 6 | 5.3 | 2.0 | 11.2 | 12 | 10.7 | 5.7 | 18.0 |
|  | Dysphagia (10013950) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
|  | Epigastric discomfort (10053155) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Flatulence (10016766) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
|  | Gastrointestinal disorder (10017944) | 1 | 0.9 | 0.0 | 4.8 | 3 | 2.7 | 0.6 | 7.6 |
|  | Gastrointestinal pain (10017999) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Gastrooesophageal reflux disease (10017885) | 3 | 2.7 | 0.6 | 7.6 | 0 | 0.0 | 0.0 | 3.2 |
|  | Gingival pain (10018286) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Glossitis (10018386) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Haemorrhoidal haemorrhage (10054787) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Haemorrhoids (10019022) | 1 | 0.9 | 0.0 | 4.8 | 2 | 1.8 | 0.2 | 6.3 |
|  | Hiatus hernia (10020028) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 3.2 | 2 | 1.8 | 0.2 | 6.3 |
|  | Nausea (10028813) | 31 | 27.4 | 19.5 | 36.6 | 28 | 25.0 | 17.3 | 34.1 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 3.2 | 3 | 2.7 | 0.6 | 7.6 |
|  | Oesophagitis (10030216) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Oral pain (10031009) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Proctalgia (10036772) | 0 | 0.0 | 0.0 | 3.2 | 2 | 1.8 | 0.2 | 6.3 |
|  | Rectal tenesmus (10057071) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Stomatitis (10042128) | 4 | 3.5 | 1.0 | 8.8 | 2 | 1.8 | 0.2 | 6.3 |
|  | Swollen tongue (10042727) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Vomiting (10047700) | 10 | 8.8 | 4.3 | 15.7 | 14 | 12.5 | 7.0 | 20.1 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 29 | 25.7 | 17.9 | 34.7 | 28 | 25.0 | 17.3 | 34.1 |
|  | Axillary pain (10048750) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Catheter site pain (10052268) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Chest pain (10008479) | 2 | 1.8 | 0.2 | 6.2 | 0 | 0.0 | 0.0 | 3.2 |
|  | Chills (10008531) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Fatigue (10016256) | 4 | 3.5 | 1.0 | 8.8 | 6 | 5.4 | 2.0 | 11.3 |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.0 | 3.2 | 2 | 1.8 | 0.2 | 6.3 |
|  | Generalised oedema (10018092) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Inflammation (10061218) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Influenza like illness (10022004) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |

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|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=113 \end{aligned}$ |  |  |  | Placebo$N=112$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | CI |  |  |  | CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.0 | 3.2 | 2 | 1.8 | 0.2 | 6.3 |
|  | Injection site pruritus (10022093) | 2 | 1.8 | 0.2 | 6.2 | 0 | 0.0 | 0.0 | 3.2 |
|  | Malaise (10025482) | 3 | 2.7 | 0.6 | 7.6 | 1 | 0.9 | 0.0 | 4.9 |
|  | Mucosal dryness (10028111) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Mucosal inflammation (10028116) | 10 | 8.8 | 4.3 | 15.7 | 6 | 5.4 | 2.0 | 11.3 |
|  | Oedema peripheral (10030124) | 3 | 2.7 | 0.6 | 7.6 | 0 | 0.0 | 0.0 | 3.2 |
|  | Pain (10033371) | 3 | 2.7 | 0.6 | 7.6 | 0 | 0.0 | 0.0 | 3.2 |
|  | Peripheral swelling (10048959) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Pyrexia (10037660) | 2 | 1.8 | 0.2 | 6.2 | 5 | 4.5 | 1.5 | 10.1 |
|  | Temperature intolerance (10057040) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Hepatic steatosis (10019708) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Hepatomegaly (10019842) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Hyperbilirubinaemia (10020578) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 3.2 | 2 | 1.8 | 0.2 | 6.3 |
|  | Hypersensitivity (10020751) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
|  | Seasonal allergy (10048908) | 0 | 0.0 | 0.0 | 3.2 | 2 | 1.8 | 0.2 | 6.3 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Bacterial infection (10060945) | 2 | 1.8 | 0.2 | 6.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Bronchitis (10006451) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Cellulitis (10007882) | 1 | 0.9 | 0.0 | 4.8 | 2 | 1.8 | 0.2 | 6.3 |
|  | Erysipelas (10015145) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Folliculitis (10016936) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Gastroenteritis (10017888) | 2 | 1.8 | 0.2 | 6.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Gingivitis (10018292) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Herpes zoster (10019974) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Infection (10021789) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |


|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=113 \end{aligned}$ |  |  |  | Placebo$N=112$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Influenza (10022000) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Lower respiratory tract infection (10024968) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Nasopharyngitis (10028810) | 3 | 2.7 | 0.6 | 7.6 | 1 | 0.9 | 0.0 | 4.9 |
|  | Neutropenic sepsis (10049151) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
|  | Oral fungal infection (10061324) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Oral herpes (10067152) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Oral infection (10048685) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Pneumonia (10035664) | 3 | 2.7 | 0.6 | 7.6 | 0 | 0.0 | 0.0 | 3.2 |
|  | Post procedural infection (10067268) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
|  | Respiratory tract infection (10062352) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Sepsis (10040047) | 2 | 1.8 | 0.2 | 6.2 | 0 | 0.0 | 0.0 | 3.2 |
|  | Sinusitis (10040753) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Upper respiratory tract infection (10046306) | 3 | 2.7 | 0.6 | 7.6 | 1 | 0.9 | 0.0 | 4.9 |
|  | Urinary tract infection (10046571) | 0 | 0.0 | 0.0 | 3.2 | 3 | 2.7 | 0.6 | 7.6 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Injury, poisoning and procedural complications (10022117) | Arthropod bite (10003399) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Gastrostomy failure (10050056) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Ligament sprain (10024453) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Post procedural complication (10058046) | 2 | 1.8 | 0.2 | 6.2 | 4 | 3.6 | 1.0 | 8.9 |
|  | Post procedural diarrhoea (10057585) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Radiation skin injury (10063562) | 1 | 0.9 | 0.0 | 4.8 | 2 | 1.8 | 0.2 | 6.3 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Investigations (10022891) | Blood iron decreased (10005619) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Body temperature fluctuation (10063488) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Haemoglobin decreased (10018884) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Platelet count decreased (10035528) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Weight decreased (10047895) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |



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|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=113 \end{aligned}$ |  |  |  | Placebo$N=112$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% Cl |  |  |  | 95\% Cl |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Dermatitis (10012431) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Dry skin (10013786) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
|  | Erythema (10015150) | 4 | 3.5 | 1.0 | 8.8 | 1 | 0.9 | 0.0 | 4.9 |
|  | Nail dystrophy (10028698) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Onychalgia (10064251) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Palmar-plantar erythrodysaesthesia syndrome (10033553) | 2 | 1.8 | 0.2 | 6.2 | 0 | 0.0 | 0.0 | 3.2 |
|  | Pruritus (10037087) | 0 | 0.0 | 0.0 | 3.2 | 4 | 3.6 | 1.0 | 8.9 |
|  | Pruritus generalised (10052576) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
|  | Rash (10037844) | 2 | 1.8 | 0.2 | 6.2 | 3 | 2.7 | 0.6 | 7.6 |
|  | Rash macular (10037867) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 3.2 | 2 | 1.8 | 0.2 | 6.3 |
|  | Scar pain (10049002) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Swelling face (10042682) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Urticaria (10046735) | 2 | 1.8 | 0.2 | 6.2 | 1 | 0.9 | 0.0 | 4.9 |
| Social circumstances (10041244) | Menopause (10027308) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Haematoma (10018852) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
|  | Hot flush (10060800) | 0 | 0.0 | 0.0 | 3.2 | 2 | 1.8 | 0.2 | 6.3 |
|  | Hypotension (10021097) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
|  | Lymphocele (10048642) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Phlebitis (10034879) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Thrombosis (10043607) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Vascular pain (10047095) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.62 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)







|  |  | $\begin{aligned} & \begin{array}{l} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=209 \end{array} \end{aligned}$ |  |  |  | Placebo$\mathrm{N}=219$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Dermatitis (10012431) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Dry skin (10013786) | 1 | 0.5 | 0.0 | 2.6 | 1 | 0.5 | 0.0 | 2.5 |
|  | Erythema (10015150) | 5 | 2.4 | 0.8 | 5.5 | 1 | 0.5 | 0.0 | 2.5 |
|  | Nail dystrophy (10028698) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Onychalgia (10064251) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Palmar-plantar erythrodysaesthesia syndrome (10033553) | 2 | 1.0 | 0.1 | 3.4 | 0 | 0.0 | 0.0 | 1.7 |
|  | Pruritus (10037087) | 0 | 0.0 | 0.0 | 1.7 | 4 | 1.8 | 0.5 | 4.6 |
|  | Pruritus generalised (10052576) | 1 | 0.5 | 0.0 | 2.6 | 1 | 0.5 | 0.0 | 2.5 |
|  | Rash (10037844) | 2 | 1.0 | 0.1 | 3.4 | 3 | 1.4 | 0.3 | 4.0 |
|  | Rash macular (10037867) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 1.7 | 2 | 0.9 | 0.1 | 3.3 |
|  | Scar pain (10049002) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Swelling face (10042682) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Urticaria (10046735) | 2 | 1.0 | 0.1 | 3.4 | 1 | 0.5 | 0.0 | 2.5 |
| Social circumstances (10041244) | Menopause (10027308) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Haematoma (10018852) | 1 | 0.5 | 0.0 | 2.6 | 1 | 0.5 | 0.0 | 2.5 |
|  | Hot flush (10060800) | 0 | 0.0 | 0.0 | 1.7 | 2 | 0.9 | 0.1 | 3.3 |
|  | Hypotension (10021097) | 1 | 0.5 | 0.0 | 2.6 | 1 | 0.5 | 0.0 | 2.5 |
|  | Lymphocele (10048642) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Phlebitis (10034879) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Thrombosis (10043607) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Vascular pain (10047095) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.63 Global Summary of unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

|  | Group |  |
| :--- | :--- | :--- |
|  |  |  |
|  | HZ/su | Placebo |
| Total |  |  |
| Number of subjects with at least one unsolicited symptom reported | 98 | 101 |
| Number of doses followed by at least one unsolicited symptom | 149 | 163 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term* | 406 | 388 |
| Number of unsolicited symptoms reported** | 421 | 400 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.64 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=113 \end{aligned}$ |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=112 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL UL | n | \% | LL | UL |
| At least one symptom |  | 18 | 15.9 | 9.724 .0 | 15 | 13.4 | 7.7 | 21.1 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 0 | 0.0 | 0.03 .2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Febrile neutropenia (10016288) | 4 | 3.5 | 1.08 .8 | 2 | 1.8 | 0.2 | 6.3 |
|  | Neutropenia (10029354) | 3 | 2.7 | 0.67 .6 | 3 | 2.7 | 0.6 | 7.6 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.03 .2 | 1 | 0.9 | 0.0 | 4.9 |
| Gastrointestinal disorders (10017947) | Abdominal pain (10000081) | 1 | 0.9 | 0.04 .8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Constipation (10010774) | 0 | 0.0 | 0.03 .2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.03 .2 | 1 | 0.9 | 0.0 | 4.9 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 0 | 0.0 | 0.03 .2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Malaise (10025482) | 0 | 0.0 | 0.03 .2 | 1 | 0.9 | 0.0 | 4.9 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 1 | 0.9 | 0.04.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.03 .2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Lower respiratory tract infection (10024968) | 1 | 0.9 | 0.04 .8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Nasopharyngitis (10028810) | 1 | 0.9 | 0.04 .8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Sepsis (10040047) | 1 | 0.9 | 0.04 .8 | 0 | 0.0 | 0.0 | 3.2 |
| Injury, poisoning and procedural complications (10022117) | Post procedural diarrhoea (10057585) | 1 | 0.9 | 0.04 .8 | 0 | 0.0 | 0.0 | 3.2 |
| Investigations (10022891) | Platelet count decreased (10035528) | 1 | 0.9 | 0.04 .8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Weight increased (10047899) | 0 | 0.0 | 0.03 .2 | 1 | 0.9 | 0.0 | 4.9 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 0.9 | 0.04 .8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Prostate cancer (10060862) | 0 | 0.0 | 0.03 .2 | 1 | 0.9 | 0.0 | 4.9 |
| Nervous system disorders (10029205) | Hepatic encephalopathy (10019660) | 1 | 0.9 | 0.04 .8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Seizure (10039906) | 1 | 0.9 | 0.04 .8 | 0 | 0.0 | 0.0 | 3.2 |
| Psychiatric disorders (10037175) | Insomnia (10022437) | 0 | 0.0 | 0.03 .2 | 1 | 0.9 | 0.0 | 4.9 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.03 .2 | 2 | 1.8 | 0.2 | 6.3 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.03 .2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Renal impairment (10062237) | 1 | 0.9 | 0.04 .8 | 0 | 0.0 | 0.0 | 3.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Pleural effusion (10035598) | 0 | 0.0 | 0.03 .2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Pulmonary embolism (10037377) | 1 | 0.9 | 0.04 .8 | 0 | 0.0 | 0.0 | 3.2 |



HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.65 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)


|  |  |  |  | $\begin{aligned} & 1 \mathrm{su} \\ & =209 \end{aligned}$ |  |  | $\begin{aligned} & \text { ceb } \\ & =21! \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | \% CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL UL | n | \% | LL | UL |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 1 | 0.5 | 0.02 .6 | 1 | 0.5 | 0.0 | 2.5 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.01 .7 | 1 | 0.5 | 0.0 | 2.5 |
| Vascular disorders (10047065) | Lymphocele (10048642) | 0 | 0.0 | 0.01 .7 | 1 | 0.5 | 0.0 | 2.5 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
n/\% = number/percentage of doses with the symptom
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit
Table 8.66 Global Summary of grade 3 unsolicited signs and symptoms reported within the $\mathbf{3 0}$-day (Days 0-29) postvaccination period (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

|  | Group |  |
| :--- | :--- | :--- |
|  |  |  |
|  | HZ/su | Placebo |
| Total |  |  |
| Number of subjects with at least one unsolicited symptom reported | 18 | 15 |
| Number of doses followed by at least one unsolicited symptom | 22 | 15 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term* | 23 | 22 |
| Number of unsolicited symptoms reported** | 23 | 22 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.67 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the $\mathbf{3 0 - d a y}$ (Days 0-29) postvaccination period (ATP cohort for safety up to 30 days post last vaccination)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=113 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=112 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL |  | \% | LL | UL |
| At least one symptom |  | 10 | 8.8 | 4.3 | 15.7 | 9 | 8.0 | 3.7 | 14.7 |
| Blood and lymphatic system disorders (10005329) | Neutropenia (10029354) | 0 | 0.0 | 0.0 | 3.2 |  | 0.9 | 0.0 | 4.9 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 0.9 | 0.0 | 4.8 |  | 0.9 | 0.0 | 4.9 |
| Gastrointestinal disorders (10017947) | Swollen tongue (10042727) | 1 | 0.9 | 0.0 | 4.8 |  | 0.0 | 0.0 | 3.2 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 2 | 1.8 | 0.2 | 6.2 |  | 0.9 | 0.0 | 4.9 |
|  | Axillary pain (10048750) | 0 | 0.0 | 0.0 | 3.2 |  | 0.9 | 0.0 | 4.9 |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.0 | 3.2 |  | 0.9 | 0.0 | 4.9 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 3.2 |  | 0.9 | 0.0 | 4.9 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.0 | 3.2 |  | 0.9 | 0.0 | 4.9 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 3.2 |  | 0.9 | 0.0 | 4.9 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.0 | 3.2 |  | 1.8 | 0.2 | 6.3 |
|  | Injection site pruritus (10022093) | 2 | 1.8 | 0.2 | 6.2 | 0 | 0.0 | 0.0 | 3.2 |
|  | Malaise (10025482) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 3.2 |  | 0.9 | 0.0 | 4.9 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 1 | 0.9 | 0.0 | 4.8 |  | 0.0 | 0.0 | 3.2 |
|  | Oral herpes (10067152) | 1 | 0.9 | 0.0 | 4.8 |  | 0.0 | 0.0 | 3.2 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 3.2 |  | 0.9 | 0.0 | 4.9 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 1 | 0.9 | 0.0 | 4.8 |  | 0.9 | 0.0 | 4.9 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 0 | 0.0 | 0.0 | 3.2 |  | 0.9 | 0.0 | 4.9 |
|  | Muscle contractions involuntary (10028293) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
| Skin and subcutaneous tissue disorders (10040785) | Erythema (10015150) | 1 | 0.9 | 0.0 | 4.8 |  | 0.0 | 0.0 | 3.2 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 3.2 |  | 0.9 | 0.0 | 4.9 |
|  | Urticaria (10046735) | 0 | 0.0 | 0.0 | 3.2 |  | 0.9 | 0.0 | 4.9 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
n/\% = number/percentage of subjects reporting the symptom at least once
$95 \%$ CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.68 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)


HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.69 Global Summary of unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days $\mathbf{0 - 2 9}$ ) post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |  |
| :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | Total |
| Number of subjects with at least one unsolicited symptom reported | 10 | 9 | 19 |
| Number of doses followed by at least one unsolicited symptom | 11 | 11 | 22 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term* | 13 | 17 | 30 |
| Number of unsolicited symptoms reported** | 13 | 17 | 30 |
| HZ/su $=$ Her |  |  |  |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.70 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30 -day (Days 0-29) post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)

|  |  |  | $\begin{aligned} & \text { Z/su } \\ & =113 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% Cl |  |  | \% Cl |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL UL | n \% | LL |  |
| At least one symptom |  | 10.9 | 0.04 .8 | 00.0 | 0.0 | 3.2 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 10.9 | 0.04 .8 | 00.0 | 0.0 | 3.2 |
| HZ/su = Herpes Zoster sub-unit vaccine group Placebo = Placebo group |  |  |  |  |  |  |
| At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term) |  |  |  |  |  |  |
| $\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once |  |  |  |  |  |  |
| 95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Lim |  |  |  |  |  |  |

Table 8.71 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=209 \end{aligned}$ | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=219 \\ & \hline \end{aligned}$ |
| :---: | :---: | :---: | :---: |
|  |  | 95\% Cl | 95\% CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% LL UL $n$ | \% LL UL |
| At least one symptom |  | 10.50 .02 .60 | 0.00 .01 .7 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 10.50 .02 .60 | 0.00 .01 .7 |
| $\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group |  |  |  |
| Placebo $=$ Placebo group |  |  |  |
| At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term) $\mathrm{N}=$ number of administered doses |  |  |  |
| $\mathrm{n} / \%=$ number/percentage of doses with the symptom |  |  |  |
| 95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Lim |  |  |  |

Table 8.72 Global Summary of grade 3 unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |
| :--- | :--- | :--- |
|  | HZ/su | Placebo |
|  | Total |  |
| Number of subjects with at least one unsolicited symptom reported | 1 | 0 |
| 1 |  |  |
| Number of doses followed by at least one unsolicited symptom | 1 | 0 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term* | 1 | 0 |
| Number of unsolicited symptoms reported** | 1 | 0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.73 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 30 -day (Days 0-29) post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)


|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=113 \end{aligned}$ |  |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=112 \end{aligned}$ |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Hepatomegaly (10019842) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 3.2 | 2 | 1.8 | 0.2 | 6.3 |
|  | Gastroenteritis (10017888) | 2 | 1.8 | 0.2 | 6.2 | 0 | 0.0 | 0.0 | 3.2 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Lower respiratory tract infection (10024968) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Nasopharyngitis (10028810) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Neutropenic sepsis (10049151) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Post procedural infection (10067268) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Respiratory tract infection (10062352) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Sepsis (10040047) | 2 | 1.8 | 0.2 | 6.2 | 0 | 0.0 | 0.0 | 3.2 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Upper respiratory tract infection (10046306) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Platelet count decreased (10035528) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Musculoskeletal and connective tissue disorders (10028395) | Back pain (10003988) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Muscle spasms (10028334) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Neck pain (10028836) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Pain in extremity (10033425) | 2 | 1.8 | 0.2 | 6.2 | 0 | 0.0 | 0.0 | 3.2 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Prostate cancer (10060862) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |


$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.74 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 30-day (Days 0-29) post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=209 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=219 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 36 | 17.2 | 12.4 | 23.0 | 41 | 18.7 | 13.8 | 24.5 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 2 | 1.0 | 0.1 | 3.4 | 3 | 1.4 | 0.3 | 4.0 |
|  | Febrile neutropenia (10016288) | 4 | 1.9 | 0.5 | 4.8 | 3 | 1.4 | 0.3 | 4.0 |
|  | Neutropenia (10029354) | 3 | 1.4 | 0.3 | 4.1 | 3 | 1.4 | 0.3 | 4.0 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 0.5 | 0.0 | 2.6 | 1 | 0.5 | 0.0 | 2.5 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Abdominal pain (10000081) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Abdominal pain upper (10000087) | 1 | 0.5 | 0.0 | 2.6 | 1 | 0.5 | 0.0 | 2.5 |
|  | Constipation (10010774) | 0 | 0.0 | 0.0 | 1.7 | 3 | 1.4 | 0.3 | 4.0 |
|  | Diarrhoea (10012735) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Dyspepsia (10013946) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Dysphagia (10013950) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Gastrooesophageal reflux disease (10017885) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Nausea (10028813) | 3 | 1.4 | 0.3 | 4.1 | 0 | 0.0 | 0.0 | 1.7 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Stomatitis (10042128) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Swollen tongue (10042727) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Vomiting (10047700) | 1 | 0.5 | 0.0 | 2.6 | 4 | 1.8 | 0.5 | 4.6 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 3 | 1.4 | 0.3 | 4.1 | 0 | 0.0 | 0.0 | 1.7 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Mucosal inflammation (10028116) | 1 | 0.5 | 0.0 | 2.6 | 1 | 0.5 | 0.0 | 2.5 |
|  | Pyrexia (10037660) | 1 | 0.5 | 0.0 | 2.6 | 1 | 0.5 | 0.0 | 2.5 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |


|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=209 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=219 \end{aligned}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Hepatomegaly (10019842) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 1.7 | 2 | 0.9 | 0.1 | 3.3 |
|  | Gastroenteritis (10017888) | 2 | 1.0 | 0.1 | 3.4 | 0 | 0.0 | 0.0 | 1.7 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Lower respiratory tract infection (10024968) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Nasopharyngitis (10028810) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Neutropenic sepsis (10049151) | 1 | 0.5 | 0.0 | 2.6 | 2 | 0.9 | 0.1 | 3.3 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Post procedural infection (10067268) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Respiratory tract infection (10062352) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Sepsis (10040047) | 2 | 1.0 | 0.1 | 3.4 | 0 | 0.0 | 0.0 | 1.7 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Upper respiratory tract infection (10046306) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Platelet count decreased (10035528) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
| Musculoskeletal and connective tissue disorders (10028395) | Back pain (10003988) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Muscle spasms (10028334) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Neck pain (10028836) | 0 | 0.0 | 0.0 | 1.7 | 1 | 0.5 | 0.0 | 2.5 |
|  | Pain in extremity (10033425) | 2 | 1.0 | 0.1 | 3.4 | 0 | 0.0 | 0.0 | 1.7 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |
|  | Prostate cancer (10060862) | 1 | 0.5 | 0.0 | 2.6 | 1 | 0.5 | 0.0 | 2.5 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 1 | 0.5 | 0.0 | 2.6 | 0 | 0.0 | 0.0 | 1.7 |


$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
n/\% = number/percentage of doses with the symptom
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.75 Global Summary of unsolicited signs and symptoms reported with medically attended visit, within the 30 -day (Days $0-29$ ) postvaccination period (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

|  | Group |  |  |
| :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | Total |
| Number of subjects with at least one unsolicited symptom reported | 31 | 32 | 63 |
| Number of doses followed by at least one unsolicited symptom | 36 | 41 | 77 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term | 60 | 60 | 120 |
| Number of unsolicited symptoms reported** | 60 | 60 | 120 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.76 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to 30 days post last vaccination (ATP cohort for safety up to 30 days post last vaccination)

No records exist in this table

Table 8.77 Global Summary of potential immune mediated diseases reported from the first vaccination up to 30 days post last vaccination (ATP cohort for safety up to 30 days post last vaccination)

No records exist in this table

Table 8.78 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from 30 days post last vaccination up to the study end (ATP cohort for safety up to the study end)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=113 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=112 \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% Cl |  | 95\% Cl |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL UL | n \% | LL UL |
| At least one symptom |  | 00.0 | 0.03 .2 | 10.9 | 0.04 .9 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 00.0 | 0.03 .2 | 10.9 | 0.04 .9 |
| $\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group Placebo = Placebo group |  |  |  |  |  |
| At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term) |  |  |  |  |  |
| $\mathrm{N}=$ number of subjects with at least one administered dose |  |  |  |  |  |
| $\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once |  |  |  |  |  |
| 95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Lim |  |  |  |  |  |

Table 8.79 Global Summary of potential immune mediated diseases reported from 30 days post last vaccination up to study end (ATP cohort for safety up to the study end)

|  | Group |  |  |
| :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | Total |
| Number of subjects with at least one unsolicited symptom reported | 0 | 1 | 1 |
| Number of doses followed by at least one unsolicited symptom | 0 | 1 | 1 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term | 0 | 1 | 1 |
| Number of unsolicited symptoms reported** | 0 | 1 | 1 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.80 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to the study end (ATP cohort for safety up to the study end)

|  |  |  | $\begin{aligned} & \text { Z/su } \\ & =113 \end{aligned}$ |  | $\begin{aligned} & \text { acebo } \\ & =112 \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  | 95\% Cl |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL UL | \% | LL UL |
| At least one symptom |  | 00.0 | 0.03 .2 | 10.9 | 0.04 .9 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) 0 | 00.0 | 0.03 .2 | 0.9 | 0.04 .9 |
| $\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group Placebo = Placebo group |  |  |  |  |  |
|  |  |  |  |  |  |
| At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term) |  |  |  |  |  |
| $\mathrm{N}=$ number of subjects with at least one administered dose |  |  |  |  |  |
| $\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once |  |  |  |  |  |
| 95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit |  |  |  |  |  |

Table 8.81 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to 30 days post last vaccination (ATP cohort for safety up to 30 days post last vaccination)

|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=113 \end{aligned}$ |  |  |  | Placebo$N=112$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 16 | 14.2 | 8.3 | 22.0 | 13 | 11.6 | 6.3 | 19.0 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 0 | 0.0 | 0.0 | 3.2 | 2 | 1.8 | 0.2 | 6.3 |
|  | Febrile neutropenia (10016288) | 4 | 3.5 | 1.0 | 8.8 | 2 | 1.8 | 0.2 | 6.3 |
|  | Neutropenia (10029354) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Gastrointestinal disorders (10017947) | Constipation (10010774) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| General disorders and administration site conditions (10018065) | Mucosal inflammation (10028116) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Hepatitis c (10019744) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Lower respiratory tract infection (10024968) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Nasopharyngitis (10028810) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Neutropenic sepsis (10049151) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
|  | Respiratory tract infection (10062352) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Sepsis (10040047) | 2 | 1.8 | 0.2 | 6.2 | 0 | 0.0 | 0.0 | 3.2 |
|  | Urinary tract infection (10046571) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 1 | 0.9 | 0.04 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Prostate cancer (10060862) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Nervous system disorders (10029205) | Hepatic encephalopathy (10019660) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Seizure (10039906) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.0 | 3.2 | 2 | 1.8 | 0.2 | 6.3 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 |  | 4.9 |



HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.82 Global Summary of serious adverse events reported from the first vaccination up to 30 days post last vaccination (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |  |
| :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | Total |
| Number of subjects with at least one unsolicited symptom reported | 16 | 13 | 29 |
| Number of doses followed by at least one unsolicited symptom | 17 | 15 | 32 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term** | 19 | 23 | 42 |
| Number of unsolicited symptoms reported** | 19 | 23 | 42 |
| HZ/su = Herpes Zoster sub-unit vaccine group |  |  |  |
| Placebo = Placebo group <br> * Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once <br> ** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start <br> date of the event, are counted once |  |  |  |

Table 8.83 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relation to vaccination from first vaccination up to 30 days post last vaccination (ATP cohort for safety up to 30 days post last vaccination)

No records exist in this table

Table 8.84 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from 30 days post last vaccination up to the study end (ATP cohort for safety up to the study end)



|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=113 \end{aligned}$ |  |  |  | Placebo$N=112$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Non-small cell lung cancer (10061873) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Ovarian cancer (10033128) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Prostate cancer (10060862) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Rectal cancer metastatic (10055097) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Squamous cell carcinoma of lung (10041826) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Tongue neoplasm malignant stage unspecified (10043966) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Tumour haemorrhage (10049750) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Uterine leiomyosarcoma (10046799) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Bronchial obstruction (10006440) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Pleural effusion (10035598) | 1 | 0.9 | 0.0 | 4.8 | 1 | 0.9 | 0.0 | 4.9 |
|  | Pulmonary embolism (10037377) | 0 | 0.0 | 0.0 | 3.2 | 2 | 1.8 | 0.2 | 6.3 |
|  | Respiratory failure (10038695) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
| Surgical and medical procedures (10042613) | Abdominal hernia repair (10060802) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Vascular disorders (10047065) | Superior vena cava occlusion (10058988) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

## Table 8.85 Global Summary of serious adverse events reported from 30 days

 post last vaccination up to study end (ATP cohort for safety up to the study end)|  | Group |  |  |
| :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | Total |
| Number of subjects with at least one unsolicited symptom reported | 30 | 30 | 60 |
| Number of doses followed by at least one unsolicited symptom | 30 | 30 | 60 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term | 54 | 39 | 93 |
| Number of unsolicited symptoms reported** | 60 | 39 | 99 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.86 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relation to vaccination from 30 days post last vaccination up to the study end (ATP cohort for safety up to the study end)

No records exist in this table

Table 8.87 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to the study end (ATP cohort for safety up to the study end)


|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=113 \end{aligned}$ |  |  |  | Placebo$N=112$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |
|  | Clostridium difficile infection (10054236) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Device related sepsis (10069802) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Diverticulitis (10013538) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Epiglottitis (10015030) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Gastroenteritis (10017888) | 2 | 1.8 | 0.2 | 6.2 | 0 | 0.0 | 0.0 | 3.2 |
|  | Hepatitis c (10019744) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Lower respiratory tract infection (10024968) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Lung infection (10061229) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Nasopharyngitis (10028810) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Neutropenic sepsis (10049151) | 1 | 0.9 | 0.0 | 4.8 | 2 | 1.8 | 0.2 | 6.3 |
|  | Oral candidiasis (10030963) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Pleural infection (10061351) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Pneumonia (10035664) | 1 | 0.9 | 0.0 | 4.8 | 2 | 1.8 | 0.2 | 6.3 |
|  | Respiratory tract infection (10062352) | 2 | 1.8 | 0.2 | 6.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Sepsis (10040047) | 3 | 2.7 | 0.6 | 7.6 | 1 | 0.9 | 0.0 | 4.9 |
|  | Staphylococcal infection (10058080) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Upper respiratory tract infection (10046306) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Urinary tract infection (10046571) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Lumbar vertebral fracture (10049947) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Metabolism and nutrition disorders (10027433) | Diabetic ketoacidosis (10012671) | 2 | 1.8 | 0.2 | 6.2 | 0 | 0.0 | 0.0 | 3.2 |
|  | Hypokalaemia (10021015) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Hyponatraemia (10021036) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Malnutrition (10061273) | 2 | 1.8 | 0.2 | 6.2 | 0 | 0.0 | 0.0 | 3.2 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
|  | Musculoskeletal chest pain (10050819) | 0 | 0.0 | 0.0 | 3.2 | 1 | 0.9 | 0.0 | 4.9 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |
|  | Bladder cancer (10005003) | 2 | 1.8 | 0.2 | 6.2 | 0 | 0.0 | 0.0 | 3.2 |
|  | Breast cancer recurrent (10006198) | 1 | 0.9 | 0.0 | 4.8 | 0 | 0.0 | 0.0 | 3.2 |



HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

## CONFIDENTIAL

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At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.88 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relation to vaccination from first vaccination up to the study end (ATP cohort for safety up to the study end)

No records exist in this table

Table 8.89 Number and percentage of subjects with fatal outcome reported up to the study end (ATP cohort for safety up to the study end)

|  | HZ/su |  | Placebo |
| :--- | :--- | :--- | :--- |
| $\mathrm{N}=113$ | $\mathrm{~N}=112$ |  |  |
| Characteristics | n | $\%$ | n |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once

Table 8.90 Percentage of subjects with concomitant medication during the 30day (Days 0-29) post-vaccination period (ATP cohort for safety up to 30 days post last vaccination)

|  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | 95\% CI |  |  |  |  |  |  |  | 95\% CI |  |
|  | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |
| Any | 113 | 108 | 95.6 | 90.0 | 98.5 | 112 | 106 | 94.6 | 88.7 | 98.0 |
| Steroids to prevent chemotherapy nausea and vomiting | 113 | 98 | 86.7 | 79.1 | 92.4 | 112 | 95 | 84.8 | 76.8 | 90.9 |
| Any in anticipation of study vaccine reaction | 113 | 0 | 0.0 | 0.0 | 3.2 | 112 | 0 | 0.0 | 0.0 | 3.2 |
| Any chronic use | 113 | 4 | 3.5 | 1.0 | 8.8 | 112 | 7 | 6.3 | 2.5 | 12.5 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |
| Any | 96 | 86 | 89.6 | 81.7 | 94.9 | 107 | 91 | 85.0 | 76.9 | 91.2 |
| Steroids to prevent chemotherapy nausea and vomiting | 96 | 78 | 81.3 | 72.0 | 88.5 | 107 | 79 | 73.8 | 64.4 | 81.9 |
| Any in anticipation of study vaccine reaction | 96 | 0 | 0.0 | 0.0 | 3.8 | 107 | 0 | 0.0 | 0.0 | 3.4 |
| Any chronic use | 96 | 2 | 2.1 | 0.3 | 7.3 | 107 | 7 | 6.5 | 2.7 | 13.0 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |
| Any | 209 | 194 | 92.8 | 88.4 | 95.9 | 219 | 197 | 90.0 | 85.2 | 93.6 |
| Steroids to prevent chemotherapy nausea and vomiting | 209 | 176 | 84.2 | 78.5 | 88.9 | 219 | 174 | 79.5 | 73.5 | 84.6 |
| Any in anticipation of study vaccine reaction | 209 | 0 | 0.0 | 0.0 | 1.7 | 219 | 0 | 0.0 | 0.0 | 1.7 |
| Any chronic use | 209 | 6 | 2.9 | 1.1 | 6.1 | 219 | 14 | 6.4 | 3.5 | 10.5 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |
| Any | 113 | 109 | 96.5 | 91.2 | 99.0 | 112 | 110 | 98.2 | 93.7 | 99.8 |
| Steroids to prevent chemotherapy nausea and vomiting | 113 | 100 | 88.5 | 81.1 | 93.7 | 112 | 98 | 87.5 | 79.9 | 93.0 |
| Any in anticipation of study vaccine reaction | 113 | 0 | 0.0 | 0.0 | 3.2 | 112 | - | 0.0 | 0.0 | 3.2 |
| Any chronic use | 113 | 6 | 5.3 | 2.0 | 11.2 | 112 | 12 | 10.7 | 5.7 | 18.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with the administered dose
$\mathrm{n} / \%=$ number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table $8.91 \quad$ Number and percentage of subjects who received vaccine dose(s) by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  | PreChemo |  |  |  | OnChemo |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  | Placebo$N=91$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  | Placebo$N=24$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=117 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=115 \end{aligned}$ |  |
| Total number of doses received | n | \% | n | \% | n | \% | n | \% | n | \% | n | \% |
| 1 | 14 | 15.6 | 4 | 4.4 | 3 | 11.1 | 1 | 4.2 | 17 | 14.5 | 5 | 4.3 |
| 2 | 76 | 84.4 | 87 | 95.6 | 24 | 88.9 | 23 | 95.8 | 100 | 85.5 | 110 | 95.7 |
| Any | 90 | 100 | 91 | 100 | 27 | 100 | 24 | 100 | 117 | 100 | 115 | 100 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in each group or in total included in the considered cohort
$\mathrm{n} / \%=$ number/percentage of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least one dose
Table 8.92 Compliance in returning symptom sheets by PreChemo/OnChemo groups (Total Vaccinated Cohort)
$\left.\begin{array}{|l|l|l|l|l|l|l|l|l|}\hline \text { Dose } & \text { Sub-group } & \text { Group } & \begin{array}{l}\text { Number } \\ \text { of } \\ \text { doses }\end{array} & \begin{array}{l}\text { Doses } \\ \text { NOT } \\ \text { according to } \\ \text { protocol }\end{array} & \begin{array}{l}\text { Number } \\ \text { of } \\ \text { general SS }\end{array} & \begin{array}{l}\text { Compliance } \\ \% \\ \text { general SS }\end{array} & \begin{array}{l}\text { Number } \\ \text { of } \\ \text { local SS }\end{array} & \begin{array}{l}\text { Compliance } \\ \%\end{array} \\ \text { local SS }\end{array}\right]$

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
SS = Symptom screens/sheets used for the collection of local and general solicited AEs
Compliance \% = (number of doses with symptom screen/sheet return / number of administered doses) X 100

Table 8.93 Incidence and nature of symptoms (solicited and unsolicited) reported during the 7 -day (Days 0-6) post-vaccination period following each dose and overall by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | PreChemo | HZ/su | 90 | 80 | 88.9 | 80.5 | 94.5 | 90 | 60 | 66.7 | 55.9 | 76.3 | 90 | 73 | 81.1 | 71.5 | 88.6 |
|  |  | Placebo | 91 | 41 | 45.1 | 34.6 | 55.8 | 91 | 40 | 44.0 | 33.6 | 54.8 | 91 | 2 | 2.2 | 0.3 | 7.7 |
|  | OnChemo | HZ/su | 27 | 26 | 96.3 | 81.0 | 99.9 | 27 | 24 | 88.9 | 70.8 | 97.6 | . 27 | 15 | 55.6 | 35.3 | 74.5 |
|  |  | Placebo | 24 | 17 | 70.8 | 48.9 | 87.4 | 24 | 17 | 70.8 | 48.9 | 87.4 | 24 | 2 | 8.3 | 1.0 | 27.0 |
| Dose 2 | PreChemo | HZ/su | 76 | 62 | 81.6 | 71.0 | 89.5 | 76 | 57 | 75.0 | 63.7 | 84.2 | 76 | 40 | 52.6 | 40.8 | 64.2 |
|  |  | Placebo | 87 | 65 | 74.7 | 64.3 | 83.4 | 87 | 65 | 74.7 | 64.3 | 83.4 | 87 | 4 | 4.6 | 1.3 | 11.4 |
|  | OnChemo | HZ/su | 24 | 20 | 83.3 | 62.6 | 95.3 | 24 | 19 | 79.2 | 57.8 | 92.9 | 24 | 16 | 66.7 | 44.7 | 84.4 |
|  |  | Placebo | 23 | 19 | 82.6 | 61.2 | 95.0 | 23 | 19 | 82.6 | 61.2 | 95.0 | 23 | 2 | 8.7 | 1.1 | 28.0 |
| Overall/dose | PreChemo | HZ/su | 166 | 142 | 85.5 | 79.3 | 90.5 | 166 | 117 | 70.5 | 62.9 | 77.3 | 166 | 113 | 68.1 | 60.4 | 75.1 |
|  |  | Placebo | 178 | 106 | 59.6 | 52.0 | 66.8 | 178 | 105 | 59.0 | 51.4 | 66.3 | 178 |  | 3.4 | 1.2 | 7.2 |
|  | OnChemo | HZ/su | 51 | 46 | 90.2 | 78.6 | 96.7 | 51 | 43 | 84.3 | 71.4 | 93.0 | 51 | 31 | 60.8 | 46.1 | 74.2 |
|  |  | Placebo | 47 | 36 | 76.6 | 62.0 | 87.7 | 47 | 36 | 76.6 | 62.0 | 87.7 | 47 | 4 | 8.5 | 2.4 | 20.4 |
| Overall/subject | PreChemo | HZ/su | 90 | 83 | 92.2 | 84.6 | 96.8 | 90 | 73 | 81.1 | 71.5 | 88.6 | 90 | 76 | 84.4 | 75.3 | 91.2 |
|  |  | Placebo | 91 | 72 | 79.1 | 69.3 | 86.9 | 91 | 72 | 79.1 | 69.3 | 86.9 | 91 | 5 | 5.5 | 1.8 | 12.4 |
|  | OnChemo | HZ/su | 27 | 26 | 96.3 | 81.0 | 99.9 | 27 | 26 | 96.3 | 81.0 | 99.9 | 27 | 18 | 66.7 | 46.0 | 83.5 |
|  |  | Placebo | 24 | 20 | 83.3 | 62.6 | 95.3 | 24 | 20 | 83.3 | 62.6 | 95.3 | 24 | 4 | 16.7 | 4.7 | 37.4 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered 95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.94 Incidence and nature of grade 3 symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 95\% Cl |  |  |  |  | 95\% Cl |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | JL |
| Dose 1 | PreChemo | HZ/su | 90 | 15 | 16.7 | 9.6 | 26.0 | 90 | 10 | 11.1 | 5.5 | 19.5 | 90 | 10 | 11.1 | 5.5 | 19.5 |
|  |  | Placebo | 91 | 6 | 6.6 | 2.5 | 13.8 | 91 | 6 | 6.6 | 2.5 | 13.8 | 91 | 0 | 0.0 | 0.0 | 4.0 |
|  | OnChemo | HZ/su | 27 | 7 | 25.9 | 11.1 | 46.3 | 27 | 7 | 25.9 | 11.1 | 46.3 | 27 | 0 | 0.0 | 0.0 | 12.8 |
|  |  | Placebo | 24 | 7 | 29.2 | 12.6 | 51.1 | 24 | 7 | 29.2 | 12.6 | 51.1 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Dose 2 | PreChemo | HZ/su | 76 | 13 | 17.1 | 9.4 | 27.5 | 76 | 12 | 15.8 | 8.4 | 26.0 | 76 | 3 | 3.9 | 0.8 | 1. |
|  |  | Placebo | 87 | 8 | 9.2 | 4.1 | 17.3 | 87 | 8 | 9.2 | 4.1 | 17.3 | 87 | 0 | 0.0 | 0.0 | 4.2 |
|  | OnChemo | HZ/su | 24 | 6 | 25.0 | 9.8 | 46.7 | 24 | 6 | 25.0 | 9.8 | 46.7 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  |  | Placebo | 23 | 4 | 17.4 | 5.0 | 38.8 | 23 | 4 | 17.4 | 5.0 | 38.8 | 23 | 0 | 0.0 | 0.0 | 14.8 |
| Overall/dose | PreChemo | HZ/su | 166 | 28 | 16.9 | 11.5 | 23.4 | 166 | 22 | 13.3 | 8.5 | 19.4 | 166 | 13 | 7.8 | 4.2 | 13.0 |
|  |  | Placebo | 178 | 14 | 7.9 | 4.4 | 12.8 | 178 | 14 | 4.9 | 4.4 | 12.8 | 178 | 0 | 0.0 | 0.0 | 2.1 |
|  | OnChemo | HZ/su | 51 | 13 | 325.5 | 14.3 | 39.6 | 51 | 13 | 32.5 | 14.3 | 39.6 | 51 | 1 | 2.0 | 0.0 | 10.4 |
|  |  | Placebo | 47 | 11 | 23.4 | 12.3 | 38.0 | 47 | 11 | 123.4 | 12.3 | 38.0 | 47 | 0 | 0.0 | 0.0 | 7.5 |
| Overall/subject | PreChemo | HZ/su | 90 | 22 | 24.4 | 16.0 | 34.6 | 90 | 19 | 21.1 | 13.2 | 31.0 | 90 | 12 | 13.3 |  | 22.1 |
|  |  | Placebo | 91 | 13 | 14.3 | 7.8 | 23.2 | 91 | 13 | 14.3 | 7.8 | 23.2 | 91 | 0 | 0.0 | 0.0 | 4.0 |
|  | OnChemo | HZ/su | 27 | 9 | 33.3 | 16.5 | 54.0 | 27 | 9 | 33.3 | 16.5 | 54.0 | 27 | 1 | 3.7 | 0.1 | 19.0 |
|  |  | Placebo | 24 | 8 | 33.3 | 15.6 | 55.3 | 24 | 8 | 33.3 | 15.6 | 55.3 | 24 | 0 | 0.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.95 Incidence and nature of symptoms (solicited only) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | PreChemo | HZ/su | 86 | 80 | 93.0 | 85.4 | 97.4 | 86 | 58 | 67.4 | 56.5 | 77.2 | 86 | 73 | 84.9 | 75.5 | 91.7 |
|  |  | Placebo | 86 | 37 | 43.0 | 32.4 | 54.2 | 86 | 36 | 41.9 | 31.3 | 53.0 | 86 | 2 | 2.3 | 0.3 | 8.1 |
|  | OnChemo | HZ/su | 26 | 24 | 92.3 | 74.9 | 99.1 | 26 | 22 | 84.6 | 65.1 | 95.6 | 26 | 15 | 57.7 | 36.9 | 76.6 |
|  |  | Placebo | 24 | 16 | 66.7 | 44.7 | 84.4 | 24 | 16 | 66.7 | 44.7 | 84.4 | 24 | 1 | 4.2 | 0.1 | 21.1 |
| Dose 2 | PreChemo | HZ/su | 74 | 55 | 74.3 | 62.8 | 83.8 | 73 | 49 | 67.1 | 55.1 | 77.7 | 74 | 40 | 54.1 | 42.1 | 65. |
|  |  | Placebo | 83 | 45 | 54.2 | 42.9 | 65.2 | 82 | 45 | 54.9 | 43.5 | 65.9 | 83 | 3 | 3.6 | 0.8 | 10.2 |
|  | OnChemo | HZ/su | 24 | 20 | 83.3 | 62.6 | 95.3 | 24 | 18 | 75.0 | 53.3 | 90.2 | 24 | 16 | 66.7 | 44.7 | 84.4 |
|  |  | Placebo | 22 | 15 | 68.2 | 45.1 | 86.1 | 22 | 15 | 68.2 | 45.1 | 86.1 | 22 | 2 | 9.1 | 1.1 | 29.2 |
| Overall/dose | PreChemo | HZ/su | 160 | 135 | 84.4 | 77.8 | 89.6 | 159 | 107 | 67.3 | 59.4 | 74.5 | 160 | 113 | 70.6 | 62.9 | 77.6 |
|  |  | Placebo | 169 | 82 | 48.5 | 40.8 | 56.3 | 168 | 81 | 48.2 | 40.5 | 56.0 | 169 | 5 | 3.0 | 1.0 | 6.8 |
|  | OnChemo | HZ/su | 50 | 44 | 88.0 | 75.7 | 95.5 | 50 | 40 | 80.0 | 66.3 | 90.0 | 50 | 31 | 62.0 | 47.2 | 75.3 |
|  |  | Placebo | 46 | 31 | 67.4 | 52.0 | 80.5 | . 46 | 31 | 67.4 | 52.0 | 80.5 | 46 | 3 | 6.5 | 1.4 | 17.9 |
| Overall/subject | PreChemo | HZ/su | 86 | 82 | 95.3 | 88.5 | 98.7 | 86 | 68 | 79.1 | 69.0 | 87.1 | 86 | 76 | 88.4 | 79.7 | 94.3 |
|  |  | Placebo | 86 | 56 | 65.1 | 54.1 | 75.1 | 86 | 56 | 65.1 | 54.1 | 75.1 | 86 | 4 | 4.7 | 1.3 | 11.5 |
|  | OnChemo | HZ/su | 26 | 25 | 96.2 | 80.4 | 99.9 | 26 | 23 | 88.5 | 69.8 | 97.6 | 26 | 18 | 69.2 | 48.2 | 85.7 |
|  |  | Placebo | 24 | 17 | 70.8 | 48.9 | 87.4 | 24 | 17 | 70.8 | 48.9 | 87.4 | 24 | 3 | 12.5 | 2.7 | 32.4 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.96 Incidence and nature of grade 3 symptoms (solicited only) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | PreChemo | HZ/su | 86 | 14 | 16.3 | 9.2 | 25.8 | 86 | 9 | 10.5 | 4.9 | 18.9 | 86 | 10 | 11.6 | 5.7 | 20.3 |
|  |  | Placebo | 86 | 6 | 7.0 | 2.6 | 14.6 | 86 | 6 | 7.0 | 2.6 | 14.6 | 86 | 0 | 0.0 | 0.0 | 4.2 |
|  | OnChemo | HZ/su | 26 | 6 | 23.1 | 9.0 | 43.6 | 26 | 6 | 23.1 | 9.0 | 43.6 | 26 | 0 | 0.0 | 0.0 | 13.2 |
|  |  | Placebo | 24 | 5 | 20.8 | 7.1 | 42.2 | 24 | 5 | 20.8 | 7.1 | 42.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Dose 2 | PreChemo | HZ/su | 74 | 11 | 14.9 | 7.7 | 25.0 | 73 | 10 | 13.7 | 6.8 | 23.8 | 74 | 3 | 4.1 | 0.8 | 11.4 |
|  |  | Placebo | 83 | 7 | 8.4 | 3.5 | 16.6 | 82 | 7 | 8.5 | 3.5 | 16.8 | 83 | 0 | 0.0 | 0.0 | 4.3 |
|  | OnChemo | HZ/su | 24 | 6 | 25.0 | 9.8 | 46.7 | 24 | 6 | 25.0 | 9.8 | 46.7 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  |  | Placebo | 22 | 3 | 13.6 | 2.9 | 34.9 | 22 | 3 | 13.6 | 2.9 | 34.9 | 22 | 0 | 0.0 | 0.0 | 15.4 |
| Overall/dose | PreChemo | HZ/su | 160 | 25 | 15.6 | 10.4 | 22.2 | 159 | 19 | 11.9 | 7.4 | 18.0 | 160 | 13 | 8.1 | 4.4 | 13.5 |
|  |  | Placebo | 169 | 13 | 7.7 | 4.2 | 12.8 | 168 | 13 | 7.7 | 4.2 | 12.9 | 169 | 0 | 0.0 | 0.0 | 2.2 |
|  | OnChemo | HZ/su | 50 | 12 | 24.0 | 13.1 | 38.2 | 50 | 12 | 24.0 | 13.1 | 38.2 | 50 | 1 | 2.0 | 0.1 | 10.6 |
|  |  | Placebo | 46 | 8 | 17.4 | 7.8 | 31.4 | 46 | 8 | 17.4 | 7.8 | 31.4 | 46 | 0 | 0.0 | 0.0 | 7.7 |
| Overall/subject | PreChemo | HZ/su | 86 | 20 | 23.3 | 14.8 | 33.6 | 86 | 17 | 19.8 | 12.0 | 29.8 | 86 | 12 | 14.0 | 7.4 | 23.1 |
|  |  | Placebo | 86 | 12 | 14.0 | 7.4 | 23.1 | 86 | 12 | 14.0 | 7.4 | 23.1 | 86 | 0 | 0.0 | 0.0 | 4.2 |
|  | OnChemo | HZ/su | 26 | 8 | 30.8 | 14.3 | 51.8 | 26 | 8 | 30.8 | 14.3 | 51.8 | 26 | 1 | 3.8 | 0.1 | 19.6 |
|  |  | Placebo | 24 | 5 | 20.8 | 7.1 | 42.2 | 24 | 5 | 20.8 | 7.1 | 42.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.97 Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |
|  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n $\%$ |  | UL | N | n | \% | LL | UL | N | n \% |  | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 86 | 68 | 79.1 | 69.0 | 87.1 | 86 | 11.2 | 0.0 | 06.3 | 26 | 15 | 57.7 | 36.9 | 76.6 | 24 | 14.2 | 0.1 | 21.1 |
|  | Grade 2 or 3 | 86 | 23 | 26.7 | 17.8 | 37.4 | 86 | 00.0 | 0.0 | 04.2 | 26 | 4 | 15.4 | 4.4 | 34.9 | 240 | 00.0 | 0.0 | 14.2 |
|  | Grade 3 | 86 | 8 | 9.3 | 4.1 | 17.5 | 86 | 00.0 | 0.0 | 04.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 240 | 00.0 | 0.0 | 14.2 |
|  | Medical advice | 86 | 1 | 1.2 | 0.0 | 6.3 | 86 | 00.0 | 0.0 | 04.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 240 | 00.0 | 0.0 | 14.2 |
| Redness (mm) | All | 86 | 30 | 34.9 | 24.9 | 45.9 | 86 | 00.0 | 0.0 | 04.2 | 26 | 3 | 11.5 | 2.4 | 30.2 | 240 | 00.0 | 0.0 | 14.2 |
|  | $>50$ | 86 | 16 | 18.6 | 11.0 | 28.4 | 86 | 00.0 | 0.0 | 04.2 | 26 | 2 | 7.7 | 0.9 | 25.1 | 240 | 00.0 | 0.0 | 14.2 |
|  | >100 | 86 | 2 | 2.3 | 0.3 | 8.1 | 86 | 00.0 | 0.0 | 04.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 240 | 00.0 | 0.0 | 14.2 |
|  | Medical advice | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 00.0 | 0.0 | 04.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 240 | 00.0 | 0.0 | 14.2 |
| Swelling (mm) | All | 86 | 14 | 16.3 | 9.2 | 25.8 | 86 | 11.2 | 0.0 | 06.3 | 26 | 1 | 3.8 | 0.1 | 19.6 | 240 | 00.0 | 0.0 | 14.2 |
|  | $>50$ | 86 | 7 | 8.1 | 3.3 | 16.1 | 86 | 00.0 | 0.0 | 04.2 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 00.0 | 0.0 | 14.2 |
|  | >100 | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 00.0 | 0.0 | 04.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 00.0 | 0.0 | 14.2 |
|  | Medical advice | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 00.0 |  | 04.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 240 | 00.0 | 0.0 | 14.2 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 74 | 36 | 48.6 | 36.9 | 60.6 | 83 | 33.6 | 0.8 | 810.2 | 24 | 16 | 66.7 | 44.7 | 84.4 | 222 | 29.1 | 1.1 | 29.2 |
|  | Grade 2 or 3 | 74 | 10 | 13.5 | 6.7 | 23.5 | 83 | 11.2 | 0.0 | 06.5 | 24 | 9 | 37.5 | 18.8 | 59.4 | 220 | 00.0 | 0.0 | 15.4 |
|  | Grade 3 | 74 | 3 | 4.1 | 0.8 | 11.4 | 83 | 00.0 | 0.0 | 04.3 | 24 | 1 | 4.2 | 0.1 | 21.1 | 220 | 00.0 | 0.0 | 15.4 |
|  | Medical advice | 74 | 0 | 0.0 | 0.0 | 4.9 | 83 | 00.0 | 0.0 | 04.3 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 00.0 | 0.0 | 15.4 |
| Redness (mm) | All | 74 | 15 | 20.3 | 11.8 | 31.2 | 83 | 00.0 | 0.0 | 04.3 | 24 | 5 | 20.8 | 7.1 | 42.2 | 22 | 00.0 | 0.0 | 15.4 |
|  | $>50$ | 74 | 6 | 8.1 | 3.0 | 16.8 | 83 | 00.0 | 0.0 | 04.3 | 24 | 2 | 8.3 | 1.0 | 27.0 | 22 | 00.0 | 0.0 | 15.4 |
|  | >100 | 74 | 0 | 0.0 | 0.0 | 4.9 | 83 | 00.0 | 0.0 | 04.3 | 24 | 0 | 0.0 | 0.0 | 14.2 | 220 | 00.0 | 0.0 | 15.4 |
|  | Medical advice | 74 | 0 | 0.0 | 0.0 | 4.9 | 83 | 00.0 | 0.0 | 04.3 | 24 | 0 | 0.0 | 0.0 | 14.2 | 220 | 00.0 | 0.0 | 15.4 |
| Swelling (mm) | All | 74 | 5 | 6.8 | 2.2 | 15.1 | 83 | 00.0 | 0.0 | 04.3 | 24 | 3 | 12.5 | 2.7 | 32.4 | 220 | 00.0 | 0.0 | 15.4 |
|  | >50 | 74 | 3 | 4.1 | 0.8 | 11.4 | 83 | 00.0 | 0.0 | 04.3 | 24 | 1 | 4.2 | 0.1 | 21.1 | 220 | 00.0 | 0.0 | 15.4 |
|  | >100 | 74 | 0 | 0.0 | 0.0 | 4.9 | 83 | 00.0 | 0.0 | 04.3 | 24 | 0 | 0.0 | 0.0 | 14.2 | 220 | 00.0 | 0.0 | 15.4 |
|  | Medical advice | 74 | 0 | 0.0 | 0.0 | 4.9 | 83 | 00.0 |  | 04.3 | 24 | 0 | 0.0 | 0.0 | 14.2 | 220 | 00.0 | 0.0 | 15.4 |

## Overall/dose

| Pain Al <br>   <br>  G | All |  |  | 65.0 |  |  |  |  | 2.40 .6 |  | 5031 | 3162. | 2.04 | 47.2 | 75.346 |  |  | 17.9 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Grade 2 or 3 | 160 | 33 | 20.6 |  | 27.7 | 169 |  | 0.60 |  | 5013 | 1326. | 26.01 | 14.6 | 40.3460 |  |  | 7.7 |
|  | Grade 3 | 160 | 11 | 6.9 | 3.5 | 12.0 | 9 | 00.0 | 0 0.0 | 02.2 | 501 | 12.0 | 2.0 | 0.1 | 10.6460 |  |  | 7 |
|  | Medical advice | 160 |  | 0.6 | 0.0 | 3.4 | 169 | 0.0 | 0.0 0.0 | 02.2 | 500 | 00.0 | 0.0 | 0.0 | 7.1460 | 00.0 |  | 7.7 |
| Redness (mm) | All | 160 | 45 | 28.1 |  | 35.8 | 169 | 00.0 | 0 0.0 | 02.2 | 508 | 816. | 6.07 | 7.2 | 29.146 |  |  | 7.7 |
|  | $>50$ | 160 | 22 | 13.8 | 8.8 | 20.1 | 169 |  | 0.0 0.0 | 02.2 | 504 | 48.0 | 8.02 | 2.2 | 19.246 |  |  | 7.7 |
|  | $>100$ | 1602 |  | 1.3 | 0.2 | 4.4 | 169 |  | 0.0 0.0 | 02.2 | 500 | 00.0 | 0.0 | 0.0 | 7.146 |  |  | 7.7 |
|  | Medical advice | 160 |  | 0.0 | 0.0 | 2.3 | 169 |  | 0 00.0 | 02.2 | 500 | 00.0 | 0.0 | 0.0 | 7.1460 |  |  | 7.7 |
| Swelling (mm) | All | 160 | 19 | 11.9 | 7.3 | 17.9 | 169 |  | 0. 0.0 | 03.3 | 504 | 48.0 | 8.02 | 2.2 | 19.2460 |  |  | 7.7 |
|  | >50 | 160 | 10 | 6.3 | 3.0 | 11.2 | 169 |  | 0.0 0.0 |  | 502 | 24.0 | 4.0 | 0.5 | 13.746 |  |  |  |
|  | $>100$ | 16 |  | 0.0 |  | 2.3 | O |  | 0.0 0.0 |  | 500 | 00.0 | 0.0 | 0.0 | 7.146 |  |  | 7.7 |
|  | Medical |  |  | 0.0 |  | 2.3 | 169 |  | 0.00 |  | 500 | 00.0 | 0.0 | 0.0 | 7.146 |  |  |  |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 86 | 72 | 83.7 |  | 90.8 | 86 |  | 4.71 .3 | 311.5 | [2618 |  | 9.24 |  | [85.7 243 |  |  |  |
|  | Grade 2 or 3 | 86 | 26 | 30.2 | 20.8 | 41.1 | 86 |  | 1.20 | 06.3 | 269 | 934. | 34.61 | 17.2 | 55.7240 | 00.0 |  |  |
|  | Grade 3 | 86 | 10 | 11.6 | 5.7 | 20.3 | 86 |  | 0. 0.0 | 04.2 | 261 | 13.8 | 3.80 | 0.1 | 19.6240 |  |  |  |
|  | Medical advice | 86 | 1 | 1.2 |  | 6.3 | 86 |  | 0 00.0 |  | 260 |  | 0.0 | 0.0 | 13.2240 |  |  |  |
| Redness (mm) | All | 86 | 34 |  |  | 50.7 | 86 |  | 0. 0.0 |  | 266 | 623. | 23.19 | 9.0 | 43.6240 |  |  |  |
|  | >50 | 86 | 17 | 19.8 |  | 29.8 | 86 | 00.0 | 00.0 | 04.2 | 262 | 27.7 | 7.70 | 0.9 | 25.1240 |  |  | 14.2 |
|  | $>100$ | 86 | 2 | 2.3 |  |  | 86 |  | 0 0.0 | 04.2 | 260 | 00.0 | 0.0 | 0.0 | 13.2240 |  |  |  |
|  | Medical advice | 86 | 0 |  | 0.0 | 4.2 | 86 |  | . 00.0 | 04.2 | 260 | 00.0 | 0.0 | 0.0 | 13.2240 | 00.0 | 0.0 | 14 |


|  |  | PreChemo |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |
|  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n \% | LL | UL | N | n | \% | LL | UL | N | n \% | LL | UL |
| Swelling (mm) | All | 86 | 15 | 17.4 | 10.1 | 27.1 | 86 | 11.2 | 0.0 | 6.3 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 0.0 | 0.0 | 14.2 |
|  | >50 | 86 | 9 | 10.5 | 4.9 | 18.9 | 86 | 00.0 | 0.0 | 4.2 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0.0 | 0.0 | 14.2 |
|  | >100 | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 00.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0.0 | 0.0 | 14.2 |
|  | Medical advice 8 | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 00.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 240 | 0.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
95\%CI = Exact 95\% confidence interval; LL = lower limit, UL = upper limit
Table 8.98 Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by PreChemo/OnChemo groups (Total Vaccinated Cohort)


|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 2 or 3 | 86 | 10 | 11.6 | 5.7 | 20.3 | 86 | 4 | 4.7 | 1.3 | 11.5 | 26 | 4 | 15.4 | 4.4 | 34.9 | 24 | 4 | 16.7 | 4.7 | 37.4 |
|  | Grade 3 | 86 | 3 | 3.5 | 0.7 | 9.9 | 86 | 0 | 0.0 | 0.0 | 4.2 | 260 | 0 | 0.0 | 0.0 | 13.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Related | 86 | 7 | 8.1 | 3.3 | 16.1 | 86 | 3 | 3.5 | 0.7 | 9.9 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Grade 2 or 3 <br> Related | 86 | 4 | 4.7 | 1.3 | 11.5 | 86 | 1 | 1.2 | 0.0 | 6.3 | 262 | 2 | 7.7 | 0.9 | 25.1 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 3 <br> Related | 86 | 2 | 2.3 | 0.3 | 8.1 | 86 | 0 | 0.0 | 0.0 | 4.2 | 260 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 260 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Myalgia | All | 86 | 41 | 47.7 | 36.8 | 58.7 | 86 | 9 | 10.5 | 4.9 | 18.9 | 26 | 9 | 34.6 | 17.2 | 55.7 | 24 | 8 | 33.3 | 15.6 | 55.3 |
|  | Grade 2 or 3 | 86 | 14 | 16.3 | 9.2 | 25.8 | 86 | 6 | 7.0 | 2.6 | 14.6 | 26 | 7 | 26.9 | 11.6 | 47.8 | 24 | 3 | 12.5 | 2.7 | 32.4 |
|  | Grade 3 | 86 | 6 | 7.0 | 2.6 | 14.6 | 86 | 1 | 1.2 | 0.0 | 6.3 | 26 | 2 | 7.7 | 0.9 | 25.1 | 24 | 2 | 8.3 | 1.0 | 27.0 |
|  | Related | 86 | 21 | 24.4 | 15.8 | 34.9 | 86 | 2 | 2.3 | 0.3 | 8.1 | 26 | 4 | 15.4 | 4.4 | 34.9 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Grade 2 or 3 <br> Related | 86 | 11 | 12.8 | 6.6 | 21.7 | 86 | 2 | 2.3 | 0.3 | 8.1 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 3 Related | 86 | 6 | 7.0 | 2.6 | 14.6 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Shivering | All | 86 | 19 | 22.1 | 13.9 | 32.3 | 86 | 7 | 8.1 | 3.3 | 16.1 | 26 |  | 30.8 | 14.3 | 51.8 | 24 | 6 | 25.0 | 9.8 | 46.7 |
|  | Grade 2 or 3 | 86 | 6 | 7.0 | 2.6 | 14.6 | 86 | 5 | 5.8 | 1.9 | 13.0 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Grade 3 | 86 | 3 | 3.5 | 0.7 | 9.9 | 86 | 2 | 2.3 | 0.3 | 8.1 | 26 | 2 | 7.7 | 0.9 | 25.1 | 24 | , | 0.0 | 0.0 | 14.2 |
|  | Related | 86 | 11 | 12.8 | 6.6 | 21.7 | 86 | 3 | 3.5 | 0.7 | 9.9 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Grade 2 or 3 <br> Related | 86 | 6 | 7.0 | 2.6 | 14.6 | 86 | 2 | 2.3 | 0.3 | 8.1 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 3 Related | 86 | 3 | 3.5 | 0.7 | 9.9 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 86 | 13 | 15.1 | 8.3 | 24.5 | 86 | 2 | 2.3 | 0.3 | 8.1 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 2 | 8.3 | 1.0 | 27.0 |
|  | $\geq 37.5$ | 86 | 13 | 15.1 | 8.3 | 24.5 | 86 | 2 | 2.3 | 0.3 | 8.1 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | , | 8.3 | 1.0 | 27.0 |
|  | >38.0 | 86 | 2 | 2.3 | 0.3 | 8.1 | 86 | 0 | 0.0 | 0.0 | 4.2 | 260 | 0 | 0.0 | 0.0 | 13.2 | 24 | - | 0.0 | 0.0 | 14.2 |
|  | >38.5 | 86 | 1 | 1.2 | 0.0 | 6.3 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | >39.0 | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | $>39.5$ | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 |  | 0.0 | 0.0 | 14.2 |
|  | >40.0 | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 |  | 0.0 | 0.0 | 14.2 |
|  | Related | 86 | 11 | 12.8 | 6.6 | 21.7 | 86 | 1 | 1.2 | 0.0 | 6.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | - | 0.0 | 0.0 | 14.2 |
|  | $\begin{aligned} & >38.0 \\ & \text { Related } \end{aligned}$ | 86 | 2 | 2.3 | 0.3 | 8.1 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | $\begin{array}{\|l\|} \hline>39.0 \\ \text { Related } \end{array}$ | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 73 | 41 | 56.2 | 44.1 | 67.8 | 82 | 43 | 52.4 | 41.1 | 63.6 | 24 | 16 | 66.7 | 44.7 | 84.4 | 22 | 14 | 63.6 | 40.7 | 82.8 |


|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 2 or 3 | 73 | 20 | 27.4 | 17.6 | 39.1 | 82 | 22 | 26.8 | 17.6 | 37.8 | 24 | 8 | 33.3 | 15.6 | 55.3 | 22 | 8 | 36.4 | 17.2 | 59.3 |
|  | Grade 3 | 73 | 5 | 6.8 | 2.3 | 15.3 | 82 | 5 | 6.1 | 2.0 | 13.7 | 24 | 4 | 16.7 | 4.7 | 37.4 | 22 | 1 | 4.5 | 0.1 | 22.8 |
|  | Related | 73 | 5 | 6.8 | 2.3 | 15.3 | 82 | 8 | 9.8 | 4.3 | 18.3 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Grade 2 or 3 <br> Related | 73 | 2 | 2.7 | 0.3 | 9.5 | 82 | 4 | 4.9 | 1.3 | 12.0 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Grade 3 <br> Related | 73 | 0 | 0.0 | 0.0 | 4.9 | 82 | 1 | 1.2 | 0.0 | 6.6 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Medical advice | 73 | 1 | 1.4 | 0.0 | 7.4 | 82 | 1 | 1.2 | 0.0 | 6.6 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
| Gastrointestinal symptoms | All | 73 | 30 | 441.1 | 29.7 | 53.2 | 82 | 29 | 35.4 | 25.1 | 46.7 | 24 | 11 | 45.8 | 25.6 | 67.2 | 22 | 10 | 45.5 | 24.4 | 67.8 |
|  | Grade 2 or 3 | 73 | 16 | 6 21.9 | 13.1 | 33.1 | 82 | 9 | 11.0 | 5.1 | 19.8 | 24 | 5 | 20.8 | 7.1 | 42.2 | 22 | 6 | 27.3 | 10.7 | 50.2 |
|  | Grade 3 | 73 | 4 | 5.5 | 1.5 | 13.4 | 82 | 1 | 1.2 | 0.0 | 6.6 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 2 | 9.1 | 1.1 | 29.2 |
|  | Related | 73 | 5 | 6.8 | 2.3 | 15.3 | 82 | 2 | 2.4 | 0.3 | 8.5 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Grade 2 or 3 <br> Related | 73 | 2 | 2.7 | 0.3 | 9.5 | 82 | 2 | 2.4 | 0.3 | 8.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Grade 3 <br> Related | 73 | 1 | 1.4 | 0.0 | 7.4 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Medical advice | 73 | 1 | 1.4 | 0.0 | 7.4 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
| Headache | All | 73 | 20 | 27.4 | 17.6 | 39.1 | 82 | 18 | 22.0 | 13.6 | 32.5 | 24 | 9 | 37.5 | 18.8 | 59.4 | 22 | 7 | 31.8 | 13.9 | 54.9 |
|  | Grade 2 or 3 | 73 | 10 | 10.7 | 6.8 | 23.8 | 82 | 5 | 6.1 | 2.0 | 13.7 | 24 | 4 | 16.7 | 4.7 | 37.4 | 22 | 2 | 9.1 | 1.1 | 29.2 |
|  | Grade 3 | 73 | 2 | 2.7 | 0.3 | 9.5 | 82 | 2 | 2.4 | 0.3 | 8.5 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Related | 73 | 5 | 6.8 | 2.3 | 15.3 | 82 | 2 | 2.4 | 0.3 | 8.5 | 24 | 2 | 8.3 | 1.0 | 27.0 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | $\begin{aligned} & \hline \text { Grade } 2 \\ & \text { or } 3 \\ & \text { Related } \\ & \hline \end{aligned}$ | 73 | 3 | 4.1 | 0.9 | 11.5 | 82 | 1 | 1.2 | 0.0 | 6.6 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Grade 3 Related | 73 | 0 | 0.0 | 0.0 | 4.9 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Medical advice | 73 | 1 | 1.4 | 0.0 | 7.4 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
| Myalgia | All | 73 | 24 | 32.9 | 22.3 | 44.9 | 82 | 17 | 20.7 | 12.6 | 31.1 | 24 | 8 | 33.3 | 15.6 | 55.3 | 22 | 6 | 27.3 | 10.7 | 50.2 |
|  | Grade 2 or 3 | 73 | 12 | 16.4 | 8.8 | 27.0 | 82 | 9 | 11.0 | 5.1 | 19.8 | 24 | 3 | 12.5 | 2.7 | 32.4 | 22 | 4 | 18.2 | 5.2 | 40.3 |
|  | Grade 3 | 73 | 2 | 2.7 | 0.3 | 9.5 | 82 | 1 | 1.2 | 0.0 | 6.6 | 24 | 2 | 8.3 | 1.0 | 27.0 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Related | 73 | 10 | 13.7 | 6.8 | 23.8 | 82 | 3 | 3.7 | 0.8 | 10.3 | 24 |  | 12.5 | 2.7 | 32.4 | 22 | 1 | 4.5 | 0.1 | 22.8 |
|  | Grade 2 or 3 <br> Related | 73 | 5 | 6.8 | 2.3 | 15.3 | 82 | 1 | 1.2 | 0.0 | 6.6 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 1 | 4.5 | 0.1 | 22.8 |
|  | Grade 3 Related | 73 | 0 | 0.0 | 0.0 | 4.9 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Medical advice | 73 | 0 | 0.0 | 0.0 | 4.9 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
| Shivering | All | 73 | 14 | 19.2 | 10.9 | 30.1 | 82 | 11 | 113.4 | 6.9 | 22.7 | 24 | - | 25.0 | 9.8 | 46.7 | 22 | 6 | 27.3 | 10.7 | 50.2 |
|  | Grade 2 or 3 | 73 | 6 | 8.2 | 3.1 | 17.0 | 82 | 1 | 1.2 | 0.0 | 6.6 | 24 | 4 | 16.7 | 4.7 | 37.4 | 22 | - | 0.0 | 0.0 | 15.4 |
|  | Grade 3 | 73 | 2 | 2.7 | 0.3 | 9.5 | 82 | 1 | 1.2 | 0.0 | 6.6 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 1 | 0.0 | 0.0 | 15.4 |
|  | Related | 73 | 5 | 6.8 | 2.3 | 15.3 | 82 | 3 | 3.7 | 0.8 | 10.3 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 1 | 4.5 | 0.1 | 22.8 |

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|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | , | \% | LL | UL |
|  | Grade 2 or 3 <br> Related | 73 | 2 | 2.7 | 0.3 | 9.5 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 1 | 4.2 | 0.1 | 21.1 | 220 |  | 0.0 | 0.0 | 15.4 |
|  | Grade 3 Related | 73 | 1 | 1.4 | 0.0 | 7.4 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 220 |  | 0.0 | 0.0 | 15.4 |
|  | Medical advice | 73 | 0 | 0.0 | 0.0 | 4.9 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 220 |  | 0.0 | 0.0 | 15.4 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 73 | 3 | 4.1 | 0.9 | 11.5 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 5 | 20.8 | 7.1 | 42.2 | 22 |  | 4.5 | 0.1 | 22.8 |
|  | $\geq 37.5$ | 73 | 3 | 4.1 | 0.9 | 11.5 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 5 | 20.8 | 7.1 | 42.2 | 22 |  | 4.5 | 0.1 | 22.8 |
|  | $>38.0$ | 73 | 1 | 1.4 | 0.0 | 7.4 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 |  | 4.5 | 0.1 | 22.8 |
|  | >38.5 | 73 | 0 | 0.0 | 0.0 | 4.9 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 |  | 0.0 | 0.0 | 15.4 |
|  | $>39.0$ | 73 | 0 | 0.0 | 0.0 | 4.9 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 |  | 0.0 | 0.0 | 15.4 |
|  | >39.5 | 73 | 0 | 0.0 | 0.0 | 4.9 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 |  | 0.0 | 0.0 | 15.4 |
|  | >40.0 | 73 | 0 | 0.0 | 0.0 | 4.9 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 |  | 0.0 | 0.0 | 15.4 |
|  | Related | 73 | 2 | 2.7 | 0.3 | 9.5 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 2 | 8.3 | 1.0 | 27.0 | 220 |  | 0.0 | 0.0 | 15.4 |
|  | $\begin{aligned} & \hline>38.0 \\ & \text { Related } \end{aligned}$ | 73 | 1 | 1.4 | 0.0 | 7.4 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 220 |  | 0.0 | 0.0 | 15.4 |
|  | $\begin{aligned} & >39.0 \\ & \text { Related } \end{aligned}$ | 73 | 0 | 0.0 | 0.0 | 4.9 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 220 |  | 0.0 | 0.0 | 15.4 |
|  | Medical advice | 73 | 0 | 0.0 | 0.0 | 4.9 | 82 | 0 | 0.0 | 0.0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 |  | 0.0 | 0.0 | 15.4 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 159 | 79 | 49.7 | 41.7 | 57.7 | 168 | 73 | 343.5 | 35.8 | 51.3 | 50 | 34 | 68.0 | 53.3 | 80.5 | 46 | 28 | 60.9 | 45.4 | 74.9 |
|  | Grade 2 or 3 | 159 | 38 | 23.9 | 17.5 | 31.3 | 168 | 30 | 017.9 | 12.4 | 24.5 | 50 | 20 | 40.0 | 26.4 | 54.8 | 46 | 5 | 32.6 | 19.5 | 48.0 |
|  | Grade 3 | 159 | 10 | 6.3 | 3.1 | 11.3 | 168 | 6 | 3.6 | 1.3 | 7.6 | 50 | 9 | 18.0 | 8.6 | 31.4 | 463 |  | 6.5 | 1.4 | 17.9 |
|  | Related | 159 | 19 | 11.9 | 7.4 | 18.0 | 168 | 18 | 810.7 | 6.5 | 16.4 | 50 | 2 | 4.0 | 0.5 | 13.7 | 46 |  | 0.0 | 0.0 | 7.7 |
|  | Grade 2 or 3 <br> Related | 159 | 10 | 6.3 | 3.1 | 11.3 | 168 | 8 | 4.8 | 2.1 | 9.2 | 50 | 1 | 2.0 | 0.1 | 10.6 | 460 |  | 0.0 | 0.0 | 7.7 |
|  | Grade 3 <br> Related | 159 | 3 | 1.9 | 0.4 | 5.4 | 168 | 1 | 0.6 | 0.0 | 3.3 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 |  | 0.0 | 0.0 | 7.7 |
|  | Medical advice | 159 | 1 | 0.6 | 0.0 | 3.5 | 168 | 1 | 0.6 | 0.0 | 3.3 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 |  | 0.0 | 0.0 | 7.7 |
| Gastrointestinal symptoms | All | 159 | 46 | 28.9 | 22.0 | 36.6 | 168 | 37 | 722.0 | 16.0 | 29.1 | 50 | 27 | 54.0 | 39.3 | 68.2 | 46 | 23 | 50.0 | 34.9 | 65.1 |
|  | Grade 2 or 3 | 159 | 22 | 13.8 | 8.9 | 20.2 | 168 | 13 | 37.7 | 4.2 | 12.9 | 50 | 13 | 26.0 | 14.6 | 40.3 | 46 | 3 | 28.3 | 16.0 | 43.5 |
|  | Grade 3 | 159 | 5 | 3.1 | 1.0 | 7.2 | 168 | 4 | 2.4 | 0.7 | 6.0 | 50 | 2 | 4.0 | 0.5 | 13.7 | 46 |  | 8.7 | 2.4 | 20.8 |
|  | Related | 159 | 11 | 6.9 | 3.5 | 12.0 | 168 | 4 | 2.4 | 0.7 | 6.0 | 50 | 4 | 8.0 | 2.2 | 19.2 | 46 |  | 0.0 | 0.0 | 7.7 |
|  | Grade 2 or 3 <br> Related | 159 | 3 | 1.9 | 0.4 | 5.4 | 168 | 3 | 1.8 | 0.4 | 5.1 | 50 | 1 | 2.0 | 0.1 | 10.6 | 46 |  | 0.0 | 0.0 | 7.7 |
|  | Grade 3 <br> Related | 159 | 1 | 0.6 | 0.0 | 3.5 | 168 | 1 | 0.6 | 0.0 | 3.3 | 50 | 0 | 0.0 | 0.0 | 7.1 | 460 |  | 0.0 | 0.0 | 7.7 |
|  | Medical advice | 159 | 1 | 0.6 | 0.0 | 3.5 | 168 | 1 | 0.6 | 0.0 | 3.3 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 |  | 2.2 | 0.1 | 11.5 |
| Headache | All | 159 | 38 | 23.9 | 17.5 | 31.3 | 168 | 30 | 017.9 | 12.4 | 24.5 | 50 | 19 | 38.0 | 24.7 | 52.8 | 46 | 19 | 41.3 | 27.0 | 56.8 |
|  | Grade 2 or 3 | 159 | 20 | 12.6 | 7.9 | 18.8 | 168 | 9 | 5.4 | 2.5 | 9.9 | 50 | 8 | 16.0 | 7.2 | 29.1 | 466 |  | 13.0 | 4.9 | 26.3 |
|  | Grade 3 | 159 | 5 | 3.1 | 1.0 | 7.2 | 168 | 2 | 1.2 | 0.1 | 4.2 | 50 | 1 | 2.0 | 0.1 | 10.6 | 46 |  | 2.2 | 0.1 | 11.5 |
|  | Related | 159 | 12 | 7.5 | 4.0 | 12.8 | 168 | 5 | 3.0 | 1.0 | 6.8 | 50 | 5 | 10.0 | 3.3 | 21.8 | 461 |  | 2.2 | 0.1 | 11.5 |

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|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  |  |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  | Placebo <br> $95 \% \mathrm{Cl}$ |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 2 or 3 Related | 159 | 7 | 4.4 | 1.8 | 8.9 | 168 | 2 | 1.2 | 0.1 | 4.2 | 50 | 3 | 6.0 | 1.3 | 16.5 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Grade 3 Related | 159 | 2 | 1.3 | 0.2 | 4.5 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Medical advice | 159 | 1 | 0.6 | 0.0 | 3.5 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
| Myalgia | All | 159 | 65 | 40.9 | 33.2 | 48.9 | 168 | 26 | 615.5 | 10.4 | 21.8 | 50 | 17 | 34.0 | 21.2 | 48.8 | 46 | 14 | 30.4 | 17.7 | 45.8 |
|  | Grade 2 or 3 | 159 | 26 | 16.4 | 11.0 | 23.0 | 168 | 15 | 58.9 | 5.1 | 14.3 | 50 | 10 | 20.0 | 10.0 | 33.7 | 46 | 7 | 15.2 | 6.3 | 28.9 |
|  | Grade 3 | 159 | 8 | 5.0 | 2.2 | 9.7 | 168 | 2 | 1.2 | 0.1 | 4.2 | 50 | 4 | 8.0 | 2.2 | 19.2 | 46 | 2 | 4.3 | 0.5 | 14.8 |
|  | Related | 159 | 31 | 19.5 | 13.6 | 26.5 | 168 | 5 | 3.0 | 1.0 | 6.8 | 50 | 7 | 14.0 | 5.8 | 26.7 | 46 | 2 | 4.3 | 0.5 | 14.8 |
|  | Grade 2 or 3 <br> Related | 159 | 16 | 10.1 | 5.9 | 15.8 | 168 | 3 | 1.8 | 0.4 | 5.1 | 50 | 4 | 8.0 | 2.2 | 19.2 | 46 | 1 | 2.2 | 0.1 | 11.5 |
|  | Grade 3 Related | 159 | 6 | 3.8 | 1.4 | 8.0 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 1 | 2.0 | 0.1 | 10.6 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Medical advice | 159 | 0 | 0.0 | 0.0 | 2.3 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
| Shivering | All | 159 | 33 | 20.8 | 14.7 | 27.9 | 168 | 18 | 810.7 | 6.5 | 16.4 | 50 | 14 | 28.0 | 16.2 | 42.5 | 46 | 12 | 26.1 | 14.3 | 41.1 |
|  | Grade 2 or 3 | 159 | 12 | 7.5 | 4.0 | 12.8 | 168 | 6 | 3.6 | 1.3 | 7.6 | 50 | 7 | 14.0 | 5.8 | 26.7 | 46 | 1 | 2.2 | 0.1 | 11.5 |
|  | Grade 3 | 159 | 5 | 3.1 | 1.0 | 7.2 | 168 | 3 | 1.8 | 0.4 | 5.1 | 50 | 3 | 6.0 | 1.3 | 16.5 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Related | 159 | 16 | 10.1 | 5.9 | 15.8 | 168 | 6 | 3.6 | 1.3 | 7.6 | 50 | 2 | 4.0 | 0.5 | 13.7 | 46 | 2 | 4.3 | 0.5 | 14.8 |
|  | Grade 2 or 3 <br> Related | 159 | 8 | 5.0 | 2.2 | 9.7 | 168 | 2 | 1.2 | 0.1 | 4.2 | 50 | 2 | 4.0 | 0.5 | 13.7 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Grade 3 <br> Related | 159 | 4 | 2.5 | 0.7 | 6.3 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 1 | 2.0 | 0.1 | 10.6 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Medical advice | 159 | 0 | 0.0 | 0.0 | 2.3 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
| Temperature/(*) | All | 159 | 16 | 10.1 | 5.9 | 15.8 | 168 | 2 | 1.2 | 0.1 | 4.2 | 50 | 5 | 10.0 | 3.3 | 21.8 | 46 | 3 | 6.5 | 1.4 | 17.9 |
|  | $\geq 37.5$ | 159 | 16 | 10.1 | 5.9 | 15.8 | 168 | 2 | 1.2 | 0.1 | 4.2 | 50 | 5 | 10.0 | 3.3 | 21.8 | 46 |  | 6.5 | 1.4 | 17.9 |
|  | $>38.0$ | 159 | 3 | 1.9 | 0.4 | 5.4 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 1 | 2.2 | 0.1 | 11.5 |
|  | >38.5 | 159 | 1 | 0.6 | 0.0 | 3.5 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | $>39.0$ | 159 | 0 | 0.0 | 0.0 | 2.3 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | $>39.5$ | 159 | 0 | 0.0 | 0.0 | 2.3 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | >40.0 | 159 | 0 | 0.0 | 0.0 | 2.3 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Related | 159 | 13 | 8.2 | 4.4 | 13.6 | 168 | 1 | 0.6 | 0.0 | 3.3 | 50 | 2 | 4.0 | 0.5 | 13.7 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | $\begin{array}{\|l\|} \hline>38.0 \\ \text { Related } \end{array}$ | 159 | 3 | 1.9 | 0.4 | 5.4 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | $>39.0$ <br> Related | 159 | 0 | 0.0 | 0.0 | 2.3 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Medical advice | 159 | 0 | 0.0 | 0.0 | 2.3 | 168 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 1 | 2.2 | 0.1 | 11.5 |
|  |  |  |  |  |  |  | Over | 这 | Il/subj | ect |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 86 | 57 | 66.3 | 55.3 | 76.1 | 86 | 52 | 260.5 | 49.3 | 70.8 | 26 | 21 | 80.8 | 60.6 | 93.4 | 24 | 16 | 66.7 | 44.7 | 84.4 |
|  | Grade 2 or 3 | 86 | 31 | 36.0 | 26.0 | 47.1 | 86 | 27 | 731.4 | 21.8 | 42.3 | 26 | 14 | 53.8 | 33.4 | 73.4 | 24 | 10 | 41.7 | 22.1 | 63.4 |
|  | Grade 3 | 86 | 10 | 11.6 | 5.7 | 20.3 | 86 | 5 | 5.8 | 1.9 | 13.0 | 26 | 6 | 23.1 | 9.0 | 43.6 | 24 | 3 | 12.5 | 2.7 | 32.4 |
|  | Related | 86 | 17 | 19.8 | 12.0 | 29.8 | 86 | 14 | 416.3 | 9.2 | 25.8 | 26 | 2 | 7.7 | 0.9 | 25.1 | 24 | 0 | 0.0 | 0.0 | 14.2 |


|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  |  |  |  | 95 \% CI |  | 95\% CI |  |  |  |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 2 or 3 Related | 86 | 10 | 11.6 | 6.7 | 20.3 | 86 | 8 | 9.3 | 4.1 | 17.5 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 3 Related | 86 | 3 | 3.5 | 0.7 | 9.9 | 86 | 1 | 1.2 | 0.0 | 6.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 86 | 1 | 1.2 | 0.0 | 6.3 | 86 | 1 | 1.2 | 0.0 | 6.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Gastrointestinal symptoms | All | 86 | 33 | 38.4 | 28.1 | 49.5 | 86 | 34 | 39.5 | 29.2 | 50.7 | 26 | 18 | 69.2 | 48.2 | 85.7 | 24 | 15 | 62.5 | 40.6 | 81.2 |
|  | Grade 2 or 3 | 86 | 18 | 20.9 | 12.9 | 31.0 | 86 | 11 | 12.8 | 6.6 | 21.7 | 26 | 8 | 30.8 | 14.3 | 51.8 | 24 | 10 | 41.7 | 22.1 | 63.4 |
|  | Grade 3 | 86 | 5 | 5.8 | 1.9 | 13.0 | 86 | 4 | 4.7 | 1.3 | 11.5 | 26 | , | 3.8 | 0.1 | 19.6 | 24 | 3 | 12.5 | 2.7 | 32.4 |
|  | Related | 86 | 7 | 8.1 | 3.3 | 16.1 | 86 | 3 | 3.5 | 0.7 | 9.9 | 26 | 4 | 15.4 | 4.4 | 34.9 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 2 or 3 <br> Related | 86 | 2 | 2.3 | 0.3 | 8.1 | 86 | 3 | 3.5 | 0.7 | 9.9 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 3 Related | 86 | 1 | 1.2 | 0.0 | 6.3 | 86 | 1 | 1.2 | 0.0 | 6.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 86 | 1 | 1.2 | 0.0 | 6.3 | 86 | 1 | 1.2 | 0.0 | 6.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |
| Headache | All | 86 | 30 | 34.9 | 24.9 | 45.9 | 86 | 26 | 30.2 | 20.8 | 41.1 | 26 | 13 | 50.0 | 29.9 | 70.1 | 24 | 14 | 58.3 | 36.6 | 77.9 |
|  | Grade 2 or 3 | 86 | 16 | 18.6 | 11.0 | 28.4 | 86 | 9 | 10.5 | 4.9 | 18.9 | 26 | 6 | 23.1 | 9.0 | 43.6 | 24 | 5 | 20.8 | 7.1 | 42.2 |
|  | Grade 3 | 86 | 5 | 5.8 | 1.9 | 13.0 | 86 | 2 | 2.3 | 0.3 | 8.1 | 26 |  | 3.8 | 0.1 | 19.6 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Related | 86 | 11 | 12.8 | 6.6 | 21.7 | 86 | 5 | 5.8 | 1.9 | 13.0 | 26 | 5 | 19.2 | 6.6 | 39.4 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Grade 2 or 3 <br> Related | 86 | 6 | 7.0 | 2.6 | 14.6 | 86 | 2 | 2.3 | 0.3 | 8.1 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 3 Related | 86 | 2 | 2.3 | 0.3 | 8.1 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 86 | 1 | 1.2 | 0.0 | 6.3 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Myalgia | All | 86 | 50 | 58.1 | 47.0 | 68.7 | 86 | 22 | 25.6 | 16.8 | 36.1 | 26 | 10 | 38.5 | 20.2 | 59.4 | 24 | 9 | 37.5 | 18.8 | 59.4 |
|  | Grade 2 or 3 | 86 | 23 | 26.7 | 17.8 | 37.4 | 86 | 14 | 16.3 | 9.2 | 25.8 | 26 | 8 | 30.8 | 14.3 | 51.8 | 24 | 5 | 20.8 | 7.1 | 42.2 |
|  | Grade 3 | 86 | 8 | 9.3 | 4.1 | 17.5 | 86 | 2 | 2.3 | 0.3 | 8.1 | 26 | 4 | 15.4 | 4.4 | 34.9 | 24 |  | 8.3 | 1.0 | 27.0 |
|  | Related | 86 | 25 | 29.1 | 19.8 | 39.9 | 86 | 4 | 4.7 | 1.3 | 11.5 | 26 | 5 | 19.2 | 6.6 | 39.4 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Grade 2 or 3 <br> Related | 86 | 14 | 16.3 | 9.2 | 25.8 | 86 | 3 | 3.5 | 0.7 | 9.9 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Grade 3 Related | 86 | 6 | 7.0 | 2.6 | 14.6 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Shivering | All | 86 | 29 | 33.7 | 23.9 | 44.7 | 86 | 16 | 18.6 | 11.0 | 28.4 | 26 | 10 | 38.5 | 20.2 | 59.4 | 24 |  | 37.5 | 18.8 | 59.4 |
|  | Grade 2 or 3 | 86 | 11 | 12.8 | 6.6 | 21.7 | 86 | 6 | 7.0 | 2.6 | 14.6 | 26 | 4 | 15.4 | 4.4 | 34.9 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Grade 3 | 86 | 4 | 4.7 | 1.3 | 11.5 | 86 | 3 | 3.5 | 0.7 | 9.9 | 26 | 2 | 7.7 | 0.9 | 25.1 | 24 | , | 0.0 | 0.0 | 14.2 |
|  | Related | 86 | 15 | 17.4 | 10.1 | 27.1 | 86 | 4 | 4.7 | 1.3 | 11.5 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Grade 2 or 3 <br> Related | 86 | 7 | 8.1 | 3.3 | 16.1 | 86 | 2 | 2.3 | 0.3 | 8.1 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |


|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 3 Related | 86 | 3 | 3.5 | 0.7 | 9.9 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 86 | 15 | 17.4 | 10.1 | 27.1 | 86 | 2 | 2.3 | 0.3 | 8.1 | 26 | 5 | 19.2 | 6.6 | 39.4 | 24 | 3 | 12.5 | 2.7 | 32.4 |
|  | $\geq 37.5$ | 86 | 15 | 17.4 | 10.1 | 27.1 | 86 | 2 | 2.3 | 0.3 | 8.1 | 26 | 5 | 19.2 | 6.6 | 39.4 | 24 | 3 | 12.5 | 2.7 | 32.4 |
|  | >38.0 | 86 | 3 | 3.5 | 0.7 | 9.9 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | >38.5 | 86 | 1 | 1.2 | 0.0 | 6.3 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | >39.0 | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | >39.5 | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | >40.0 | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Related | 86 | 12 | 14.0 | 7.4 | 23.1 | 86 | 1 | 1.2 | 0.0 | 6.3 | 26 | 2 | 7.7 | 0.9 | 25.1 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | $\begin{aligned} & >38.0 \\ & \text { Related } \end{aligned}$ | 86 | 3 | 3.5 | 0.7 | 9.9 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | $\begin{aligned} & \hline>39.0 \\ & \text { Related } \\ & \hline \end{aligned}$ | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; $\mathrm{LL}=$ lower limit, $\mathrm{UL}=$ upper limit
$\left(^{*}\right)=$ Temperature is measured by oral, axillary or tympanic routes
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for oral, axillary or tympanic route

Table $8.99 \quad$ Number and percentage of subjects who reported temperature by half degree measured via oral route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |
|  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |
| Symptom | Type | N | n \% | \% L | LL U | UL | N | n \% | LL | L UL | N | n \% | \% LL | LL U | UL | N | n \% |  | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 86 |  | 4.71 | 1.31 | 11.5 | 86 | 11.2 | 0.0 | . 6.3 | 26 |  | 0.00. | 0.01 | 13.2 | 24 | 00.0 | 0.0 | O 14.2 |
|  | $\geq 35.5$ | 86 | 44.7 | 4.71 | 1.31 | 11.5 | 86 | 11.2 | 0.0 | . 06.3 | 26 | 00.0 | 0.00. | 0.0 | 13.2 | 24 | 00.0 | 0.0 | 014.2 |
|  | $>36.0$ | 86 | 44.7 | 4.71 | 1.31 | 11.5 | 86 | 11.2 |  | . 06.3 | 26 | 00.0 | 0.00. | 0.01 | 13.2 | 24 | 00.0 | 0.0 | . 14.2 |
|  | >36.5 | 86 | 44.7 | 4.71 | 1.31 | 11.5 | 86 | 11.2 | 0.0 | . 06.3 | 26 | 00.0 | 0.00. | 0.0 | 13.2 | 24 | 00.0 | 0.0 | . 14.2 |
|  | >37.0 | 86 | 44.7 | 4.71 | 1.31 | 11.5 | 86 | 11.2 | 0.0 | . 06.3 | 26 | 00.0 | 0.00. | 0.01 | 13.2 | 24 | 00.0 | 0.0 | . 14.2 |
|  | >37.5 | 86 | 11.2 | 1.20 | 0.06 | 6.3 | 86 | 11.2 | 0.0 | . 06.3 | 26 | 00.0 | 0.00. | 0.01 | 13.2 | 24 | 00.0 | 0.0 | . 14.2 |
|  | >38.0 8 | 86 |  | 0.00 | 0.04 | 4.2 | 86 | 00.0 | 0.0 | . 4.2 | 26 |  | 0.00. | 0.0 | 13.2 | 24 | 00.0 | 0.0 | 014.2 |
|  | $>38.5$ | 86 | 00.0 | 0.00 | 0.04 | 4.2 | 86 | 00.0 | 0.0 | . 4.2 | 26 |  | 0.00. | 0.0 | 13.2 | 24 | 00.0 | 0.0 | . 14.2 |
|  | >39.0 8 | 86 | 00.0 | 0.00 | 0.04 | 4.2 | 86 | 00.0 | 0.0 | . 4.2 | 26 |  | 0.00. | 0.0 | 13.2 | 24 | 00.0 | 0.0 | O 14.2 |
|  | >39.5 | 86 |  | 0.00 | 0.04 | 4.2 | 86 | 00.0 | 0.0 | . 04.2 | 26 |  | 0.00. | 0.01 | 13.2 | 24 | 00.0 | 0.0 | . 14.2 |
|  | >40.0 | 86 | 00.0 | 0.00 | 0.04 | 4.2 | 86 | 00.0 |  | . 4.2 | 26 | 00.0 | 0.00. | 0.01 | 13.2 | 24 |  | 0.0 | 014.2 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 73 | 22.7 | 2.70 | 0.39 | 9.5 | 82 | 00.0 | 0.0 | . 4.4 | 24 |  | 4.20. | 0.12 | 21.1 | 22 | 00.0 | 0.0 | O 115.4 |
|  | $\geq 35.57$ | 73 | 22.7 | 2.70 | 0.39 | 9.5 | 82 | 00.0 | 0.0 | . 04.4 | 24 |  | 4.20. | 0.12 | 21.1 | 22 | 00.0 | 0.0 | . 115.4 |
|  | >36.0 | 73 | 22.7 | 2.70 | 0.39 | 9.5 | 82 | 00.0 | 0.0 | . 04.4 | 24 |  | 4.20. | 0.12 | 21.1 | 22 | 00.0 | 0.0 | O 15.4 |
|  | >36.5 7 | 73 | 22.7 | 2.70 | 0.39 | 9.5 | 82 | 00.0 |  | . 4.4 | 24 |  | 4.20. | 0.12 | 21.1 | 22 | 00.0 | 0.0 | 015.4 |
|  | $>37.0$ | 73 |  | 2.70 | 0.39 | 9.5 | 82 | 00.0 |  | . 4.4 | 24 |  | 4.20. | 0.12 | 21.1 | 220 | 00.0 | 0.0 | O 15.4 |
|  | >37.5 7 | 73 | 22.7 | 2.70 | 0.39 | 9.5 | 82 | 00.0 |  | . 4.4 | 24 |  | 4.20. | 0.12 | 21.1 | 22 | 00.0 | 0.0 | O 15.4 |
|  | >38.0 | 73 |  | 1.40 | 0.07 | 7.4 | 82 | 00.0 | 0.0 | . 4.4 | 24 |  | 0.00. | 0.0 | 14.2 | 22 | 00.0 | 0.0 | 015.4 |
|  | $>38.5$ | 73 |  | 0.00 | 0.04 | 4.9 | 82 | 00.0 |  | . 04.4 | 24 |  | 0.00. | 0.01 | 14.2 | 22 | 00.0 | 0.0 | . 15.4 |
|  | >39.0 7 | 73 |  | 0.00 | 0.04 | 4.9 | 82 | 00.0 |  | . 4.4 | 24 |  | 0.00. | 0.01 | 14.2 | 22 | 00.0 | 0.0 | O 15.4 |
|  | >39.5 7 | 73 |  | 0.00 | 0.04 | 4.9 | 82 | 00.0 |  | . 4.4 | 24 |  | 0.00. | 0.01 | 14.2 | 22 | 00.0 | 0.0 | O 15.4 |
|  | >40.0 | 73 |  | 0.00 | 0.04 | 4.9 | 82 | 00.0 |  | . 4.4 | 24 |  | 0.00. | 0.01 | 14.2 | 22 |  |  | 015.4 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 159 |  | 3.81 | 1.48 | 8.0 | 168 | 10.6 | 0.0 | . 33.3 | 50 |  | 2.00. | 0.110 | 10.6 | 46 | 00.0 | 0.0 | 017.7 |
|  | $\geq 35.5$ | 159 |  | 3.81 | 1.48 | 8.0 | 168 | 10.6 | 0.0 | . 3.3 | 50 |  | 2.00. | 0.11 | 10.6 | 46 | 00.0 | 0.0 | 07.7 |
|  | >36.0 | 159 | 63.8 | 3.81 | 1.48 | 8.0 | 168 | 10.6 | 0.0 | . 3.3 | 50 |  | 2.00. | 0.11 | 10.6 | 46 | 00.0 | 0.0 | 0 7.7 |
|  | >36.5 | 159 | 63.8 | 3.81 | 1.48 | 8.0 | 168 | 10.6 | 0.0 | . 3.3 | 50 |  | 2.00. | 0.110 | 10.6 | 46 | 00.0 | 0.0 | 0 7.7 |
|  | >37.0 | 159 | 63.8 | 3.81 | 1.48 | 8.0 | 168 | 10.6 | 0.0 | . 3.3 | 50 |  | 2.00. | 0.110 | 10.6 | 46 | 00.0 | 0.0 | 07.7 |
|  | >37.5 | 159 |  | 1.90 | 0.45 | 5.4 | 168 | 10.6 | 0.0 | . 3.3 | 50 |  | 2.00. | 0.110 | 10.6 | 46 | 00.0 | 0.0 | 07.7 |
|  | >38.0 | 159 |  | 0.60 | 0.03 | 3.5 | 168 | 00.0 | 0.0 | . 2.2 | 50 |  | 0.00. | 0.07 | 7.1 | 46 | 00.0 | 0.0 | 07.7 |
|  | >38.5 | 159 |  | 0.00 | 0.02 | 2.3 | 168 | 00.0 | 0.0 | . 2.2 | 50 |  | 0.00. | 0.07 | 7.1 | 46 | 00.0 | 0.0 | 07.7 |
|  | >39.0 | 159 | 00.0 | 0.00 | 0.02 | 2.3 | 168 | 00.0 | 0.0 | . 2.2 | 50 | 00.0 | 0.00. | 0.07 | 7.1 | 46 | 00.0 | 0.0 | 07.7 |
|  | >39.5 | 159 | 00.0 | 0.00 | 0.02 | 2.3 | 168 | 00.0 | 0.0 | . 2.2 | 50 | 00.0 | 0.00. | 0.07 | 7.1 | 46 | 00.0 | 0.0 | 07.7 |
|  | >40.0 | 159 |  | 0.00 | 0.02 | 2.3 | 168 | 00.0 | 0.0 | . 2.2 | 50 |  | 0.00. | 0.07 | 7.1 | 46 | 00.0 | 0.0 | 07.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 86 | 55.8 | 5.81 | 1.91 | 13.0 | 86 | 11.2 |  | . 06.3 | 26 |  | 3.80. | 0.11 | 19.6 | 24 | 00.0 | 0.0 | O 14.2 |
|  | $\geq 35.5$ | 86 | 55.8 | 5.81 | 1.91 | 13.0 | 86 | 11.2 |  | . 6.3 | 26 |  | 3.80. | 0.119 | 19.6 | 24 | 00.0 | 0.0 | 014.2 |
|  | >36.0 86 | 86 | 55.8 | 5.81 | 1.91 | 13.0 | 86 | 11.2 | 0.0 | . 06.3 | 26 |  | 3.80. | 0.11 | 19.6 | 24 | 00.0 | 0.0 | 014.2 |
|  | >36.5 | 86 | 55.8 | 5.81 | 1.91 | 13.0 | 86 | 11.2 | 0.0 | . 06.3 | 26 |  | 3.80. | 0.11 | 19.6 | 24 | 00.0 | 0.0 | . 14.2 |
|  | >37.0 8 | 86 | 55.8 | 5.81 | 1.91 | 13.0 | 86 | 11.2 |  | . 6.3 | 26 |  | 3.80. | 0.11 | 19.6 | 24 | 00.0 | 0.0 | . 14.2 |
|  | $>37.5$ | 86 | 22.3 | 2.30 | 0.38 | 8.1 | 86 | 11.2 |  | . 06.3 | 26 |  | 3.80. | 0.11 | 19.6 | 24 | 00.0 | 0.0 | 014.2 |
|  | >38.0 8 | 86 | 11.2 | 1.20 | 0.06 | 6.3 | 86 | 00.0 | 0.0 | . 4.2 | 26 | 00.0 | 0.00. | 0.0 | 13.2 | 24 | 00.0 | 0.0 | O 14.2 |
|  | $>38.5$ | 86 | 00.0 | 0.00 | 0.04 | 4.2 | 86 | 00.0 | 0.0 | . 4.2 | 26 | 00.0 | 0.00. | 0.0 | 13.2 | 24 | 00.0 | 0.0 | O 14.2 |
|  | >39.0 8 | 86 |  | 0.00 | 0.04 | 4.2 | 86 | 00.0 | 0.0 | . 4.2 | 26 |  | 0.00. | 0.01 | 13.2 | 24 | 00.0 | 0.0 | O 14.2 |
|  | >39.5 | 86 | 00.0 | 0.00 | 0.04 | 4.2 | 86 | 00.0 |  | . 4.2 | 26 | 00.0 | 0.00. | 0.01 | 13.2 | 24 | 00.0 | 0.0 | 014.2 |


|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  | Placebo |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% Cl |  |  |  | 95 \% Cl |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type | N | n \% | LL | UL | N | n \% | LL | UL | N | n | \% | LL | UL | N |  | \% | LL | UL |
|  | >40.0 | 86 | 00.0 | 0.0 | 4.2 | 86 | 00.0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for oral route
Table 8.100 Number and percentage of subjects who reported temperature by half degree measured via axillary route during the 7-day (Days 0-6) post-vaccination period following each dose (no conversion) by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type | N | n | \% | LL U | UL | N |  | \% | LL | U | UL | N |  | \% | LL | UL | N |  | \% |  | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 86 | 9 | 10.5 | 4.91 | 18.9 | 86 | 1 | 1.2 | 0.0 | 0 | 6.3 | 26 | 0 | 0.0 | 0.0 | 13.2 |  |  | 8.3 | 1.0 | (1.027.0 |
|  | $\geq 35.5$ | 86 | 9 | 10.5 | 4.91 | 18.9 | 86 | 1 | 1.2 | 0.0 | 0 | 6.3 | 26 | 0 | 0.0 | 0.0 | 13.2 |  |  | 8.3 | 1.0 | 1.0 27.0 |
|  | >36.0 | 86 | 9 | 10.5 | 4.91 | 18.9 | 86 | 1 | 1.2 | 0.0 | 0 | 6.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 4 | 8.3 | 1.0 | 1.027.0 |
|  | >36.5 | 86 | 9 | 10.5 | 4.91 | 18.9 | 86 | 1 | 1.2 | 0.0 | 0 | 6.3 | 26 | 0 | 0.0 | 0.0 | 13.2 |  | 2 | 8.3 | 1.0 | 1.027.0 |
|  | $>37.0$ | 86 | 9 | 10.5 | 4.91 | 18.9 | 86 | 1 | 1.2 | 0.0 | 0 | 6.3 | 26 | 0 | 0.0 | 0.0 | 13.2 |  | 4 | 8.3 | 1.0 | 1.027.0 |
|  | >37.5 | 86 | 7 | 8.1 | 3.31 | 16.1 | 86 | 1 | 1.2 | 0.0 | 0 | 6.3 | 26 | 0 | 0.0 | 0.0 | 13.2 |  | 4 | 8.3 | 1.0 | 1.027.0 |
|  | $>38.0$ | 86 | 2 | 2.3 | 0.38 | 8.1 | 86 | 0 | 0.0 | 0.0 | 04 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | . 14.2 |
|  | $>38.5$ | 86 | 1 | 1.2 | 0.06 | 6.3 | 86 | 0 | 0.0 | 0.0 | 04 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | . 14.2 |
|  | $>39.0$ | 86 | 0 | 0.0 | 0.04 | 4.2 | 86 | 0 | 0.0 | 0.0 | 04 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | . 14.2 |
|  | $>39.5$ | 86 | 0 | 0.0 | 0.04 | 4.2 | 86 | 0 | 0.0 | 0.0 | 04 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | . 14.2 |
|  | >40.0 | 86 | 0 | 0.0 | 0.04 | 4.2 | 86 | 0 | 0.0 | 0.0 | 04 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 |  | 0.0 |  | . 14.2 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 73 | 1 | 1.4 | 0.07 | 7.4 | 82 | 0 | 0.0 | 0.0 | 04 | 4.4 | 24 | 43 | 12.5 | 2.7 | 32.4 | 22 |  | 4.5 |  | 122.8 |
|  | $\geq 35.5$ | 73 | 1 | 1.4 | 0.07 | 7.4 | 82 | 0 | 0.0 | 0.0 | 04 | 4.4 | 24 | 4 | 12.5 | 2.7 | 32.4 | 22 |  | 4.5 | 0.1 | . 122.8 |
|  | >36.0 | 73 | 1 | 1.4 | 0.07 | 7.4 | 82 | 0 | 0.0 | 0.0 | 04 | 4.4 | 24 | 43 | 12.5 | 2.7 | 32.4 | 22 |  | 4.5 | 0.1 | . 122.8 |
|  | >36.5 | 73 | 1 | 1.4 | 0.07 | 7.4 | 82 | 0 | 0.0 | 0.0 | 04 | 4.4 | 24 | 4 | 12.5 | 2.7 | 32.4 | 22 |  | 4.5 | 0.1 | . 122.8 |
|  | >37.0 | 73 | 1 | 1.4 | 0.07 | 7.4 | 82 | 0 | 0.0 | 0.0 | 04 | 4.4 | 24 | 4 | 12.5 | 2.7 | 32.4 | 22 |  | 4.5 | 0.1 | . 122.8 |
|  | $>37.5$ | 73 | 0 | 0.0 | 0.04 | 4.9 | 82 | 0 | 0.0 | 0.0 | 04 | 4.4 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 |  | 4.5 | 0.1 | . 122.8 |
|  | >38.0 | 73 | 0 | 0.0 | 0.04 | 4.9 | 82 | 0 | 0.0 | 0.0 | 04 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 |  | 4.5 | 0.1 | 122.8 |
|  | $>38.5$ | 73 | 0 | 0.0 | 0.04 | 4.9 | 82 | 0 | 0.0 | 0.0 | 04 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 |  | 0.0 | 0.0 | . 15.4 |
|  | $>39.0$ | 73 | 0 | 0.0 | 0.04 | 4.9 | 82 | 0 | 0.0 | 0.0 | 04 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 |  | 0.0 | 0.0 | . 15.4 |
|  | >39.5 | 73 | 0 | 0.0 | 0.04 | 4.9 | 82 | 0 | 0.0 | 0.0 | 0 | 4.4 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 |  | 0.0 | 0.0 | 0.0 15.4 |
|  | >40.0 | 73 | 0 | 0.0 | 0.04 | 4.9 | 82 |  | 0.0 | 0.0 | 04 | 4.4 | 24 |  | 0.0 | 0.0 | 14.2 | 22 |  | 0.0 | 0.0 | . 15.4 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 159 | 10 | 0.3 | 3.11 | 11.3 | 168 | 1 | 0.6 | 0.0 | 03 | 3.3 | 50 | 3 | 6.0 | 1.3 | 16.5 | 46 | 3 | 6.5 | 1.4 | 417.9 |
|  | $\geq 35.5$ | 159 | 10 | 06.3 | 3.11 | 11.3 | 168 | 1 | 0.6 | 0.0 | 0 | 3.3 | 50 | 3 | 6.0 | 1.3 | 16.5 | 46 |  | 6.5 | 1.4 | 417.9 |
|  | >36.0 | 159 | 10 | 0.3 | 3.11 | 11.3 | 168 |  | 0.6 | 0.0 |  | 3.3 | 50 | 3 | 6.0 | 1.3 | 16.5 | 46 |  | 6.5 | 1.4 | 1417.9 |
|  | >36.5 | 159 | 10 | 10.3 | 3.11 | 11.3 | 168 |  | 0.6 | 0.0 | 03 | 3.3 | 50 |  | 6.0 | 1.3 | 16.5 | 46 | 3 | 6.5 |  | 417.9 |

116427 (ZOSTER-028)
Report Final

|  |  | PreChemo |  |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type | N | n | \% | LL U | UL | N | n | \% | LL | UL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | >37.0 | 159 | 10 | 6.3 | 3.1 | 11.3 | 168 |  | 0.6 | 0.0 | 0 | 3.3 | 50 | 3 | 6.0 | 1.3 | 16.5 | 46 |  | 6.5 | 1.4 | 17.9 |
|  | >37.5 | 159 | 7 | 4.4 | 1.8 | 8.9 | 168 |  | 0.6 | 0.0 | 0 | 3.3 | 50 |  | 2.0 | 0.1 | 10.6 | 46 |  | 6.5 | 1.4 | 17.9 |
|  | >38.0 | 159 | 2 | 1.3 | 0.24 | 4.5 | 168 | 0 | 0.0 | 0.0 | 0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 1 | 2.2 | 0.1 | 111.5 |
|  | >38.5 | 159 | 1 | 0.6 | 0.0 | 3.5 | 168 | 0 | 0.0 | 0.0 | 02 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | >39.0 | 159 | 0 | 0.0 | 0.0 | 2.3 | 168 | 0 | 0.0 | 0.0 | 0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | >39.5 | 159 | 0 | 0.0 | 0.0 | 2.3 | 168 | 0 | 0.0 | 0.0 | 02 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | >40.0 | 159 | 0 | 0.0 | 0.0 | 2.3 | 168 | 0 | 0.0 | 0.0 | 0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 86 | 10 | 11.6 | 5.7 | 20.3 | 86 | 1 | 1.2 | 0.0 | 06 | 6.3 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 3 | 12.5 | 52.7 | 32.4 |
|  | $\geq 35.5$ | 86 | 10 | 11.6 | 5.7 | 20.3 | 86 | 1 | 1.2 | 0.0 | 0 | 6.3 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 3 | 12.5 | 2.7 | 32.4 |
|  | >36.0 | 86 | 10 | 11.6 | 5.7 | 20.3 | 86 | 1 | 1.2 | 0.0 | 0 | 6.3 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 3 | 12.5 | 2.7 | 32.4 |
|  | >36.5 | 86 | 10 | 11.6 | 5.7 | 20.3 | 86 | 1 | 1.2 | 0.0 | 0 | 6.3 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 3 | 12.5 | 52.7 | 32.4 |
|  | >37.0 | 86 | 10 | 11.6 | 5.7 | 20.3 | 86 | 1 | 1.2 | 0.0 | 0 | 6.3 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 3 | 12.5 | 2.7 | 22.4 |
|  | >37.5 | 86 | 7 | 8.1 | 3.3 | 16.1 | 86 | 1 | 1.2 | 0.0 | 0 | 6.3 | 26 |  | 3.8 | 0.1 | 19.6 | 24 | 3 | 12.5 | 2.7 | 732.4 |
|  | $>38.0$ | 86 | 2 | 2.3 | 0.38 | 8.1 | 86 | 0 | 0.0 | 0.0 | 04 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 1 | 4.2 | 0.1 | . 21.1 |
|  | >38.5 | 86 | 1 | 1.2 | 0.0 | 6.3 | 86 | 0 | 0.0 | 0.0 | 04 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | >39.0 | 86 | 0 | 0.0 | 0.0 | 4.2 | 86 | 0 | 0.0 | 0.0 | 04 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | >39.5 | 86 | 0 | 0.0 | 0.04 | 4.2 | 86 | 0 | 0.0 | 0.0 | 04 | 4.2 | 26 |  | 0.0 | 0.0 | 13.2 | 24 |  | 0.0 | 0.0 | 14.2 |
|  | $>40.0$ | 86 | 0 | 0.0 | 0.04 | 4.2 | 86 | 0 | 0.0 | 0.0 | 04 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$N=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for axillary route

Table 8.101 Number and percentage of subjects who reported temperature by half degree measured via tympanic route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type | N | n \% |  | LL | UL N | N | n \% | \% L | LL | UL | N | n \% | \% LL | LL U | UL | N |  |  |  |  |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 86 | 00. | 0.00. | 0.0 | 4.2 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 |  | 0.014 | 14.2 |
|  | $\geq 35.5$ | 86 | 00. | 0.00. | 0.0 | 4.28 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 |  | 0.014 | 14.2 |
|  | >36.0 | 86 | 00. | 0.00. | 0.0 | 4.2 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 |  | 0.0 | 14.2 |
|  | >36.5 | 86 | 00. | 0.00. | 0.0 | 4.28 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 |  | 0.014 | 14.2 |
|  | >37.0 | 86 |  | 0.00. | 0.0 | 4.28 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 |  | 0.014 | 14.2 |
|  | >37.5 | 86 |  | 0.00. | 0.0 | 4.2 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 |  | 0.014 | 14.2 |
|  | >38.0 | 86 |  | 0.00. | 0.0 | 4.28 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 |  | 0.014 | 14.2 |
|  | >38.5 | 86 |  | 0.00. | 0.0 | 4.2 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 |  | 0.014 | 14.2 |
|  | >39.0 | 86 | 00. | 0.00. | 0.0 | 4.2 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 |  | 0.014 | 14.2 |
|  | >39.5 | 86 | 00. | 0.00. | 0.0 | 4.28 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 |  | 0.014 | 14.2 |
|  | $>40.0$ | 86 | 00. | 0.00. | 0.0 | 4.28 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 |  | 0.014 | 14.2 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 73 |  | 0.00. | 0.0 | 4.98 | 82 |  | 0.00 | 0.0 | 4.4 | 24 |  | 4.20. | 0.12 | 21.1 | 220 | 00.0 |  | 0.0 | 5.4 |
|  | $\geq 35.5$ | 73 |  | 0.00. | 0.0 | 4.98 | 82 |  | 0.00 | 0.0 | 4.4 | 24 |  | 4.20. | 0.12 | 21.1 | 220 | 00.0 |  | 0.0 | 15.4 |
|  | >36.0 | 73 |  | 0.00. | 0.0 | 4.98 | 82 |  | 0.00 | 0.0 | 4.4 | 24 | 14.2 | 4.20. | 0.12 | 21.1 | 220 | 00.0 |  | 0.0 | 15.4 |
|  | $>36.5$ | 73 |  | 0.00. | 0.0 | 4.982 | 82 | 00. | 0.00 | 0.0 | 4.4 | 24 |  | 4.20. | 0.12 | 21.1 | 220 | 00.0 |  | 0.0 | 15.4 |
|  | >37.0 | 73 |  | 0.00. | 0.0 | 4.98 | 82 | 00. | 0.00 | 0.0 | 4.4 | 24 | 14.2 | 4.20. | 0.121 | 21.1 | 220 | 00.0 |  | 0.01 | 15.4 |
|  | >37.5 | 73 |  | 0.00. | 0.0 | 4.98 | 82 |  | 0.00 | 0.0 | 4.4 | 24 | 00. | 0.00 .0 | 0.014 | 14.2 | 220 | 00.0 |  | 0.01 | 15.4 |
|  | >38.0 | 73 |  | 0.00. | 0.0 | 4.98 | 82 |  | 0.00 | 0.0 | 4.4 | 24 | 00. | 0.00 .0 | 0.014 | 14.2 | 220 | 00.0 |  | 0.0 | 15.4 |
|  | >38.5 | 73 |  | 0.00. | 0.0 | 4.98 | 82 |  | 0.00 | 0.0 | 4.4 | 24 | 00. | 0.00 .0 | 0.014 | 14.2 | 220 | 00.0 |  | 0.0 | 15.4 |
|  | $>39.0$ | 73 | 00. | 0.00. | 0.04 | 4.98 | 82 | 00. | 0.00 | 0.0 | 4.4 | 24 | 00. | 0.00 .0 | 0.014 | 14.2 | 220 | 00.0 |  | 0.015 | 15.4 |
|  | >39.5 7 | 73 | 00. | 0.00. | 0.04 | 4.98 | 82 | 00. | 0.00 | 0.0 | 4.4 | 24 | 00. | 0.00 .0 | 0.014 | 14.2 | 220 | 00.0 |  | 0.015 | 15.4 |
|  | >40.0 | 73 | 00. | 0.00. | 0.04 | 4.98 | 82 |  | 0.00 | 0.0 | 4.4 | 24 | 00. | 0.00 .0 | 0.014 | 14.2 | 220 |  |  | 0.0 | 15.4 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 159 | 00. | 0.00. | 0.02 | 2.3 | 168 | 00. | 0.00 | 0.0 | 2.2 | 50 |  | 2.00. | 0.110 | 10.6 | 460 | 00.0 |  | 0.07 | 7.7 |
|  | $\geq 35.5$ | 159 | 00. | 0.00. | 0.02 | 2.3 | 168 | 00. | 0.00 | 0.0 | 2.2 | 50 |  | 2.00. | 0.110 | 10.6 | 460 | 00.0 |  | 0.07 | 7.7 |
|  | >36.0 | 159 | 00. | 0.00. | 0.02 | 2.3 | 168 | 00. | 0.00 | 0.0 | 2.2 | 50 |  | 2.00. | 0.110 | 10.6 | 460 | 00.0 |  | 0.07 | 7.7 |
|  | >36.5 | 159 | 00. | 0.00. | 0.02 | 2.3 | 168 |  | 0.00 | 0.0 | 2.2 | 50 |  | 2.00. | 0.110 | 10.6 | 460 | 00.0 |  | 0.0 | 7.7 |
|  | >37.0 | 159 | 00. | 0.00. | 0.02 | 2.3 | 168 | 00. | 0.00 | 0.0 | 2.2 | 50 |  | 2.00. | 0.110 | 10.6 | 460 | 00.0 |  | 0.0 | 7.7 |
|  | >37.5 | 159 |  | 0.00. | 0.02 | 2.3 | 168 |  | 0.00 | 0.0 | 2.2 | 50 | 00. | 0.00 .0 | 0.07. | 7.1 | 460 | 00.0 |  | 0.0 | 7.7 |
|  | >38.0 | 159 | 00. | 0.00. | 0.02 | 2.3 | 168 | 00. | 0.00 | 0.0 | 2.2 | 50 | 00. | 0.00 .0 | 0.07. | 7.1 | 460 | 00.0 | 00.0 | 0.0 | 7.7 |
|  | >38.5 | 159 | 00. | 0.00. | 0.02 | 2.3 | 168 | 00. | 0.00 | 0.0 | 2.2 | 50 | 00. | 0.00 .0 | 0.07. | 7.1 | 460 | 00.0 |  | 0.0 | 7.7 |
|  | >39.0 | 159 | 00. | 0.00. | 0.02 | 2.3 | 168 | 00. | 0.00 | 0.0 | 2.2 | 50 | 00. | 0.00 .0 | 0.07. | 7.1 | 460 | 00.0 | 00.0 | 0.0 | 7.7 |
|  | >39.5 | 159 | 00. | 0.00. | 0.02 | 2.3 | 168 |  | 0.00 | 0.0 | 2.2 | 50 | 00. | 0.00 .0 | 0.07. | 7.1 | 460 | 00.0 | 00.0 | 0.0 | 7.7 |
|  | >40.0 | 159 | 00. | 0.00. | 0.02 | 2.31 | 168 |  | 0.00 | 0.0 | 2.2 | 50 | 00. | 0.00 .0 | 0.07. | 7.1 | 460 | 00.0 |  | 0.0 | 7.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 86 | 00. | 0.00. | 0.04 | 4.28 | 86 |  | 0.00 | 0.0 | 4.2 | 26 |  | 3.80. | 0.119 | 19.6 | 24 | 00.0 | 00.0 | 0.01 | 14.2 |
|  | $\geq 35.5$ | 86 | 00. | 0.00. | 0.04 | 4.28 | 86 |  | 0.00 | 0.0 | 4.2 | 26 | 13.8 | 3.80. | 0.119 | 19.6 | 240 | 00.0 | 00.0 | 0.014 | 14.2 |
|  | >36.0 | 86 | 00. | 0.00. | 0.04 | 4.28 | 86 |  | 0.00 | 0.0 | 4.2 | 26 | 13.8 | 3.80. | 0.119 | 19.6 | 240 | 00.0 | 00.0 | 0.014 | 14.2 |
|  | >36.5 | 86 | 00. | 0.00. | 0.04 | 4.28 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 13.8 | 3.80. | 0.119 | 19.6 | 240 | 00.0 | 00.0 | 0.014 | 14.2 |
|  | >37.0 | 86 | 00. | 0.00. | 0.04 | 4.2 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 13. | 3.80. | 0.119 | 19.6 | 240 | 00.0 | 00.0 | 0.014 | 14.2 |
|  | $>37.5$ | 86 | 00. | 0.00. | 0.04 | 4.28 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 | 00.0 | 0.01 | 14.2 |
|  | $>38.0$ | 86 | 00. | 0.00. | 0.04 | 4.28 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 | 00.0 | 0.014 | 14.2 |
|  | $>38.5$ | 86 | 00. | 0.00. | 0.04 | 4.28 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 | 00.0 | 0.014 | 14.2 |
|  | >39.0 | 86 | 00. | 0.00. | 0.04 | 4.28 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 | 00.0 | 00.0 | 0.014 | 14.2 |
|  | >39.5 | 86 | 00. | 0.00. | 0.04 | 4.28 | 86 | 00. | 0.00 | 0.0 | 4.2 | 26 | 00. | 0.00 .0 | 0.013 | 13.2 | 240 |  |  | 0.014 | 14.2 |


|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  | Placebo |  |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% Cl |  |  |  | 95 \% Cl |  |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type | N | n \% | LL | UL | N |  | n \% |  | LL | UL | N | n | \% | LL | UL | N |  | \% | LL | UL |
|  | >40.0 | 86 | 00.0 | 0.0 | 4.2 | 86 |  | 00.0 | 0 | 0.0 | 4.2 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | O | 0.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; $\mathrm{LL}=$ lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for tympanic route
Table 8.102 Number and percentage of subjects who reported temperature by half degree measured via rectal route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) by PreChemo/OnChemo groups (Total Vaccinated Cohort)

No records exist in this table

Table 8.103 Number of days with grade 3 local symptoms during the solicited post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Pain | Dose 1 | PreChemo | HZ/su | 8 | 1.1 | 1.0 | 1.0 | 1.0 | 1.0 | 2.0 |
|  | Dose 2 | PreChemo | HZ/su | 3 | 2.3 | 1.0 | 1.0 | 3.0 | 3.0 | 3.0 |
|  |  | OnChemo | HZ/su | 1 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
|  | Overall/dose | PreChemo | HZ/su | 11 | 1.5 | 1.0 | 1.0 | 1.0 | 2.0 | 3.0 |
|  |  | OnChemo | HZ/su | 1 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
| Redness | Dose 1 | PreChemo | HZ/su | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | PreChemo | HZ/su |  | 1.0 | 1.0 |  | 1.0 |  | 1.0 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.104 Number of days with grade 3 general symptoms during the solicited post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Fatigue | Dose 1 | PreChemo | HZ/su | 5 | 1.8 | 1.0 | 1.0 | 1.0 | 2.0 | 4.0 |
|  |  |  | Placebo | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  | OnChemo | HZ/su | 5 | 2.4 | 1.0 | 2.0 | 2.0 | 3.0 | 4.0 |
|  |  |  | Placebo | 2 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  | Dose 2 | PreChemo | HZ/su | 5 | 2.6 | 1.0 | 1.0 | 2.0 | 2.0 | 7.0 |
|  |  |  | Placebo | 5 | 2.0 | 1.0 | 1.0 | 1.0 | 3.0 | 4.0 |
|  |  | OnChemo | HZ/su | 4 | 4.0 | 2.0 | 2.5 | 3.5 | 5.5 | 7.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | PreChemo | HZ/su | 10 | 2.2 | 1.0 | 1.0 | 1.5 | 2.0 | 7.0 |
|  |  |  | Placebo | 6 | 2.0 | 1.0 | 1.0 | 1.5 | 3.0 | 4.0 |
|  |  | OnChemo | HZ/su | 9 | 3.1 | 1.0 | 2.0 | 3.0 | 4.0 | 7.0 |
|  |  |  | Placebo | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
| Gastrointestinal symptoms | Dose 1 | PreChemo | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  |  | OnChemo | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
|  | Dose 2 | PreChemo | HZ/su | 4 | 2.3 | 1.0 | 1.5 | 2.0 | 3.0 | 4.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | OnChemo | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 2.5 | 1.0 | 1.0 | 2.5 | 4.0 | 4.0 |
|  | Overall/dose | PreChemo | HZ/su | 5 | 2.2 | 1.0 | 2.0 | 2.0 | 2.0 | 4.0 |
|  |  |  | Placebo | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
|  |  | OnChemo | HZ/su | 2 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 4 | 2.8 | 1.0 | 2.0 | 3.0 | 3.5 | 4.0 |
| Headache | Dose 1 | PreChemo | HZ/su | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  |  | OnChemo | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Dose 2 | PreChemo | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | OnChemo | HZ/su | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | PreChemo | HZ/su | 5 | 1.6 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | OnChemo | HZ/su | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Myalgia | Dose 1 | PreChemo | HZ/su | 6 | 2.2 | 1.0 | 1.0 | 1.5 | 2.0 | 6.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | OnChemo | HZ/su | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  |  | Placebo | 2 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
|  | Dose 2 | PreChemo | HZ/su | 2 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 1 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 |
|  |  | OnChemo | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  | Overall/dose | PreChemo | HZ/su | 8 | 2.1 | 1.0 | 1.0 | 2.0 | 2.0 | 6.0 |
|  |  |  | Placebo | 2 | 3.0 | 1.0 | 1.0 | 3.0 | 5.0 | 5.0 |
|  |  | OnChemo | HZ/su | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
|  |  |  | Placebo | 2 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
| Shivering | Dose 1 | PreChemo | HZ/su | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | OnChemo | HZ/su | 2 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  | Dose 2 | PreChemo | HZ/su | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | OnChemo | HZ/su | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | PreChemo | HZ/su | 5 | 1.2 | 1.0 | 1.0 | 1.0 | 1.0 | 2.0 |


| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  |  |  | Placebo | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  | OnChemo | HZ/su | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |  |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.105 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=91 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |  |
|  |  | 95\% CI |  |  |  | - $95 \% \mathrm{Cl}$ |  |  |  |  | 95\% CI |  |  | 95\% Cl |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% L | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 74 | 82.27 | 72.7 | 89.5 | 81 | 89.0 | 80.7 | 94.6 | 26 | 96.3 | 81.0 | 99.9 | 22 | 91.7 | 73.0 | 99.0 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 4 | 4.41 | 1.2 | 11.0 | 5 | 5.5 | 1.8 | 12.4 | 1 | 3.7 | 0.1 | 19.0 | 1 | 4.2 | 0.1 | 21.1 |
|  | Febrile neutropenia (10016288) | 2 | 2.20 | 0.3 | 7.8 | 1 | 1.1 | 0.0 | 6.0 | 2 | 7.4 | 0.9 | 24.3 | 1 | 4.2 | 0.1 | 21.1 |
|  | Iron deficiency anaemia (10022972) | 1 | 1.10 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Leukocytosis (10024378) | 1 | 1.10 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.80 | 0 | 0.0 | 0.0 | 14.2 |
|  | Leukopenia (10024384) | 1 | 1.10 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.80 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lymphopenia (10025327) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neutropenia (10029354) | 10 | 11.15 | 5.5 | 19.5 | 12 | 13.2 | 7.0 | 21.9 | 1 | 3.7 | 0.1 | 19.0 | 3 | 12.5 | 2.7 | 32.4 |
|  | Thrombocytopenia (10043554) | 5 | 5.61 | 1.8 | 12.5 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Cardiac disorders (10007541) | Palpitations (10033557) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Tachycardia (10043071) | 2 | 2.2 | 0.3 | 7.8 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 1 | 1.10 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Tinnitus (10043882) | 1 | 1.10 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 2 | 8.3 | 1.0 | 27.0 |
| Eye disorders (10015919) | Eye discharge (10015915) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Eye irritation (10015946) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Eye swelling (10015967) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lacrimation increased (10023644) | 1 | 1.10 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 2 | 7.4 | 0.9 | 24.3 | 1 | 4.2 | 0.1 | 21.1 |
|  | Myopia (10028651) | 1 | 1.10 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Visual acuity reduced (10047531) | 1 | 1.10 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.80 | 0 | 0.0 | 0.0 | 14.2 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 1 | 1.10 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Abdominal pain (10000081) | 2 | 2.20 | 0.3 | 7.8 | 1 | 1.1 | 0.0 | 6.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Abdominal pain upper (10000087) | 3 | 3.30 | 0.7 | 9.4 | 3 | 3.3 | 0.7 | 9.3 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Aerophagia (10052813) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Aphthous ulcer (10002959) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Constipation (10010774) | 11 | 12.2 | 6.3 | 20.8 | 10 | 11.0 | 5.4 | 19.3 | 5 | 18.5 | 6.3 | 38.12 | 2 | 8.3 | 1.0 | 27.0 |
|  | Diarrhoea (10012735) | 8 | 8.9 | 3.9 | 16.8 | 7 | 7.7 | 3.1 | 15.2 | 1 | 3.7 | 0.1 | 19.0 | 3 | 12.5 | 2.7 | 32.4 |

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116427 (ZOSTER-028)
Report Final

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | Placebo$N=91$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | Placebo$N=24$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Dry mouth (10013781) | 1 | 1.1 | 0.0 | 6.0 | 2 | 2.2 | 0.3 | 7.7 | 1 | 3.7 | 0.1 | 19.0 | 1 | 4.2 | 0.1 | 21.1 |
|  | Dyspepsia (10013946) | 5 | 5.6 | 1.8 | 12.5 | 8 | 8.8 | 3.9 | 16.6 | 1 | 3.7 | 0.1 | 19.0 | 5 | 20.8 | 7.1 | 42.2 |
|  | Dysphagia (10013950) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Epigastric discomfort (10053155) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Flatulence (10016766) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Gastrointestinal disorder (10017944) | 1 | 1.1 | 0.0 | 6.0 | 3 | 3.3 | 0.7 | 9.3 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Gastrointestinal pain (10017999) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Gastrooesophageal reflux disease (10017885) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 2 | 7.4 | 0.9 | 24.3 | 0 | 0.0 | 0.0 | 14.2 |
|  | Gingival pain (10018286) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Glossitis (10018386) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Haemorrhoidal haemorrhage (10054787) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Haemorrhoids (10019022) | 1 | 1.1 | 0.0 | 6.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hiatus hernia (10020028) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 2 | 8.3 | 1.0 | 27.0 |
|  | Nausea (10028813) | 23 | 25.6 | 16.9 | 35.8 | 23 | 25.3 | 16.7 | 35.5 | 8 | 29.6 | 13.8 | 50.2 | 5 | 20.8 | 7.1 | 42.2 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 2 | 8.3 | 1.0 | 27.0 |
|  | Oesophagitis (10030216) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oral pain (10031009) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Proctalgia (10036772) | 0 | 0.0 | 0.0 | 4.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Rectal tenesmus (10057071) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Stomatitis (10042128) | 2 | 2.2 | 0.3 | 7.8 | 1 | 1.1 | 0.0 | 6.0 | 2 | 7.4 | 0.9 | 24.3 | 1 | 4.2 | 0.1 | 21.1 |
|  | Swollen tongue (10042727) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Vomiting (10047700) | 6 | 6.7 | 2.5 | 13.9 | 12 | 13.2 | 7.0 | 21.9 | 4 | 14.8 | 4.2 | 33.7 | 2 | 8.3 | 1.0 | 27.0 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 23 | 25.6 | 16.9 | 35.8 | 25 | 27.5 | 18.6 | 37.8 | 7 | 25.9 | 11.1 | 46.3 | 3 | 12.5 | 2.7 | 32.4 |
|  | Axillary pain (10048750) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Catheter site pain (10052268) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Chest pain (10008479) | 2 | 2.2 | 0.3 | 7.8 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Chills (10008531) | 1 | 1.1 | 0.0 | 6.0 | O | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Fatigue (10016256) | 2 | 2.2 | 0.3 | 7.8 | 5 | 5.5 | 1.8 | 12.4 | 2 | 7.4 | 0.9 | 24.3 | 1 | 4.2 | 0.1 | 21.1 |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.0 | 4.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | Placebo$N=91$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | Placebo$N=24$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Generalised oedema (10018092) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Inflammation (10061218) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Influenza like illness (10022004) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.0 | 4.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Injection site pruritus (10022093) | 2 | 2.2 | 0.3 | 7.8 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Malaise (10025482) | 3 | 3.3 | 0.7 | 9.4 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Mucosal dryness (10028111) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Mucosal inflammation (10028116) | 6 | 6.7 | 2.5 | 13.9 | 5 | 5.5 | 1.8 | 12.4 | 4 | 14.8 | 4.2 | 33.7 | 1 | 4.2 | 0.1 | 21.1 |
|  | Oedema peripheral (10030124) | 3 | 3.3 | 0.7 | 9.4 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pain (10033371) | 2 | 2.2 | 0.3 | 7.8 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Peripheral swelling (10048959) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pyrexia (10037660) | 2 | 2.2 | 0.3 | 7.8 | 4 | 4.4 | 1.2 | 10.9 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Temperature intolerance (10057040) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hepatic steatosis (10019708) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hepatomegaly (10019842) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hyperbilirubinaemia (10020578) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 1 | 1.1 | 0.0 | 6.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypersensitivity (10020751) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Seasonal allergy (10048908) | 0 | 0.0 | 0.0 | 4.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Bacterial infection (10060945) | 2 | 2.2 | 0.3 | 7.8 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Bronchitis (10006451) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 4.0 | 2 | 2.2 | 0.3 | 7.7 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Cystitis (10011781) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Erysipelas (10015145) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Folliculitis (10016936) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=91 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=24 \end{gathered}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Gastroenteritis (10017888) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Gingivitis (10018292) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Herpes zoster (10019974) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Infection (10021789) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Influenza (10022000) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.80 | 0 | 0.0 | 0.0 | 14.2 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.80 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Nasopharyngitis (10028810) | 2 | 2.2 | 0.3 | 7.8 | 1 | 1.1 | 0.0 | 6.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neutropenic sepsis (10049151) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oral fungal infection (10061324) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oral herpes (10067152) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oral infection (10048685) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.80 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pneumonia (10035664) | 2 | 2.2 | 0.3 | 7.8 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Post procedural infection (10067268) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 1 | 4.2 | 0.1 | 21.1 |
|  | Respiratory tract infection (10062352) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Sepsis (10040047) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Sinusitis (10040753) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Upper respiratory tract infection (10046306) | 3 | 3.3 | 0.7 | 9.4 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urinary tract infection (10046571) | 0 | 0.0 | 0.0 | 4.0 | 3 | 3.3 | 0.7 | 9.3 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Injury, poisoning and procedural complications (10022117) | Arthropod bite (10003399) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.80 | 0 | 0.0 | 0.0 | 14.2 |
|  | Gastrostomy failure (10050056) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Ligament sprain (10024453) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Post procedural complication (10058046) | 2 | 2.2 | 0.3 | 7.8 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 2 | 8.3 | 1.0 | 27.0 |
|  | Post procedural diarrhoea (10057585) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Radiation skin injury (10063562) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.82 | 2 | 8.3 | 1.0 | 27.0 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.80 | 0 | 0.0 | 0.0 | 14.2 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.80 | 0 | 0.0 | 0.0 | 14.2 |

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|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | Placebo$N=91$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=97 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |  |
|  |  | 95\% Cl |  |  |  | N $\quad 95 \%$ CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| Investigations (10022891) | Blood iron decreased (10005619) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Body temperature fluctuation (10063488) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Haemoglobin decreased (10018884) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Platelet count decreased (10035528) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Weight decreased (10047895) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Weight increased (10047899) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | - | 0.0 | 0.0 | 14.2 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) | 8 | 8.9 | 3.9 | 16.8 | 3 | 3.3 | 0.7 | 9.3 | 1 | 3.7 | 0.1 | 19.0 | 2 | 8.3 | 1.0 | 27.0 |
|  | Hypercholesterolaemia (10020603) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hyperglycaemia (10020635) | 2 | 2.2 | 0.3 | 7.8 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypocalcaemia (10020947) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Iron deficiency (10022970) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 3 | 3.3 | 0.7 | 9.4 | 3 | 3.3 | 0.7 | 9.3 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Back pain (10003988) | 2 | 2.2 | 0.3 | 7.8 | 2 | 2.2 | 0.3 | 7.7 | 1 | 3.7 | 0.1 | 19.0 |  | 0.0 | 0.0 | 14.2 |
|  | Bone pain (10006002) | 4 | 4.4 | 1.2 | 11.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Groin pain (10018735) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Muscle contracture (10062575) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Muscle spasms (10028334) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Musculoskeletal discomfort (10053156) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Musculoskeletal pain (10028391) | 2 | 2.2 | 0.3 | 7.8 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Musculoskeletal stiffness (10052904) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Myalgia (10028411) | 5 | 5.6 | 1.8 | 12.5 | 5 | 5.5 | 1.8 | 12.4 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neck pain (10028836) | 2 | 2.2 | 0.3 | 7.8 | 1 | 1.1 | 0.0 | 6.0 | 1 | 3.7 | 0.1 | 19.0 | - | 0.0 | 0.0 | 14.2 |
|  | Osteoarthritis (10031161) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | - | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pain in extremity (10033425) | 2 | 2.2 | 0.3 | 7.8 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 1.1 | 0.0 | 6.0 | - | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Prostate cancer (10060862) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 3 | 3.3 | 0.7 | 9.4 | 3 | 3.3 | 0.7 | 9.3 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=91 \end{gathered}$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=24 \end{gathered}$ |  |  |  |
|  |  | 95\% CI |  |  |  | - $95 \% \mathrm{Cl}$ |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Dizziness postural (10013578) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Dysaesthesia (10013886) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Dysgeusia (10013911) | 0 | 0.0 | 0.0 | 4.0 | 4 | 4.4 | 1.2 | 10.9 | 1 | 3.7 | 0.1 | 19.0 | 2 | 8.3 | 1.0 | 27.0 |
|  | Headache (10019211) | 3 | 3.3 | 0.7 | 9.4 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Hepatic encephalopathy (10019660) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypoaesthesia (10020937) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lethargy (10024264) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Motor dysfunction (10061296) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Muscle contractions involuntary (10028293) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neuropathy peripheral (10029331) | 2 | 2.2 | 0.3 | 7.8 | 3 | 3.3 | 0.7 | 9.3 | 3 | 11.1 | 2.4 | 29.2 | 1 | 4.2 | 0.1 | 21.1 |
|  | Neurotoxicity (10029350) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Paraesthesia (10033775) | 3 | 3.3 | 0.7 | 9.4 | 3 | 3.3 | 0.7 | 9.3 | 2 | 7.4 | 0.9 | 24.3 | 1 | 4.2 | 0.1 | 21.1 |
|  | Paresis (10033985) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Peripheral sensory neuropathy (10034620) | 2 | 2.2 | 0.3 | 7.8 | 3 | 3.3 | 0.7 | 9.3 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Syncope (10042772) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Tremor (10044565) | 0 | 0.0 | 0.0 | 4.0 | 2 | 2.2 | 0.3 | 7.7 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
| Psychiatric disorders (10037175) | Aggression (10001488) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Anxiety (10002855) | 4 | 4.4 | 1.2 | 11.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Depression (10012378) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Insomnia (10022437) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 3 | 11.1 | 2.4 | 29.2 | 2 | 8.3 | 1.0 | 27.0 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Bladder spasm (10048994) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Chronic kidney disease (10064848) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Dysuria (10013990) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Renal impairment (10062237) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urinary retention (10046555) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Reproductive system and breast disorders (10038604) | Oedema genital (10030104) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Asthma (10003553) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Catarrh (10007774) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=91 \end{gathered}$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=24 \end{gathered}$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Cough (10011224) | 3 | 3.3 | 0.7 | 9.4 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Dysaesthesia pharynx (10062665) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Dysphonia (10013952) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Dyspnoea (10013968) | 1 | 1.1 | 0.0 | 6.0 | 2 | 2.2 | 0.3 | 7.7 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Epistaxis (10015090) | 2 | 2.2 | 0.3 | 7.8 | 4 | 4.4 | 1.2 | 10.9 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Haemoptysis (10018964) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hiccups (10020039) | 1 | 1.1 | 0.0 | 6.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Nasal congestion (10028735) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oropharyngeal discomfort (10068318) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oropharyngeal pain (10068319) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pulmonary embolism (10037377) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 16 | 17.8 | 10.5 | 27.3 | 17 | 18.7 | 11.3 | 28.2 | 5 | 18.5 | 6.3 | 38.1 | 6 | 25.0 | 9.8 | 46.7 |
|  | Dermatitis (10012431) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Dry skin (10013786) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Erythema (10015150) | 4 | 4.4 | 1.2 | 11.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Nail dystrophy (10028698) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Onychalgia (10064251) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Palmar-plantar erythrodysaesthesia syndrome (10033553) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pruritus (10037087) | 0 | 0.0 | 0.0 | 4.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 2 | 8.3 | 1.0 | 27.0 |
|  | Pruritus generalised (10052576) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Rash (10037844) | 1 | 1.1 | 0.0 | 6.0 | 4 | 4.4 | 1.2 | 10.9 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Rash macular (10037867) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Scar pain (10049002) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Skin disorder (10040831) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Swelling face (10042682) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urticaria (10046735) | 2 | 2.2 | 0.3 | 7.8 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

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|  |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =90 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { cebc } \\ & =91 \end{aligned}$ |  |  |  | $\begin{aligned} & \mathrm{Z} / \mathrm{su} \\ & -20 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { aceb } \\ & =24 \end{aligned}$ |  |
|  |  |  |  |  | CI |  |  |  | Cl |  |  |  | Cl |  |  |  | \% CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| Social circumstances (10041244) | Menopause (10027308) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Haematoma (10018852) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hot flush (10060800) | 0 | 0.0 | 0.0 | 4.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypotension (10021097) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lymphocele (10048642) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Phlebitis (10034879) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Thrombosis (10043607) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Vascular pain (10047095) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
n/\% = number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{CI}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.106 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the $\mathbf{3 0}$-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{gathered} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=166 \end{gathered}$ |  |  |  | Placebo$N=178$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | Placebo$N=47$ |  |  |  |
|  |  | 95\% CI |  |  |  | N $95 \% \mathrm{Cl}$ |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 113 | 68.1 | 60.4 | 75.1 | 132 | 74.2 | 67.1 | 80.4 | 40 | 78.4 | 64.7 | 88.7 | 34 | 72.3 | 57.4 | 84.4 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 4 | 2.4 | 0.7 | 6.1 | 5 | 2.8 | 0.9 | 6.4 | 1 | 2.0 | 0.0 | 10.4 | 1 | 2.1 | 0.1 | 11.3 |
|  | Febrile neutropenia (10016288) | 2 | 1.2 | 0.1 | 4.3 | 1 | 0.6 | 0.0 | 3.1 | 2 | 3.9 | 0.5 | 13.5 | 2 | 4.3 | 0.5 | 14.5 |
|  | Iron deficiency anaemia (10022972) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Leukocytosis (10024378) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Leukopenia (10024384) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | - | 0.0 | 0.0 | 7.5 |
|  | Lymphopenia (10025327) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Neutropenia (10029354) | 11 | 6.6 | 3.4 | 11.5 | 13 | 7.3 | 3.9 | 12.2 | 1 | 2.0 | 0.0 | 10.4 | 4 | 8.5 | 2.4 | 20.4 |
|  | Thrombocytopenia (10043554) | 6 | 3.6 | 1.3 | 7.7 | 3 | 1.7 | 0.3 | 4.8 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
| Cardiac disorders (10007541) | Palpitations (10033557) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 |  | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Tachycardia (10043071) | 2 | 1.2 | 0.1 | 4.3 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Tinnitus (10043882) | 1 | 0.6 | 0.0 | 3.3 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 2 | 4.3 | 0.5 | 14.5 |
| Eye disorders (10015919) | Eye discharge (10015915) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Eye irritation (10015946) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Eye swelling (10015967) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Lacrimation increased (10023644) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 2 | 3.9 | 0.5 | 13.5 | 1 | 2.1 | 0.1 | 11.3 |
|  | Myopia (10028651) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Visual acuity reduced (10047531) | 1 | 0.6 | 0.0 | 3.3 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Abdominal pain (10000081) | 2 | 1.2 | 0.1 | 4.3 | 1 | 0.6 | 0.0 | 3.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Abdominal pain upper (10000087) | 3 | 1.8 | 0.4 | 5.2 | 3 | 1.7 | 0.3 | 4.8 | 2 | 3.9 | 0.5 | 13.5 | 0 | 0.0 | 0.0 | 7.5 |
|  | Aerophagia (10052813) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Aphthous ulcer (10002959) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Constipation (10010774) | 13 | 7.8 | 4.2 | 13.0 | 10 | 5.6 | 2.7 | 10.1 | 5 | 9.8 | 3.3 | 21.4 | 2 | 4.3 | 0.5 | 14.5 |
|  | Diarrhoea (10012735) | 10 | 6.0 | 2.9 | 10.8 | 7 | 3.9 | 1.6 | 7.9 | 1 | 2.0 | 0.0 | 10.4 | 3 | 6.4 | 1.3 | 17.5 |

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Report Final

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=166 \end{aligned}$ |  |  |  | Placebo$N=178$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  |  | Placebo$N=47$ |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.0 | 2.2 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Generalised oedema (10018092) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Inflammation (10061218) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Influenza like illness (10022004) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.0 | 2.2 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Injection site pruritus (10022093) | 2 | 1.2 | 0.1 | 4.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Malaise (10025482) | 4 | 2.4 | 0.7 | 6.1 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Mucosal dryness (10028111) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Mucosal inflammation (10028116) | 7 | 4.2 | 1.7 | 8.5 | 6 | 3.4 | 1.2 | 7.2 | 4 | 7.8 | 2.2 | 18.9 | 2 | 4.3 | 0.5 | 14.5 |
|  | Oedema peripheral (10030124) | 3 | 1.8 | 0.4 | 5.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Pain (10033371) | 2 | 1.2 | 0.1 | 4.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Peripheral swelling (10048959) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Pyrexia (10037660) | 2 | 1.2 | 0.1 | 4.3 |  | 2.2 | 0.6 | 5.7 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Temperature intolerance (10057040) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hepatic steatosis (10019708) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hepatomegaly (10019842) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hyperbilirubinaemia (10020578) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 1 | 0.6 | 0.0 | 3.3 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hypersensitivity (10020751) | 1 | 0.6 | 0.0 | 3.3 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Seasonal allergy (10048908) | 0 | 0.0 | 0.0 | 2.2 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Bacterial infection (10060945) | 2 | 1.2 | 0.1 | 4.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Bronchitis (10006451) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 2.2 | 2 | 1.1 | 0.1 | 4.0 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Cystitis (10011781) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Erysipelas (10015145) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=166 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=178 \end{aligned}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | Placebo$N=47$ |  |  |  |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Folliculitis (10016936) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Gastroenteritis (10017888) | 1 | 0.6 | 0.0 | 3.3 | 1 | 0.6 | 0.0 | 3.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Gingivitis (10018292) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Herpes zoster (10019974) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Infection (10021789) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Influenza (10022000) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Nasopharyngitis (10028810) | 2 | 1.2 | 0.1 | 4.3 | 1 | 0.6 | 0.0 | 3.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Neutropenic sepsis (10049151) | 1 | 0.6 | 0.0 | 3.3 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oral fungal infection (10061324) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oral herpes (10067152) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oral infection (10048685) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Pneumonia (10035664) | 2 | 1.2 | 0.1 | 4.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Post procedural infection (10067268) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 1 | 2.1 | 0.1 | 11.3 |
|  | Respiratory tract infection (10062352) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Sepsis (10040047) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Sinusitis (10040753) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Upper respiratory tract infection (10046306) | 3 | 1.8 | 0.4 | 5.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Urinary tract infection (10046571) | 0 | 0.0 | 0.0 | 2.2 | 3 | 1.7 | 0.3 | 4.8 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Injury, poisoning and procedural complications (10022117) | Arthropod bite (10003399) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Gastrostomy failure (10050056) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Ligament sprain (10024453) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Post procedural complication (10058046) | 2 | 1.2 | 0.1 | 4.3 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 2 | 4.3 | 0.5 | 14.5 |
|  | Post procedural diarrhoea (10057585) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 2 | 3.9 | 0.5 | 13.5 | 0 | 0.0 | 0.0 | 7.5 |
|  | Radiation skin injury (10063562) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 2 | 4.3 | 0.5 | 14.5 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=166 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=178 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | Placebo$N=47$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | -95\% CI |  |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Investigations (10022891) | Blood iron decreased (10005619) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Body temperature fluctuation (10063488) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Haemoglobin decreased (10018884) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Platelet count decreased (10035528) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Weight decreased (10047895) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Weight increased (10047899) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) | 9 | 5.4 | 2.5 | 10.0 | 3 | 1.7 | 0.3 | 4.8 | 2 | 3.9 | 0.5 | 13.5 | 2 | 4.3 | 0.5 | 14.5 |
|  | Hypercholesterolaemia (10020603) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hyperglycaemia (10020635) | 2 | 1.2 | 0.1 | 4.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hypocalcaemia (10020947) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Iron deficiency (10022970) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 3 | 1.8 | 0.4 | 5.2 | 3 | 1.7 | 0.3 | 4.8 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Back pain (10003988) | 2 | 1.2 | 0.1 | 4.3 | 2 | 1.1 | 0.1 | 4.0 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Bone pain (10006002) | 4 | 2.4 | 0.7 | 6.1 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Groin pain (10018735) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Muscle contracture (10062575) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Muscle spasms (10028334) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Musculoskeletal discomfort (10053156) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Musculoskeletal pain (10028391) | 2 | 1.2 | 0.1 | 4.3 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Musculoskeletal stiffness (10052904) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Myalgia (10028411) | 6 | 3.6 | 1.3 | 7.7 | 5 | 2.8 | 0.9 | 6.4 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Neck pain (10028836) | 2 | 1.2 | 0.1 | 4.3 | 1 | 0.6 | 0.0 | 3.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Osteoarthritis (10031161) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Pain in extremity (10033425) | 2 | 1.2 | 0.1 | 4.3 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Prostate cancer (10060862) | 1 | 0.6 | 0.0 | 3.3 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |

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Report Final

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=166 \end{aligned}$ |  |  |  | Placebo$N=178$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  | Placebo$N=47$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| Nervous system disorders (10029205) | Dizziness (10013573) | 3 | 1.8 | 0.4 | 5.2 | 3 | 1.7 | 0.3 | 4.8 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Dizziness postural (10013578) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Dysaesthesia (10013886) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Dysgeusia (10013911) | 0 | 0.0 | 0.0 | 2.2 | 4 | 2.2 | 0.6 | 5.7 | 1 | 2.0 | 0.0 | 10.4 | 2 | 4.3 | 0.5 | 14.5 |
|  | Headache (10019211) | 4 | 2.4 | 0.7 | 6.1 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Hepatic encephalopathy (10019660) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hypoaesthesia (10020937) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Lethargy (10024264) | 0 | 0.0 | 0.0 | 2.2 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Motor dysfunction (10061296) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 |  | 0.0 | 0.0 | 7.5 |
|  | Muscle contractions involuntary (10028293) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Neuropathy peripheral (10029331) | 2 | 1.2 | 0.1 | 4.3 | 4 | 2.2 | 0.6 | 5.7 | 3 | 5.9 | 1.2 | 16.2 | 1 | 2.1 | 0.1 | 11.3 |
|  | Neurotoxicity (10029350) | 1 | 0.6 | 0.0 | 3.3 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Paraesthesia (10033775) | 5 | 3.0 | 1.0 | 6.9 | 4 | 2.2 | 0.6 | 5.7 | 2 | 3.9 | 0.5 | 13.5 | 1 | 2.1 | 0.1 | 11.3 |
|  | Paresis (10033985) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 |  | 0.0 | 0.0 | 7.5 |
|  | Peripheral sensory neuropathy (10034620) | 2 | 1.2 | 0.1 | 4.3 | 3 | 1.7 | 0.3 | 4.8 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Syncope (10042772) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | - | 0.0 | 0.0 | 7.5 |
|  | Tremor (10044565) | 0 | 0.0 | 0.0 | 2.2 | 3 | 1.7 | 0.3 | 4.8 | 1 | 2.0 | 0.0 | 10.4 | - | 0.0 | 0.0 | 7.5 |
| Psychiatric disorders (10037175) | Aggression (10001488) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Anxiety (10002855) | 6 | 3.6 | 1.3 | 7.7 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 |  | 0.0 | 0.0 | 7.5 |
|  | Depression (10012378) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | - | 0.0 | 0.0 | 7.5 |
|  | Insomnia (10022437) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 3 | 5.9 | 1.2 | 16.2 | 2 | 4.3 | 0.5 | 14.5 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Bladder spasm (10048994) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Chronic kidney disease (10064848) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 |  | 0.0 | 0.0 | 7.5 |
|  | Dysuria (10013990) | 1 | 0.6 | 0.0 | 3.3 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 |  | 0.0 | 0.0 | 7.5 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Renal impairment (10062237) | 2 | 1.2 | 0.1 | 4.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Urinary retention (10046555) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 |  | 0.0 | 0.0 | 7.0 |  | 2.1 | 0.1 | 11.3 |
| Reproductive system and breast disorders (10038604) | Oedema genital (10030104) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |

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116427 (ZOSTER-028)
Report Final

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{gathered} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=166 \end{gathered}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=178 \end{aligned}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | Placebo$N=47$ |  |  |  |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% Cl |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| Respiratory, thoracic and mediastinal disorders (10038738) | Asthma (10003553) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Catarrh (10007774) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Cough (10011224) | 3 | 1.8 | 0.4 | 5.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Dysaesthesia pharynx (10062665) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Dysphonia (10013952) | 1 | 0.6 | 0.0 | 3.3 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Dyspnoea (10013968) | 1 | 0.6 | 0.0 | 3.3 | 2 | 1.1 | 0.1 | 4.0 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Epistaxis (10015090) | 2 | 1.2 | 0.1 | 4.3 | 4 | 2.2 | 0.6 | 5.7 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Haemoptysis (10018964) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hiccups (10020039) | 1 | 0.6 | 0.0 | 3.3 | 3 | 1.7 | 0.3 | 4.8 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Nasal congestion (10028735) | 1 | 0.6 | 0.0 | 3.3 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oropharyngeal discomfort (10068318) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oropharyngeal pain (10068319) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Pulmonary embolism (10037377) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 16 | 9.6 | 5.6 | 15.2 | 17 | 9.6 | 5.7 | 14.9 | 5 | 9.8 | 3.3 | 21.4 | 6 | 12.8 | 4.8 | 25.7 |
|  | Dermatitis (10012431) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Dry skin (10013786) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Erythema (10015150) | 5 | 3.0 | 1.0 | 6.9 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Nail dystrophy (10028698) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Onychalgia (10064251) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Palmar-plantar erythrodysaesthesia syndrome (10033553) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Pruritus (10037087) | 0 | 0.0 | 0.0 | 2.2 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 2 | 4.3 | 0.5 | 14.5 |
|  | Pruritus generalised (10052576) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Rash (10037844) | 1 | 0.6 | 0.0 | 3.3 | 4 | 2.2 | 0.6 | 5.7 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Rash macular (10037867) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 |  | 2.1 | 0.1 | 11.3 |
|  | Scar pain (10049002) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Skin disorder (10040831) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |



PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
$n / \%=$ number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.107 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30 -day (Days $0-29$ ) post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)


|  |  | PreChemo |  |  |  |  |  | OnChemo |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  | Placebo$N=91$ |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |
|  |  | 95\% CI |  |  | 95\% CI |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL UL | n \% | \% LL | LL UL |  | \% | LL | UL | n \% | LL | UL |
|  | Renal impairment (10062237) | 1 | 1.1 | 0.06 .0 |  | 0.00 .0 | 0.04 .0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Pleural effusion (10035598) | 0 | 0.0 | 0.04 .0 |  | 1.10 .0 | 0.06 .0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Pulmonary embolism (10037377) | 1 | 1.1 | 0.06 .0 |  | 0.00 .0 | 0.04 .0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 1 | 1.1 | 0.06 .0 |  | 0.00 .0 | 0.04 .0 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.04 .0 |  | 1.10 .0 | 0.06 .0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Vascular disorders (10047065) | Lymphocele (10048642) | 0 | 0.0 | 0.04 .0 | 00.0 | . 00.0 | 0.04 .0 | 0 | 0.0 | 0.0 | 12.8 | 14.2 |  | 21.1 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.108 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the $\mathbf{3 0 - d a y}$ (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=166 \end{aligned}$ |  |  |  | Placebo$N=178$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  | $\begin{aligned} & \text { Placebo } \\ & N=47 \end{aligned}$ |  |  |
|  |  | 95\% CI |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n \% | \% | LL | UL | n \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 16 | 9.6 | 5.6 | 615.2 | 95. | 5.1 | 2.3 | 9.4 | 611.8 | 4.4 | 23.9 | 612.8 | 4.8 | 25.7 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 0 | 0.0 | 0.0 | 02.2 |  | 0.60 | 0.0 | 3.1 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Febrile neutropenia (10016288) | 2 | 1.2 | 0.1 | 14.3 |  | 0.60 | 0.0 | 3.1 | 23.9 | 0.5 | 13.5 | 12.1 | 0.1 | 11.3 |
|  | Neutropenia (10029354) | 4 | 2.4 |  | 76.1 | 31. | 1.70 | 0.3 | 4.8 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 02.2 |  | 0.0 | 0.0 | 2.1 | 00.0 | 0.0 | 7.0 | 12.1 | 0.1 | 11.3 |
| Gastrointestinal disorders (10017947) | Abdominal pain (10000081) | 1 | 0.6 | 0.0 | 03.3 |  | 0.0 | 0.0 | 2.1 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Constipation (10010774) | 0 | 0.0 | 0.0 | 02.2 | 00.0 | 0.0 | 0.0 | 2.1 | 00.0 | 0.0 | 7.0 | 12.1 | 0.1 | 11.3 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.0 | 02.2 |  | 0.6 | 0.0 | 3.1 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 0 | 0.0 | 0.0 | 02.2 |  | 0.0 | 0.0 | 2.1 | 00.0 | 0.0 | 7.0 | 12.1 | 0.1 | 11.3 |
|  | Malaise (10025482) | 0 | 0.0 | 0.0 | 02.2 |  | 0.6 | 0.0 | 3.1 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 1 | 0.6 | 0.0 | 03.3 |  | 0.0 | 0.0 | 2.1 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 02.2 |  | 0.6 | 0.0 | 3.1 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 02.2 |  | 0.0 | 0.0 | 2.1 | 12.0 | 0.0 | 10.4 | 00.0 | 0.0 | 7.5 |
|  | Nasopharyngitis (10028810) | 1 | 0.6 | 0.0 | 03.3 |  | 0.0 | 0.0 | 2.1 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Sepsis (10040047) | 1 | 0.6 | 0.0 | 03.3 |  | 0.0 | 0.0 | 2.1 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| Injury, poisoning and procedural complications (10022117) | Post procedural diarrhoea (10057585) | 0 | 0.0 | 0.0 | 02.2 |  | 0.0 | 0.0 | 2.1 | 23.9 | 0.5 | 13.5 | 00.0 | 0.0 | 7.5 |
| Investigations (10022891) | Platelet count decreased (10035528) | 1 | 0.6 | 0.0 | 03.3 |  | 0.00 | 0.0 | 2.1 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Weight increased (10047899) | 0 | 0.0 | 0.0 | 02.2 |  | 0.60 | 0.0 | 3.1 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 0.6 | 0.0 | 03.3 | 00. | 0.0 | 0.0 | 2.1 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Prostate cancer (10060862) | 0 | 0.0 | 0.0 | 02.2 |  | 0.6 | 0.0 | 3.1 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| Nervous system disorders (10029205) | Hepatic encephalopathy (10019660) | 1 | 0.6 | 0.0 | 03.3 | 00. | 0.00 | 0.0 | 2.1 | 00.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 02.2 | 00.0 | 0.0 | 0.0 | 2.1 | 12.0 | 0.0 | 10.4 | 00.0 | 0.0 | 7.5 |
| Psychiatric disorders (10037175) | Insomnia (10022437) | 0 | 0.0 | 0.0 | 02.2 | 00.0 | 0.0 | 0.0 | 2.1 | 00.0 | 0.0 | 7.0 | 12.1 | 0.1 | 11.3 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 |  | 02.2 |  | 0.6 | 0.0 | 3.1 | 00.0 |  | 7.0 | 12.1 |  | 11.3 |



PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.109 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) postvaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  | OnChemo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  | Placebo$N=91$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | Placebo$N=24$ |  |  |
|  |  |  | 95\% CI |  | 95\% Cl |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL UL | n $\%$ | LL | UL |  | \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 10 | 11.1 | 5.519 .5 | 77.7 | 3.1 | 15.2 | 0 | 0.0 | 0.0 | 12.8 | 28.3 | 1.0 | 27.0 |
| Blood and lymphatic system disorders (10005329) | Neutropenia (10029354) | 0 | 0.0 | 0.04 .0 | 00.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 1.1 | 0.06 .0 | 11.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Gastrointestinal disorders (10017947) | Swollen tongue (10042727) | 1 | 1.1 | 0.06 .0 | 00.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 2 | 2.2 | 0.37 .8 | 11.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Axillary pain (10048750) | 0 | 0.0 | 0.04 .0 | 11.10 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.04 .0 | 11.10 | 0.0 | 6.0 |  | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.04 .0 | 00.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.04 .0 | 11.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.04 .0 | 11.10 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.04 .0 | 22.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Injection site pruritus (10022093) | 2 | 2.2 | 0.37 .8 | 00.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Malaise (10025482) | 1 | 1.1 | 0.06 .0 | 00.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.04 .0 | 11.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 1 | 1.1 | 0.06 .0 | 00.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Oral herpes (10067152) | 1 | 1.1 | 0.06 .0 | 00.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.04 .0 | 11.10 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 1 | 1.1 | 0.06 .0 | 11.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 0 | 0.0 | 0.04 .0 | 11.10 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Muscle contractions involuntary (10028293) | 1 | 1.1 | 0.06 .0 | 00.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Skin and subcutaneous tissue disorders (10040785) | Erythema (10015150) | 1 | 1.1 | 0.06 .0 | 00.0 | 0.0 | 4.0 |  | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.04 .0 | 11.1 | 0.0 | 6.0 | - | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Urticaria (10046735) | 0 | 0.0 | 0.04 .0 | 11.10 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group

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116427 (ZOSTER-028)
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At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.110 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{gathered} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=166 \end{gathered}$ |  |  |  | Placebo$N=178$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | Placebo$N=47$ |  |  |
|  |  | 95\% Cl |  |  |  | 95\% CI |  |  |  | 95\% Cl |  |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n \% |  | LL | UL |  | \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 11 | 6.6 | 3.4 | 11.5 | 95. | . 12 | 2.3 | 9.4 |  | 0.0 | 0.0 | 7.0 | 24.3 | 0.5 | 514.5 |
| Blood and lymphatic system disorders (10005329) | Neutropenia (10029354) | 0 | 0.0 | 0.0 | 2.2 | 00.0 | 0 0 | 0.0 | 2.1 |  | 0.0 | 0.0 | 7.0 | 12.1 | 0.1 | 111.3 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 0.6 | 0.0 | 3.3 | 10. | . 60 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O7.5 |
| Gastrointestinal disorders (10017947) | Swollen tongue (10042727) | 1 | 0.6 | 0.0 | 3.3 | 00.0 | . 00 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O7.5 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 2 | 1.2 | 0.1 | 4.3 | 10. | . 60 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O7.5 |
|  | Axillary pain (10048750) | 0 | 0.0 | 0.0 | 2.2 | 21. | . 10 | 0.1 | 4.0 |  | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O7.5 |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.0 | 2.2 | 10. | . 60 | 0.0 | 3.1 |  | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O 7.5 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 2.2 |  | . 00 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 12.1 | 0.1 | 111.3 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.0 | 2.2 | 10. | . 60 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O7.5 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 2.2 | 10. | . 60 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O7.5 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.0 | 2.2 | 21. | . 10 | 0.1 | 4.0 |  | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O 7.5 |
|  | Injection site pruritus (10022093) | 2 | 1.2 | 0.1 | 4.3 |  | . 00 | 0.0 | 2.1 |  | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O 7.5 |
|  | Malaise (10025482) | 2 | 1.2 | 0.1 | 4.3 | 00.0 | . 00 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O 7.5 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 2.2 | 10. | . 60 | 0.0 | 3.1 |  | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O7.5 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 1 | 0.6 | 0.0 | 3.3 | 00. | . 00 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O7.5 |
|  | Oral herpes (10067152) | 1 | 0.6 | 0.0 | 3.3 |  | . 00 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O 7.5 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 2.2 | 10. | . 60 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O 7.5 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 1 | 0.6 | 0.0 | 3.3 | 10. | . 60 | 0.0 | 3.1 |  | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 07.5 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 0 | 0.0 | 0.0 | 2.2 | 10. | . 60 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O 7.5 |
|  | Muscle contractions involuntary (10028293) | 1 | 0.6 | 0.0 | 3.3 |  | . 00 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O 7.5 |
| Skin and subcutaneous tissue disorders (10040785) | Erythema (10015150) | 1 | 0.6 | 0.0 | 3.3 | 00. | . 00 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O 7.5 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 2.2 | 10. | . 60 | 0.0 | 3.1 |  | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O7.5 |
|  | Urticaria (10046735) | 0 | 0.0 | 0.0 | 2.2 | 10. | . 60 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | O 7.5 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group

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At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of administered doses
n/\% = number/percentage of doses with the symptom
$95 \% \mathrm{CI}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.111 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30 -day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)


PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit
Table 8.112 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \text { HZ/su } \\ & \mathrm{N}=166 \end{aligned}$ |  |  | Placebo$\mathrm{N}=178$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | Placebo$N=47$ |  |  |  |
|  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL | UL n | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |
| At least one symptom |  | 10.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 10.6 | 0.0 | 3.30 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.113 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 30 -day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=91 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 19 | 21.1 | 13.2 | 31.0 | 28 | 30 | 21.5 | 41.3 | 12 | 44.4 | 25.5 | 64.7 | 520.8 | 7.1 | 42.2 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 2 | 2.2 | 0.3 | 7.8 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
|  | Febrile neutropenia (10016288) | 2 | 2.2 | 0.3 | 7.8 | 1 | 1.1 | 0.0 | 6.0 | 2 | 7.4 | 0.9 | 24.3 | 14.2 | 0.1 | 21.1 |
|  | Neutropenia (10029354) | 2 | 2.2 | 0.3 | 7.8 | 3 | 3.3 | 0.7 | 9.3 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Abdominal pain (10000081) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Abdominal pain upper (10000087) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Constipation (10010774) | 0 | 0.0 | 0.0 | 4.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
|  | Diarrhoea (10012735) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Dyspepsia (10013946) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 00.0 | 0.0 | 14.2 |
|  | Dysphagia (10013950) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Gastrooesophageal reflux disease (10017885) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 00.0 | 0.0 | 14.2 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
|  | Nausea (10028813) | 3 | 3.3 | 0.7 | 9.4 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Stomatitis (10042128) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 00.0 | 0.0 | 14.2 |
|  | Swollen tongue (10042727) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Vomiting (10047700) | 1 | 1.1 | 0.0 | 6.0 | 3 | 3.3 | 0.7 | 9.3 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 2 | 2.2 | 0.3 | 7.8 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 00.0 | 0.0 | 14.2 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |

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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | Placebo$N=91$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=24 \end{aligned}$ |  |  |  |
|  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  | 95\% Cl |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |
|  | Mucosal inflammation (10028116) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 1 | 3.7 | 0.1 | 19.0 |  | 0.0 | 0.0 | 14.2 |
|  | Pyrexia (10037660) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hepatomegaly (10019842) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 4.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Cystitis (10011781) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Gastroenteritis (10017888) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Nasopharyngitis (10028810) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neutropenic sepsis (10049151) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Post procedural infection (10067268) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Respiratory tract infection (10062352) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Sepsis (10040047) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Upper respiratory tract infection (10046306) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Platelet count decreased (10035528) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =90 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { cebc } \\ & =91 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =07 \end{aligned}$ |  |  | $\begin{aligned} & \text { acebo } \\ & =24 \end{aligned}$ |
|  |  |  |  |  | CI |  |  |  | Cl |  |  |  | Cl |  | 95\% CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n \% | LL UL |
|  | Thrombosis (10043607) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 00.0 | 0.014 .2 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.114 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=166 \end{aligned}$ |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=178 \end{aligned}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | Placebo$N=47$ |  |  |
|  |  | 95\% CI |  |  | 95\% CI |  |  |  |  |  | 95\% CI |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL UL | n | \% | LL | UL | n | \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 23 | 13.9 | 9.020 .1 | 36 | 20.2 | 14.6 | 26.9 | 13 | 25.5 | 14.3 | 39.6 | 714.9 | 6.2 | 28.3 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 2 | 1.2 | 0.14 .3 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 12.1 | 0.1 | 11.3 |
|  | Febrile neutropenia (10016288) | 2 | 1.2 | 0.14 .3 | 1 | 0.6 | 0.0 | 3.1 | 2 | 3.9 | 0.5 | 13.5 | 24.3 | 0.5 | 14.5 |
|  | Neutropenia (10029354) | 3 | 1.8 | 0.45 .2 | 3 | 1.7 | 0.3 | 4.8 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.02 .2 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 12.1 | 0.1 | 11.3 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 0.6 | 0.03 .3 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.02 .2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 1 | 0.6 | 0.03 .3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 1 | 0.6 | 0.03 .3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Abdominal pain (10000081) | 1 | 0.6 | 0.03 .3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Abdominal pain upper (10000087) | 1 | 0.6 | 0.03 .3 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Constipation (10010774) | 0 | 0.0 | 0.02 .2 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 12.1 | 0.1 | 11.3 |
|  | Diarrhoea (10012735) | 1 | 0.6 | 0.03 .3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Dyspepsia (10013946) | 0 | 0.0 | 0.02 .2 | - | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 00.0 | 0.0 | 7.5 |
|  | Dysphagia (10013950) | 0 | 0.0 | 0.02 .2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Gastrooesophageal reflux disease (10017885) | 0 | 0.0 | 0.02 .2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 00.0 | 0.0 | 7.5 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.02 .2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.02 .2 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 12.1 | 0.1 | 11.3 |
|  | Nausea (10028813) | 3 | 1.8 | 0.45 .2 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.02 .2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Stomatitis (10042128) | 0 | 0.0 | 0.02 .2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 00.0 | 0.0 | 7.5 |
|  | Swollen tongue (10042727) | 1 | 0.6 | 0.03 .3 | - | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Vomiting (10047700) | 1 | 0.6 | 0.03 .3 | 3 | 1.7 | 0.3 | 4.8 | 0 | 0.0 | 0.0 | 7.0 | 12.1 | 0.1 | 11.3 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 2 | 1.2 | 0.14 .3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 00.0 | 0.0 | 7.5 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.02 .2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Mucosal inflammation (10028116) | 0 | 0.0 | 0.02 .2 | 1 | 0.6 | 0.0 | 3.1 | 1 | 2.0 | 0.0 | 10.4 | 00.0 | 0.0 | 7.5 |

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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=166 \end{aligned}$ |  |  |  | Placebo$N=178$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  | Placebo$N=47$ |  |  |  |
|  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |
|  | Pyrexia (10037660) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 |  | 2.1 | 0.1 | 11.3 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hepatomegaly (10019842) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 2.2 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Cystitis (10011781) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Gastroenteritis (10017888) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 |  | 2.1 | 0.1 | 11.3 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Nasopharyngitis (10028810) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Neutropenic sepsis (10049151) | 1 | 0.6 | 0.0 | 3.3 | 2 | 1.1 | 0.1 | 4.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Post procedural infection (10067268) | 0 | 0.0 | 0.0 | 2.2 | - | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Respiratory tract infection (10062352) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Sepsis (10040047) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Upper respiratory tract infection (10046306) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 0 | 0.0 | 0.0 | 2.2 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Platelet count decreased (10035528) | 1 | 0.6 | 0.0 | 3.3 |  | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) | 1 | 0.6 | 0.0 | 3.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Musculoskeletal and connective tissue disorders (10028395) | Back pain (10003988) | 0 | 0.0 | 0.0 | 2.2 | 1 | 0.6 | 0.0 | 3.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |

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PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
n/\% = number/percentage of doses with the symptom
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.115 Global Summary of unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  | Group |  |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :---: | :---: | :---: | :---: | :---: |
|  | PreChemo |  |  |  |  |  |  |  |  | OnChemo | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |  |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 74 | 81 | 26 | 22 | 100 | 103 |  |  |  |  |  |
| Number of doses followed by at least one unsolicited symptom | 113 | 132 | 40 | 34 | 153 | 166 |  |  |  |  |  |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 308 | 314 | 107 | 84 | 415 | 398 |  |  |  |  |  |
| Number of unsolicited symptoms reported** | 321 | 325 | 109 | 85 | 430 | 410 |  |  |  |  |  |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.116 Global Summary of grade 3 unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  | Group |  |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :---: | :---: | :---: | :---: | :---: |
|  | PreChemo |  |  |  |  |  |  |  | OnChemo |  | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |  |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 13 | 9 | 5 | 6 | 18 | 15 |  |  |  |  |  |
| Number of doses followed by at least one unsolicited symptom | 16 | 9 | 6 | 6 | 22 | 15 |  |  |  |  |  |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 17 | 14 | 6 | 8 | 23 | 22 |  |  |  |  |  |
| Number of unsolicited symptoms reported** | 17 | 14 | 6 | 8 | 23 | 22 |  |  |  |  |  |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once ** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.117 Global Summary of unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  | Group |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  | PreChemo |  | OnChemo |  | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su |
|  | Placebo |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 10 | 7 | 0 | 2 | 10 |
| Number of doses followed by at least one unsolicited symptom | 11 | 9 | 0 | 2 | 11 |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term | 13 | 15 | 0 | 2 | 13 |
| Number of unsolicited symptoms reported** | 13 | 15 | 0 | 2 | 13 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.118 Global Summary of grade 3 unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  | Group |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | PreChemo |  | OnChemo |  | All |  |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |
| Number of subjects with at least one unsolicited symptom reported | 1 | 0 | 0 | 0 | 1 | 0 |
| Number of doses followed by at least one unsolicited symptom | 1 | 0 | 0 | 0 | 1 | 0 |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 1 | 0 | 0 | 0 | 1 | 0 |
| Number of unsolicited symptoms reported** | 1 | 0 | 0 | 0 | 1 | 0 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.119 Global Summary of unsolicited signs and symptoms reported with medically attended visit, within the 30 -day (Days $0-29$ ) postvaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  | Group |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | PreChemo |  | OnChemo |  | All |  |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |
| Number of subjects with at least one unsolicited symptom reported | 19 | 28 | 12 | 5 | 31 | 33 |
| Number of doses followed by at least one unsolicited symptom | 23 | 36 | 13 | 7 | 36 | 43 |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 40 | 50 | 20 | 12 | 60 | 62 |
| Number of unsolicited symptoms reported** | 40 | 50 | 20 | 12 | 60 | 62 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.120 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to 30 days post last vaccination by PreChemo/OnChemo groups (Total Vaccinated Cohort)

No records exist in this table

Table 8.121 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from 30 days post last vaccination up to the study end by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  | OnChemo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  | $\begin{gathered} \hline \text { Placebo } \\ \mathrm{N}=91 \end{gathered}$ |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=24 \end{gathered}$ |  |  |
|  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  | 95\% CI |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL UL | n $\%$ | LL | UL n | n \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 00.0 | 0.04 .0 | 00.0 | 0.0 | 4.0 | 00.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 00.0 | 0.04 .0 | 00.0 | 0.0 | 4.00 | 00.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.122 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to the study end by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | Placebo$N=91$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |
|  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  |  | 95\% CI |  |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) |  | \% \% | LL | UL |  | \% | LL |  | UL | n | \% | LL | UL | n \% | LL | UL |
| At least one symptom |  |  | 00.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 |  | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) |  | 00.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 |  | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit
Table 8.123 Global Summary of serious adverse events reported from the first vaccination up to 30 days post last vaccination by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  | Group |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :---: | :---: | :---: | :---: | :---: |
|  | PreChemo |  |  |  |  |  |  |  | OnChemo | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su |  |  |  |  |  |
|  | Placebo |  |  |  |  |  |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 9 | 10 | 7 | 4 | 16 |  |  |  |  |  |
| 14 |  |  |  |  |  |  |  |  |  |  |
| Number of doses followed by at least one unsolicited symptom | 9 | 11 | 8 | 5 | 17 |  |  |  |  |  |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 9 | 16 | 10 | 8 | 19 |  |  |  |  |  |
| Number of unsolicited symptoms reported** | 9 | 16 | 10 | 8 | 19 |  |  |  |  |  |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.124 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from the first vaccination up to 30 days post last vaccination by PreChemo/OnChemo groups (Total Vaccinated Cohort)


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|  |  | PreChemo |  |  |  |  | OnChemo |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=91 \\ \hline \end{gathered}$ |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | Placebo$N=24$ |  |
|  |  | 95\% Cl |  |  | 95\% Cl |  |  | 95\% CI |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL UL | n | \% | LL UL | n \% | LL | UL | n \% | LL UL |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 00.0 | 0.04 .0 | 1 | 1.1 | 0.06 .0 | 00.0 | 0.0 | 12.8 | 14.2 | 0.121 .1 |
|  | Hydronephrosis (10020524) | 00.0 | 0.04 .0 | 1 | 1.1 | 0.06 .0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.014 .2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Pleural effusion (10035598) | 00.0 | 0.04 .0 | 1 | 1.1 | 0.06 .0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.014 .2 |
|  | Pulmonary embolism (10037377) | 11.1 | 0.06 .0 | 0 | 0.0 | 0.04 .0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.014 .2 |
| Skin and subcutaneous tissue disorders (10040785) | Rash (10037844) | 00.0 | 0.04 .0 | 1 | 1.1 | 0.06 .0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.014 .2 |
|  | Skin haemorrhage (10064265) | 00.0 | 0.04 .0 | 1 | 1.1 | 0.06 .0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.014 .2 |
| Vascular disorders (10047065) | Thrombosis (10043607) | 00.0 | 0.04 .0 | 0 | 0.0 | 0.04 .0 | 13.7 | 0.1 | 19.0 | 00.0 | 0.014 .2 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; $\mathrm{LL}=$ Lower Limit, UL = Upper Limit

Table 8.125 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, from the first vaccination up to 30 days post last vaccination by PreChemo/OnChemo groups (Total Vaccinated Cohort)

No records exist in this table

Table 8.126 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from 30 days post last vaccination up to the study end by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=91 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=24 \end{gathered}$ |  |  |
|  |  | 95\% CI |  |  |  | - 95\% CI |  |  |  |  | 95\% CI |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 22 | 24.4 | 16.0 | 34.6 | 25 | 27.5 | 18.6 | 37.8 | 829.6 | 13.8 | 50.2 | 625.0 | 9.8 | U46.7 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 2 | 2.2 | 0.3 | 7.8 | 1 | 1.1 | 0.0 | 6.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | . 14.2 |
|  | Febrile neutropenia (10016288) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 27.4 | 0.9 | 24.3 | 00.0 | 0.0 | . 14.2 |
|  | Neutropenia (10029354) | 1 | 1.1 | 0.0 | 6.0 | 3 | 3.3 | 0.7 | 9.3 | 13.7 | 0.1 | 19.0 | 00.0 | 0.0 | 0.0 14.2 |
|  | Pancytopenia (10033661) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 13.7 | 0.1 | 19.0 | 00.0 | 0.0 | O 14.2 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | 0.0 14.2 |
| Cardiac disorders (10007541) | Cardiac arrest (10007515) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Cardiac failure (10007554) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | . 14.2 |
|  | Cardiac failure congestive (10007559) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | 0.0 14.2 |
|  | Myocardial infarction (10028596) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | . 14.2 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 00.0 | 0.0 | 12.8 | 14.2 | 0.1 | 121.1 |
| Gastrointestinal disorders (10017947) | Constipation (10010774) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | . 14.2 |
|  | Diarrhoea (10012735) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 13.7 | 0.1 | 19.0 | 00.0 | 0.0 | 0.0 14.2 |
|  | Dysphagia (10013950) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | 0. 14.2 |
|  | Enteritis (10014866) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | 0.0 14.2 |
|  | Mouth ulceration (10028034) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | 0.0 14.2 |
|  | Nausea (10028813) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | O 14.2 |
|  | Odynophagia (10030094) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | . 14.2 |
|  | Oesophagitis (10030216) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | 0.0 14.2 |
| General disorders and administration site conditions (10018065) | Death (10011906) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | (14.2 |
|  | Mucosal inflammation (10028116) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 13.7 | 0.1 | 19.0 | 00.0 | 0.0 | O 14.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 13.7 | 0.1 | 19.0 | 00.0 | 0.0 | . 14.2 |
| Hepatobiliary disorders (10019805) | Cholangitis acute (10008605) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | 0.0 14.2 |
| Infections and infestations (10021881) | Anal abscess (10048946) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | 0.0 14.2 |
|  | Bacteraemia (10003997) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | . 14.2 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 13.7 | 0.1 | 19.0 | 00.0 | 0.0 | 14.2 |

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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | Placebo$\mathrm{N}=91$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |  |
|  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL | n | \% | LL | UL |
|  | Clostridium bacteraemia (10058852) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Clostridium difficile infection (10054236) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Device related sepsis (10069802) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Diverticulitis (10013538) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Epiglottitis (10015030) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Gastroenteritis (10017888) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lung infection (10061229) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neutropenic sepsis (10049151) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oral candidiasis (10030963) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pleural infection (10061351) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pneumonia (10035664) | 0 | 0.0 | 0.0 | 4.0 | 2 | 2.2 | 0.3 | 7.7 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Respiratory tract infection (10062352) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Sepsis (10040047) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Staphylococcal infection (10058080) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Upper respiratory tract infection (10046306) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Injury, poisoning and procedural complications (10022117) | Lumbar vertebral fracture (10049947) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Metabolism and nutrition disorders (10027433) | Diabetic ketoacidosis (10012671) | 2 | 2.2 | 0.3 | 7.8 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypokalaemia (10021015) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hyponatraemia (10021036) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Malnutrition (10061273) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Musculoskeletal chest pain (10050819) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Bladder cancer (10005003) |  | 2.2 | 0.3 | 7.8 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Breast cancer recurrent (10006198) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Cholangiocarcinoma (10008593) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Colon cancer (10009944) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Colorectal cancer (10061451) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Colorectal cancer metastatic (10052358) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Head and neck cancer (10067821) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 |  | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Liposarcoma (10024627) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | Placebo$\mathrm{N}=91$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% Cl |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |  | \% | LL | UL |
|  | Lung neoplasm malignant (10058467) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Malignant melanoma (10025650) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Metastases to central nervous system (10059282) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Metastases to liver (10027457) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Non-small cell lung cancer (10061873) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Ovarian cancer (10033128) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Prostate cancer (10060862) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Rectal cancer metastatic (10055097) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Squamous cell carcinoma of lung (10041826) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Tongue neoplasm malignant stage unspecified (10043966) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Tumour haemorrhage (10049750) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Uterine leiomyosarcoma (10046799) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Bronchial obstruction (10006440) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pleural effusion (10035598) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pulmonary embolism (10037377) | 0 | 0.0 | 0.0 | 4.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Respiratory failure (10038695) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Surgical and medical procedures (10042613) | Abdominal hernia repair (10060802) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 |  | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Vascular disorders (10047065) | Superior vena cava occlusion (10058988) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%$ = number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.127 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, from 30 days post last vaccination up to the study end by PreChemo/OnChemo groups (Total Vaccinated Cohort)

No recors exist in this table

Table 8.128 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to the study end by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | Placebo$N=91$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% Cl |  |  |  | 95\% Cl |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 27 | 30.0 | 20.8 | 40.6 | 34 | 37.4 | 27.4 | 48.1 | 9 | 33.3 | 16.5 | 54.0 | 833.3 | 15.6 | 55.3 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 2 | 2.2 | 0.3 | 7.8 | 3 | 3.3 | 0.7 | 9.3 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Febrile neutropenia (10016288) | 3 | 3.3 | 0.7 | 9.4 | 1 | 1.1 | 0.0 | 6.0 | 3 | 11.1 | 2.4 | 29.2 | 14.2 | 0.1 | 21.1 |
|  | Neutropenia (10029354) | 1 | 1.1 | 0.0 | 6.0 | 4 | 4.4 | 1.2 | 10.9 | 1 | 3.7 | 0.1 | 19.0 | 00.0 | 0.0 | 14.2 |
|  | Pancytopenia (10033661) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 00.0 | 0.0 | 14.2 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
| Cardiac disorders (10007541) | Cardiac arrest (10007515) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Cardiac failure (10007554) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Cardiac failure congestive (10007559) |  | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Myocardial infarction (10028596) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
| Gastrointestinal disorders (10017947) | Constipation (10010774) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
|  | Diarrhoea (10012735) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 00.0 | 0.0 | 14.2 |
|  | Dysphagia (10013950) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Enteritis (10014866) | 0 | 0.0 | 0.0 | 4.0 | , | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Mouth ulceration (10028034) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Nausea (10028813) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Odynophagia (10030094) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Oesophagitis (10030216) |  | 1.1 | 0.0 | 6.0 | - | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| General disorders and administration site conditions (10018065) | Death (10011906) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Mucosal inflammation (10028116) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 2 | 7.4 | 0.9 | 24.3 | 00.0 | 0.0 | 14.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 14.2 | 0.1 | 21.1 |
| Hepatobiliary disorders (10019805) | Cholangitis acute (10008605) |  | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Infections and infestations (10021881) | Anal abscess (10048946) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Bacteraemia (10003997) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |

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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  |  | Placebo$N=91$ |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ N=24 \end{gathered}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% Cl |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) |  | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |  | \% | LL | UL |
|  | Candida infection (10074170) | - | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Clostridium bacteraemia (10058852) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Clostridium difficile infection (10054236) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Device related sepsis (10069802) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Diverticulitis (10013538) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Epiglottitis (10015030) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Gastroenteritis (10017888) |  | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hepatitis c (10019744) |  | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lung infection (10061229) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Nasopharyngitis (10028810) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neutropenic sepsis (10049151) | 1 | 1.1 | 0.0 | 6.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oral candidiasis (10030963) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pleural infection (10061351) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pneumonia (10035664) | 0 | 0.0 | 0.0 | 4.0 | 2 | 2.2 | 0.3 | 7.7 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Respiratory tract infection (10062352) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Sepsis (10040047) | 2 | 2.2 | 0.3 | 7.8 | 1 | 1.1 | 0.0 | 6.0 |  | 3.7 | 0.1 | 19.0 | 1 | 4.2 | 0.1 | 21.1 |
|  | Staphylococcal infection (10058080) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Upper respiratory tract infection (10046306) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urinary tract infection (10046571) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urosepsis (10048709) | - | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lumbar vertebral fracture (10049947) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Metabolism and nutrition disorders (10027433) | Diabetic ketoacidosis (10012671) | 2 | 2.2 | 0.3 | 7.8 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypokalaemia (10021015) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hyponatraemia (10021036) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Malnutrition (10061273) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | - | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Musculoskeletal chest pain (10050819) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 |  | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=90 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=91 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=24 \end{gathered}$ |  |  |  |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% Cl |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |  | \% | LL | UL |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Bladder cancer (10005003) | 2 | 2.2 | 0.3 | 7.8 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Breast cancer recurrent (10006198) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Cholangiocarcinoma (10008593) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Colon cancer (10009944) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Colorectal cancer (10061451) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Colorectal cancer metastatic (10052358) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Head and neck cancer (10067821) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Liposarcoma (10024627) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lung neoplasm malignant (10058467) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Malignant melanoma (10025650) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Metastases to central nervous system (10059282) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Metastases to liver (10027457) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Non-small cell lung cancer (10061873) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Ovarian cancer (10033128) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Prostate cancer (10060862) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Rectal cancer metastatic (10055097) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Squamous cell carcinoma of lung (10041826) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Tongue neoplasm malignant stage unspecified (10043966) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Tumour haemorrhage (10049750) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Uterine leiomyosarcoma (10046799) | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Nervous system disorders (10029205) | Hepatic encephalopathy (10019660) | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 4.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 1 | 1.1 | 0.0 | 6.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Bronchial obstruction (10006440) | 0 | 0.0 | 0.0 | 4.0 | 1 | 1.1 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pleural effusion (10035598) | 1 | 1.1 | 0.0 | 6.0 | 2 | 2.2 | 0.3 | 7.7 |  | 0.0 | 0.0 | 12.8 | - | 0.0 | 0.0 | 14.2 |
|  | Pulmonary embolism (10037377) | 1 | 1.1 | 0.0 | 6.0 | 2 | 2.2 | 0.3 | 7.7 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

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PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \%$ CI $=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.129 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, from first vaccination up to the study end by PreChemo/OnChemo groups (Total Vaccinated Cohort)

No records exist in this table

Table 8.130 Global Summary of potential immune mediated diseases reported from the first vaccination up to 30 days post last vaccination by PreChemo/OnChemo groups (Total Vaccinated Cohort)

No records exist in this table

Table 8.131 Number and percentage of subjects with fatal outcome reported up to the study end by PreChemo/OnChemo groups (Total Vaccinated Cohort)


PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once

Table 8.132 Percentage of subjects with concomitant medication during the 30day (Day 0-29) post vaccination period by PreChemo/OnChemo groups (Total Vaccinated Cohort)

|  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  | 95\% Cl |  |  |  |  |  |  |  | 95\% CI |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  |
|  | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 90 | 83 | 92.2 | 84.6 | 96.8 | 91 | 85 | 93.4 | 86.2 | 97.5 | 27 | 26 | 96.3 | 81.0 | 99.9 | 24 | 24 | 100 | 85.8 | 100 |
| Steroids to prevent chemotherapy nausea and vomiting | 90 | 76 | 84.4 | 75.3 | 91.2 | 91 | 77 | 84.6 | 75.5 | 91.3 | 27 | 23 | 85.2 | 66.3 | 95.8 | 24 | 21 | 87.5 | 67.6 | 97.3 |
| Any in anticipation of study vaccine reaction | 90 | 0 | 0.0 | 0.0 | 4.0 | 91 | 0 | 0.0 | 0.0 | 4.0 | 27 | 0 | 0.0 | 0.0 | 12.8 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Any chronic use | 90 | 4 | 4.4 | 1.2 | 11.0 | 91 | 5 | 5.5 | 1.8 | 12.4 | 27 | 0 | 0.0 | 0.0 | 12.8 | 24 | 3 | 12.5 | 2.7 | 32.4 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 76 | 69 | 90.8 | 81.9 | 96.2 | 87 | 76 | 87.4 | 78.5 | 93.5 | 24 | 21 | 87.5 | 67.6 | 97.3 | 23 | 18 | 78.3 | 56.3 | 92.5 |
| Steroids to prevent chemotherapy nausea and vomiting | 76 | 62 | 81.6 | 71.0 | 89.5 | 87 | 65 | 74.7 | 64.3 | 83.4 | 24 | 20 | 83.3 | 62.6 | 95.3 | 23 | 17 | 73.9 | 51.6 | 89.8 |
| Any in anticipation of study vaccine reaction | 76 | 0 | 0.0 | 0.0 | 4.7 | 87 | 0 | 0.0 | 0.0 | 4.2 | 24 | 0 | 0.0 | 0.0 | 14.2 | 230 | 0 | 0.0 | 0.0 | 14.8 |
| Any chronic use | 76 | 1 | 1.3 | 0.0 | 7.1 | 87 | 6 | 6.9 | 2.6 | 14.4 | 24 | 1 | 4.2 | 0.1 | 21.1 | 23 | 1 | 4.3 | 0.1 | 21.9 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 166 | 152 | 91.6 | 86.3 | 95.3 | 178 | 161 | 90.4 | 85.1 | 94.3 | 51 | 47 | 92.2 | 81.1 | 97.8 | 47 | 42 | 89.4 | 76.9 | 96.5 |
| Steroids to prevent chemotherapy nausea and vomiting | 166 | 138 | 83.1 | 76.6 | 88.5 | 178 | 142 | 79.8 | 73.1 | 85.4 | 51 | 43 | 84.3 | 71.4 | 93.0 | 47 | 38 | 80.9 | 66.7 | 90.9 |
| Any in anticipation of study vaccine reaction | 166 | 0 | 0.0 | 0.0 | 2.2 | 178 | 0 | 0.0 | 0.0 | 2.1 | 51 | 0 | 0.0 | 0.0 | 7.0 | 470 | 0 | 0.0 | 0.0 | 7.5 |
| Any chronic use | 166 | 5 | 3.0 | 1.0 | 6.9 | 178 | 11 | 6.2 | 3.1 | 10.8 | 51 | 1 | 2.0 | 0.0 | 10.4 | 47 | , | 8.5 | 2.4 | 20.4 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 90 | 87 | 96.7 | 90.6 | 99.3 | 91 | 89 | 97.8 | 92.3 | 99.7 | 27 | 26 | 96.3 | 81.0 | 99.9 | 24 | 24 | 100 | 85.8 | 100 |
| Steroids to prevent chemotherapy nausea and vomiting | 90 | 80 | 88.9 | 80.5 | 94.5 | 91 | 80 | 87.9 | 79.4 | 93.8 | 27 | 24 | 88.9 | 70.8 | 97.6 | 24 | 21 | 87.5 | 67.6 | 97.3 |
| Any in anticipation of study vaccine reaction | 90 | 0 | 0.0 | 0.0 | 4.0 | 91 | 0 | 0.0 | 0.0 | 4.0 | 27 | 0 | 0.0 | 0.0 | 12.8 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Any chronic use | 90 | 5 | 5.6 | 1.8 | 12.5 | 91 | 9 | 9.9 | 4.6 | 17.9 | 27 | 1 | 3.7 | 0.1 | 19.0 | 24 | 4 | 16.7 | 4.7 | 37.4 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.133 Number and percentage of subjects who received vaccine dose(s) by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  | PreChemo |  |  |  | OnChemo |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  | Placebo$N=88$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  | Placebo$N=24$ |  | $\begin{array}{c\|} \hline \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=113 \end{array}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=112 \end{gathered}$ |  |
| Total number of doses received | n | \% | n | \% | n | \% | n | \% | n | \% | n | \% |
| 1 | 14 | 16.3 | 4 | 4.5 | 3 | 11.1 | 1 | 4.2 | 17 | 15.0 | 5 | 4.5 |
| 2 | 72 | 83.7 | 84 | 95.5 | 24 | 88.9 | 23 | 95.8 | 96 | 85.0 | 107 | 95.5 |
| Any | 86 | 100 | 88 | 100 | 27 | 100 | 24 | 100 | 113 | 100 | 112 | 100 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in each group or in total included in the considered cohort
$\mathrm{n} / \%=$ number/percentage of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least one dose
Table 8.134 Compliance in returning symptom sheets by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

| Dose | Sub-group | Group | Number of doses | Doses NOT according to protocol | Number of general SS | Compliance \% general SS | Number of local SS | ```Compliance % local SS``` |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 1 | PreChemo | HZ/su | 86 | 2 | 82 | 95.3 | 82 | 95.3 |
|  |  | Placebo | 88 | 5 | 83 | 94.3 | 83 | 94.3 |
|  | OnChemo | HZ/su | 27 | 1 | 26 | 96.3 | 26 | 96.3 |
|  |  | Placebo | 24 | 1 | 24 | 100 | 24 | 100 |
| 2 | PreChemo | HZ/su | 72 | 4 | 69 | 95.8 | 70 | 97.2 |
|  |  | Placebo | 84 | 5 | 81 | 96.4 | 81 | 96.4 |
|  | OnChemo | HZ/su | 24 | 0 | 24 | 100 | 24 | 100 |
|  |  | Placebo | 23 | 2 | 22 | 95.7 | 22 | 95.7 |
| Total | PreChemo | HZ/su | 158 | 6 | 151 | 95.6 | 152 | 96.2 |
|  |  | Placebo | 172 | 10 | 164 | 95.3 | 164 | 95.3 |
|  | OnChemo | HZ/su | 51 | 1 | 50 | 98.0 | 50 | 98.0 |
|  |  | Placebo | 47 | 3 | 46 | 97.9 | 46 | 97.9 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
SS = Symptom screens/sheets used for the collection of local and general solicited AEs
Compliance \% = (number of doses with symptom screen/sheet return / number of administered doses) X 100

Table 8.135 Incidence and nature of symptoms (solicited and unsolicited) reported during the 7 -day (Days 0-6) post-vaccination period following each dose and overall by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  |  |  |  |  | 95\% CI |  | N | n | \% | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL |  |  |  | LL | UL |
| Dose 1 | PreChemo | HZ/su | 86 | 76 | 88.4 | 79.7 | 94.3 | 86 | 57 | 66.3 | 55.3 | 76.1 | 86 | 69 | 80.2 | 70.2 | 88.0 |
|  |  | Placebo | 88 | 39 | 44.3 | 33.7 | 55.3 | 88 | 38 | 43.2 | 32.7 | 54.2 | 88 | 2 | 2.3 | 0.3 | 8.0 |
|  | OnChemo | HZ/su | 27 | 26 | 96.3 | 81.0 | 99.9 | 27 | 24 | 88.9 | 70.8 | 97.6 | 27 | 15 | 55.6 | 35.3 | 74.5 |
|  |  | Placebo | 24 | 17 | 70.8 | 48.9 | 87.4 | 24 | 17 | 70.8 | 48.9 | 87.4 | 24 | 2 | 8.3 | 1.0 | 27.0 |
| Dose 2 | PreChemo | HZ/su | 72 | 58 | 80.6 | 69.5 | 88.9 | 72 | 53 | 73.6 | 61.9 | 83.3 | 72 | 37 | 51.4 | 39.3 | 63.3 |
|  |  | Placebo | 84 | 63 | 75.0 | 64.4 | 83.8 | 84 | 63 | 75.0 | 64.4 | 83.8 | 84 | 4 | 4.8 | 1.3 | 11.7 |
|  | OnChemo | HZ/su | 24 | 20 | 83.3 | 62.6 | 95.3 | 24 | 19 | 79.2 | 57.8 | 92.9 | 24 | 16 | 66.7 | 44.7 | 84. |
|  |  | Placebo | 23 | 19 | 82.6 | 61.2 | 95.0 | 23 | 19 | 82.6 | 61.2 | 95.0 | 23 | 2 | 8.7 | 1.1 | 28.0 |
| Overall/dose | PreChemo | HZ/su | 158 | 134 | 84.8 | 78.2 | 90.0 | 158 | 110 | 69.6 | 61.8 | 76.7 | 158 | 106 | 67.1 | 59.2 | 74.3 |
|  |  | Placebo | 172 | 102 | 59.3 | 51.6 | 66.7 | 172 | 101 | 58.7 | 51.0 | 66.2 | 172 | 6 | 3.5 | 1.3 | 7.4 |
|  | OnChemo | HZ/su | 51 | 46 | 90.2 | 78.6 | 96.7 | 51 | 43 | 84.3 | 71.4 | 93.0 | 51 | 31 | 60.8 | 46.1 | 74.2 |
|  |  | Placebo | 47 | 36 | 76.6 | 62.0 | 87.7 | 47 | 36 | 76.6 | 62.0 | 87.7 | 47 | 4 | 8.5 | 2.4 | 20.4 |
| Overall/subject | PreChemo | HZ/su | 86 | 79 | 91.9 | 83.9 | 96.7 | 86 | 69 | 80.2 | 70.2 | 88.0 | 86 | 72 | 83.7 | 74.2 | 90.8 |
|  |  | Placebo | 88 | 70 | 79.5 | 69.6 | 87.4 | 88 | 70 | 79.5 | 69.6 | 87.4 | 88 | 5 | 5.7 | 1.9 | 12.8 |
|  | OnChemo | HZ/su | 27 | 26 | 96.3 | 81.0 | 99.9 | 27 | 26 | 96.3 | 81.0 | 99.9 | 27 | 18 | 66.7 | 46.0 | 83.5 |
|  |  | Placebo | 24 | 20 | 83.3 | 62.6 | 95.3 | 24 | 20 | 83.3 | 62.6 | 95.3 | 24 | 4 | 16.7 | 4.7 | 37.4 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$N$ = number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.136 Incidence and nature of grade 3 symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 95\% Cl |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | JL |
| Dose 1 | PreChemo | HZ/su | 86 | 14 | 146.3 | 9.2 | 25.8 | 86 | 10 | 11.6 | 5.7 | 20.3 | 86 | 9 | 10.5 | 4.9 | 18.9 |
|  |  | Placebo | 88 | 6 | 6.8 | 2.5 | 14.3 | 88 | 6 | 6.8 | 2.5 | 14.3 | 88 | 0 | 0.0 | 0.0 | 4.1 |
|  | OnChemo | HZ/su | 27 | 7 | 25.9 | 11.1 | 46.3 | 27 | 7 | 25.9 | 11.1 | 46.3 | 27 | 0 | 0.0 | 0.0 | 12.8 |
|  |  | Placebo | 24 | 7 | 29.2 | 12.6 | 51.1 | 24 | 7 | 29.2 | 12.6 | 51.1 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Dose 2 | PreChemo | HZ/su | 72 | 12 | 216.7 | 8.9 | 27.3 | 72 | 11 | 115.3 | 7.9 | 25.7 | 72 | 3 | 4.2 | 0.9 | 11.7 |
|  |  | Placebo | 84 | 8 | 9.5 | 4.2 | 17.9 | 84 | 8 | 9.5 | 4.2 | 17.9 | 84 | 0 | 0.0 | 0.0 | 4.3 |
|  | OnChemo | HZ/su | 24 | 6 | 25.0 | 9.8 | 46.7 | 24 | 6 | 25.0 | 9.8 | 46.7 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  |  | Placebo | 23 | 4 | 17.4 | 5.0 | 38.8 | 23 | 4 | 17.4 | 5.0 | 38.8 | 23 | 0 | 0.0 | 0.0 | 14.8 |
| Overall/dose | PreChemo | HZ/su | 158 | 26 | 616.5 | 11.0 | 23.2 | 158 | 21 | 13.3 | 8.4 | 19.6 | 158 | 12 | 7.6 | 4.0 | 12.9 |
|  |  | Placebo | 172 | 14 | 48.1 | 4.5 | 13.3 | 172 | 14 | 8.1 | 4.5 | 13.3 | 172 | 0 | 0.0 | 0.0 | 2.1 |
|  | OnChemo | HZ/su | 51 | 13 | 325.5 | 14.3 | 39.6 | 51 | 13 | 35.5 | 14.3 | 39.6 | 51 | 1 | 2.0 | 0.0 | 10.4 |
|  |  | Placebo | 47 | 11 | 123.4 | 12.3 | 38.0 | 47 | 11 | 123.4 | 12.3 | 38.0 | 47 | 0 | 0.0 | 0.0 | 7.5 |
| Overall/subject | PreChemo | HZ/su | 86 | 20 | 023.3 | 14.8 | 33.6 | 86 | 18 | 20.9 | 12.9 | 31.0 | 86 | 11 | 12.8 | 6.6 | 21.7 |
|  |  | Placebo | 88 | 13 | 314.8 | 8.1 | 23.9 | 88 | 13 | 14.8 | 8.1 | 23.9 | 88 | 0 | 0.0 | 0.0 | 4.1 |
|  | OnChemo | HZ/su | 27 | 9 | 33.3 | 16.5 | 54.0 | 27 | 9 | 33.3 | 16.5 | 54.0 | 27 | 1 | 3.7 | 0.1 | 19.0 |
|  |  | Placebo | 24 | 8 | 33.3 | 15.6 | 55.3 | 24 | 8 | 33.3 | 15.6 | 55.3 | 24 | 0 | 0.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered 95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.137 Incidence and nature of symptoms (solicited only) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by PreChemo/OnChemo groups (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% Cl |  |  |  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | PreChemo | HZ/su | 82 | 76 | 92.7 | 84.8 | 97.3 | 82 | 55 | 67.1 | 55.8 | 77.1 | 82 | 69 | 84.1 | 74.4 | 91.3 |
|  |  | Placebo | 83 | 35 | 42.2 | 31.4 | 53.5 | 83 | 34 | 41.0 | 30.3 | 52.3 | 83 | 2 | 2.4 | 0.3 | 8.4 |
|  | OnChemo | HZ/su | 26 | 24 | 92.3 | 74.9 | 99.1 | 26 | 22 | 84.6 | 65.1 | 95.6 | 26 | 15 | 57.7 | 36.9 | 76. |
|  |  | Placebo | 24 | 16 | 66.7 | 44.7 | 84.4 | 24 | 16 | 66.7 | 44.7 | 84.4 | 24 | 1 | 4.2 | 0.1 | 21.1 |
| Dose 2 | PreChemo | HZ/su | 70 | 51 | 72.9 | 60.9 | 82.8 | 69 | 45 | 65.2 | 52.8 | 76.3 | 70 | 37 | 52.9 | 40.6 | 64.9 |
|  |  | Placebo | 81 | 44 | 54.3 | 42.9 | 65.4 | 81 | 44 | 54.3 | 42.9 | 65.4 | 81 | 3 | 3.7 | 0.8 | 10.4 |
|  | OnChemo | HZ/su | 24 | 20 | 83.3 | 62.6 | 95.3 | 24 | 18 | 75.0 | 53.3 | 90.2 | 24 | 16 | 66.7 | 44.7 | 84 |
|  |  | Placebo | 22 | 15 | 68.2 | 45.1 | 86.1 | 22 | 15 | 68.2 | 45.1 | 86.1 | 22 | 2 | 9.1 | 1.1 | 29.2 |
| Overall/dose | PreChemo | HZ/su | 152 | 127 | 83.6 | 76.7 | 89.1 | 151 | 100 | 66.2 | 58.1 | 73.7 | 152 | 106 | 69.7 | 61.8 | 76.9 |
|  |  | Placebo | 164 | 79 | 48.2 | 40.3 | 56.1 | 164 | 78 | 47.6 | 39.7 | 55.5 | 164 | 5 | 3.0 | 1.0 | 7.0 |
|  | OnChemo | HZ/su | 50 | 44 | 88.0 | 75.7 | 95.5 | 50 | 40 | 80.0 | 66.3 | 90.0 | 50 | 31 | 62.0 | 47.2 | 75.3 |
|  |  | Placebo | 46 | 31 | 67.4 | 52.0 | 80.5 | 46 | 31 | 67.4 | 52.0 | 80.5 | 46 | 3 | 6.5 | 1.4 | 17.9 |
| Overall/subject | PreChemo | HZ/su | 82 | 78 | 95.1 | 88.0 | 98.7 | 82 | 64 | 78.0 | 67.5 | 86.4 | 82 | 72 | 87.8 | 78.7 | 94.0 |
|  |  | Placebo | 83 | 54 | 65.1 | 53.8 | 75.2 | 83 | 54 | 65.1 | 53.8 | 75.2 | 83 | 4 | 4.8 | 1.3 | 11.9 |
|  | OnChemo | HZ/su | 26 | 25 | 96.2 | 80.4 | 99.9 | 26 | 23 | 88.5 | 69.8 | 97.6 | 26 | 18 | 69.2 | 48.2 | 85.7 |
|  |  | Placebo | 24 | 17 | 70.8 | 48.9 | 87.4 | 24 | 17 | 70.8 | 48.9 | 87.4 | 24 | 3 | 12.5 | 2.7 | 32.4 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.138 Incidence and nature of grade 3 symptoms (solicited only) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% Cl |  |  |  |  |  |  |  | 95\% Cl |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | JL |
| Dose 1 | PreChemo | HZ/su | 82 | 13 | 15.9 | 8.7 | 25.6 | 82 | 9 | 11.0 | 5.1 | 19.8 | 82 | 9 | 11.0 | 5.1 | 19.8 |
|  |  | Placebo | 83 | 6 | 7.2 | 2.7 | 15.1 | 83 | 6 | 7.2 | 2.7 | 15.1 | 83 | - | 0.0 | 0.0 | 4.3 |
|  | OnChemo | HZ/su | 26 | 6 | 23.1 | 9.0 | 43.6 | 26 | 6 | 23.1 | 9.0 | 43.6 | 26 | 0 | 0.0 | 0.0 | 13.2 |
|  |  | Placebo | 24 | 5 | 20.8 | 7.1 | 42.2 | 24 | 5 | 20.8 | 7.1 | 42.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Dose 2 | PreChemo | HZ/su | 70 | 10 | 14.3 | 7.1 | 24.7 | 69 | 9 | 13.0 | 6.1 | 23.3 | 70 |  | 4.3 | 0.9 | 12.0 |
|  |  | Placebo | 81 | 7 | 8.6 | 3.5 | 17.0 | 81 | 7 | 8.6 | 3.5 | 17.0 | 81 |  | 0.0 | 0.0 | 4.5 |
|  | OnChemo | HZ/su | 24 | 6 | 25.0 | 9.8 | 46.7 | 24 | 6 | 25.0 | 9.8 | 46.7 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  |  | Placebo | 22 | 3 | 13.6 | 2.9 | 34.9 | 22 | 3 | 13.6 | 2.9 | 34.9 | 22 | 0 | 0.0 | 0.0 | 15.4 |
| Overall/dose | PreChemo | HZ/su | 152 | 23 | 15.1 | 9.8 | 21.8 | 151 | 18 | 11.9 | 7.2 | 18.2 | 152 | 12 | 7.9 | 4.1 | 13.4 |
|  |  | Placebo | 164 | 13 | 7.9 | 4.3 | 13.2 | 164 | 13 | 7.9 | 4.3 | 13.2 | 164 | 0 | 0.0 | 0.0 | 2.2 |
|  | OnChemo | HZ/su | 50 | 12 | 24.0 | 13.1 | 38.2 | 50 | 12 | 24.0 | 13.1 | 38.2 | 50 | 1 | 2.0 | 0.1 | 10.6 |
|  |  | Placebo | 46 | 8 | 17.4 | 7.8 | 31.4 | 46 | 8 | 17.4 | 7.8 | 31.4 | 46 | 0 | 0.0 | 0.0 | 7.7 |
| Overall/subject | PreChemo | HZ/su | 82 | 18 | 22.0 | 13.6 | 32.5 | 82 | 16 | 19.5 | 11.6 | 29.7 | 82 | 11 | 13.4 | 6.9 | 22.7 |
|  |  | Placebo | 83 | 12 | 14.5 | 7.7 | 23.9 | 83 | 12 | 14.5 | 7.7 | 23.9 | 83 | 0 | 0.0 | 0.0 | 4.3 |
|  | OnChemo | HZ/su | 26 | 8 | 30.8 | 14.3 | 51.8 | 26 | 8 | 30.8 | 14.3 | 51.8 | 26 | 1 | 3.8 | 0.1 | 19.6 |
|  |  | Placebo | 24 | 5 | 20.8 | 7.1 | 42.2 | 24 | 5 | 20.8 | 7.1 | 42.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered 95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.139 Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |
|  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n \% | \% | LL | UL | N | n | \% | LL | UL | N | n \% |  | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 82 | 64 | 78.0 | 67.5 | 86.4 | 83 | 11. | 1.2 | 0.0 | 6.5 | 26 | 15 | 57.7 | 36.9 | 76.6 | 24 | 14.2 |  | 121.1 |
|  | Grade 2 or 3 | 82 | 21 | 25.6 | 16.6 | 36.4 | 83 | 00. | 0.0 | 0.0 | 4.3 | 26 | 4 | 15.4 | 4.4 | 34.9 | 24 | 00.0 | 0.0 | 14.2 |
|  | Grade 3 | 82 | 7 | 8.5 | 3.5 | 16.8 | 83 | 00. | 0.0 | 0.0 | 4.3 | 26 | , | 0.0 | 0.0 | 13.2 | 24 | 00.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 1 | 1.2 | 0.0 | 6.6 | 83 | 00. | 0.0 | 0.0 | 4.3 | 26 | , | 0.0 | 0.0 | 13.2 | 24 | 00.0 | 0.0 | 14.2 |
| Redness (mm) | All | 82 | 27 | 32.9 | 22.9 | 44.2 | 83 | 00. | 0.0 | 0.0 | 4.3 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 00.0 | 0.0 | 14.2 |
|  | $>50$ | 82 | 15 | 18.3 | 10.6 | 28.4 | 83 | 00. | 0.0 | 0.0 | 4.3 | 26 | 2 | 7.7 | 0.9 | 25.1 | 24 | 00.0 | 0.0 | 14.2 |
|  | >100 | 82 | 2 | 2.4 | 0.3 | 8.5 | 83 |  | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 00.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 |  | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 00.0 | 0.0 | 14.2 |
| Swelling (mm) | All | 82 | 13 | 15.9 | 8.7 | 25.6 | 83 | 11. | 1.2 | 0.0 | 6.5 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 00.0 | 0.0 | 14.2 |
|  | $>50$ | 82 | 7 | 8.5 | 3.5 | 16.8 | 83 | 00. | 0.0 | 0.0 | 4.3 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 00.0 | 0.0 | 14.2 |
|  | >100 | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 00. | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 00.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 00. | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 00.0 | 0.0 | 14.2 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 70 | 33 | 47.1 | 35.1 | 59.4 | 81 | 33. | 3.70 | 0.8 | 10.4 | 24 | 16 | 66.7 | 44. | 84.4 | 22 | 29.1 | 1.1 | 129.2 |
|  | Grade 2 or 3 | 70 | 9 | 12.9 | 6.1 | 23.0 | 81 | 11. | 1.2 | 0.0 | 6.7 | 24 | 9 | 37.5 | 18.8 | 59.4 | 22 | 00.0 | 0.0 | 15.4 |
|  | Grade 3 | 70 | 3 | 4.3 | 0.9 | 12.0 | 81 | 00. | 0.0 | 0.0 | 4.5 | 24 |  | 4.2 | 0.1 | 21.1 | 22 | 00.0 | 0.0 | 15.4 |
|  | Medical advice | 70 | 0 | 0.0 | 0.0 | 5.1 | 81 |  | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 00.0 | 0.0 | 15.4 |
| Redness (mm) | All | 70 | 13 | 18.6 | 10.3 | 29.7 | 81 |  | 0.0 | 0.0 | 4.5 | 24 | 5 | 20.8 | 7.1 | 42.2 | 22 | 00.0 | 0.0 | 15.4 |
|  | >50 | 70 | 5 | 7.1 | 2.4 | 15.9 | 81 |  | 0.0 | 0.0 | 4.5 | 24 | 2 | 8.3 | 1.0 | 27.0 | 22 | 00.0 | 0.0 | 15.4 |
|  | >100 | 70 | 0 | 0.0 | 0.0 | 5.1 | 81 |  | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 00.0 | 0.0 | 15.4 |
|  | Medical advice | 70 | 0 | 0.0 | 0.0 | 5.1 | 81 |  | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 00.0 | 0.0 | 15.4 |
| Swelling (mm) | All | 70 | 5 | 7.1 | 2.4 | 15.9 | 81 |  | 0.0 | 0.0 | 4.5 | 24 | 3 | 12.5 | 2.7 | 32.4 | 22 | 00.0 | 0.0 | 15.4 |
|  | $>50$ | 70 | 3 | 4.3 | 0.9 | 12.0 | 81 |  | 0.0 | 0.0 | 4.5 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 00.0 | 0.0 | 15.4 |
|  | >100 | 70 | 0 | 0.0 | 0.0 | 5.1 | 81 |  | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 00.0 | 0.0 | 15.4 |
|  | Medical advice | 70 | 0 | 0.0 | 0.0 | 5.1 | 81 | 00.0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 00.0 | 0.0 | 15.4 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 152 | 97 | 63.8 | 55.6 | 71.4 | 164 | 42. | 2.4 | 0.7 | 6.1 | 50 | 31 | 62.0 | 47.2 | 75.3 | 46 | 36.5 | 1.4 | 417.9 |
|  | Grade 2 or 3 | 152 | 30 | 19.7 | 13.7 | 27.0 | 164 |  | 0.6 | 0.0 | 3.4 | 50 | 13 | 26.0 | 14.6 | 40.3 | 46 | 00.0 | 0.0 | 7.7 |
|  | Grade 3 | 152 | 10 | 6.6 | 3.2 | 11.8 | 164 |  | 0.0 | 0.0 | 2.2 | 50 | 1 | 2.0 | 0.1 | 10.6 | 46 | 00.0 | 0.0 | 7.7 |
|  | Medical advice | 152 | 1 | 0.7 | 0.0 | 3.6 | 164 | 00. | 0.0 | 0.0 | 2.2 | 50 | , | 0.0 | 0.0 | 7.1 | 46 | 00.0 | 0.0 | 7.7 |
| Redness (mm) | All | 152 | 40 | 26.3 | 19.5 | 34.1 | 164 |  | 0.0 | 0.0 | 2.2 | 50 | 8 | 16.0 | 7.2 | 29.1 | 46 | 00.0 | 0.0 | 7.7 |
|  | $>50$ | 152 | 20 | 13.2 | 8.2 | 19.6 | 164 | 00. | 0.0 | 0.0 | 2.2 | 50 |  | 8.0 | 2.2 | 19.2 | 46 | 00.0 | 0.0 | 7.7 |
|  | >100 | 152 | 2 | 1.3 | 0.2 | 4.7 | 164 |  | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 00.0 | 0.0 | 7.7 |
|  | Medical advice | 152 | 0 | 0.0 | 0.0 | 2.4 | 164 | 00. | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 00.0 | 0.0 | 7.7 |
| Swelling (mm) | All | 152 | 18 | 11.8 | 7.2 | 18.1 | 164 |  | 0.60 | 0.0 | 3.4 | 50 | 4 | 8.0 | 2.2 | 19.2 | 46 | 00.0 | 0.0 | 7.7 |
|  | $>50$ | 152 | 10 | 6.6 | 3.2 | 11.8 | 164 |  | 0.0 | 0.0 | 2.2 | 50 | 2 | 4.0 | 0.5 | 13.7 | 46 | 00.0 | 0.0 | 7.7 |
|  | >100 | 152 | 0 | 0.0 | 0.0 | 2.4 | 164 |  | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 00.0 | 0.0 | 7.7 |
|  | Medical advice | 152 | 0 | 0.0 | 0.0 | 2.4 | 164 | 00.0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 00.0 | 0.0 | 7.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 82 | 68 | 82.9 | 73.0 | 90.3 | 83 |  | 4.8 | 1.3 | 11.9 | 26 | 18 | 69.2 | 48.2 | 85.7 | 24 | 312.5 | 2.7 | 32.4 |
|  | Grade 2 or 3 | 82 | 23 | 28.0 | 18.7 | 39.1 | 83 | 11. | 1.2 | 0.0 | 6.5 | 26 | 9 | 34.6 | 17.2 | 55.7 | 24 | 00.0 | 0.0 | 14.2 |
|  | Grade 3 | 82 | 9 | 11.0 | 5.1 | 19.8 | 83 | 00. | 0.0 | 0.0 | 4.3 | 26 |  | 3.8 | 0.1 | 19.6 | 24 | 00.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 1 | 1.2 | 0.0 | 6.6 | 83 | 00. | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 00.0 | 0.0 | 14.2 |
| Redness (mm) | All | 82 | 31 | 37.8 | 27.3 | 49.2 | 83 | 00. | 0.0 | 0.0 | 4.3 | 26 | 6 | 23.1 | 9.0 | 43.6 | 24 | 00.0 | 0.0 | 14.2 |
|  | $>50$ | 82 | 16 | 19.5 | 11.6 | 29.7 | 83 | 00. | 0.0 | 0.0 | 4.3 | 26 | 2 | 7.7 | 0.9 | 25.1 | 24 | 00.0 | 0.0 | 14.2 |
|  | >100 | 82 | 2 | 2.4 | 0.3 | 8.5 | 83 | 00.0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 00.0 | 0.0 | 14.2 |


|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N |  | \% | LL | UL |
|  | Medical advice | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Swelling (mm) | All | 82 | 14 | 17.1 | 9.7 | 27.0 | 83 | 1 | 1.2 | 0.0 | 6.5 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | $>50$ | 82 | 9 | 11.0 | 5.1 | 19.8 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | >100 | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 |  | 0.0 |  | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom $95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; $\mathrm{LL}=$ lower limit, UL = upper limit

Table 8.140 Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  | PreChemo |  |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  |  |  |  | 95 \% Cl |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% |  | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 82 | 35 | 42.7 | 31.8 | 54.1 | 83 | 28 | 33 |  | 23.7 | 44.9 | 26 | 18 | 69.2 | 48.2 | 85.7 | 241 | 14 | 58.3 | 36.6 | 77.9 |
|  | Grade 2 or 3 | 82 | 17 | 20.7 | 12.6 | 31.1 | 83 | 8 | 9.6 |  | 4.3 | 18.1 | 26 | 12 | 46.2 | 26.6 | 66.6 | 247 | 7 | 29.2 | 12.6 | 51.1 |
|  | Grade 3 | 82 | 5 | 6.1 | 2.0 | 13.7 | 83 | 1 | 1.2 |  | 0.0 | 6.5 | 26 | 5 | 19.2 | 6.6 | 39.4 | 242 | 2 | 8.3 | 1.0 | 27.0 |
|  | Related | 82 | 12 | 14.6 | 7.8 | 24.2 | 83 | 10 | 12. |  | 5.9 | 21.0 | 26 | 1 | 3.8 | 0.1 | 19.6 | 240 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 2 <br> or 3 <br> Related | 82 | 7 | 8.5 | 3.5 | 16.8 | 83 | 4 | 4.8 |  | 1.3 | 11.9 | 26 | 1 | 3.8 | 0.1 | 19.6 | 240 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 3 <br> Related | 82 | 3 | 3.7 | 0.8 | 10.3 | 83 | 0 | 0.0 |  | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 |  | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Gastrointestinal symptoms | All | 82 | 16 | 619.5 | 11.6 | 29.7 | 83 | 8 | 9.6 |  | 4.3 | 18.1 | 26 | 16 | 61.5 | 40.6 | 79.8 | 24 | 13 | 54.2 | 32.8 | 74.4 |
|  | Grade 2 or 3 | 82 | 6 | 7.3 | 2.7 | 15.2 | 83 | 4 | 4.8 |  | 1.3 | 11.9 | 26 | 8 | 30.8 | 14.3 | 51.8 | 24 | 7 | 29.2 | 12.6 | 51.1 |
|  | Grade 3 | 82 | 1 | 1.2 | 0.0 | 6.6 | 83 | 3 | 3.6 |  | 0.8 | 10.2 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 2 | 8.3 | 1.0 | 27.0 |
|  | Related | 82 | 6 | 7.3 | 2.7 | 15.2 | 83 | 2 | 2.4 |  | 0.3 | 8.4 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 2 or 3 Related | 82 | 1 | 1.2 | 0.0 | 6.6 | 83 | 1 | 1.2 |  | 0.0 | 6.5 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 3 <br> Related | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 1 | 1.2 |  | 0.0 | 6.5 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 1 | 1.2 |  | 0.0 | 6.5 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |
| Headache | All | 82 | 16 | 19.5 | 11.6 | 29.7 | 83 | 11 | 13. |  | 6.8 | 22.5 | 26 | 10 | 38.5 | 20.2 | 59.4 | 24 | 12 | 50.0 | 29.1 | 70.9 |
|  | Grade 2 or 3 | 82 | 9 | 11.0 | 5.1 | 19.8 | 83 | 3 | 3.6 |  | 0.8 | 10.2 | 26 | 4 | 15.4 | 4.4 | 34.9 | 24 | 4 | 16.7 | 4.7 | 37.4 |
|  | Grade 3 | 82 | 3 | 3.7 | 0.8 | 10.3 | 83 | 0 | 0.0 |  | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Related | 82 | 6 | 7.3 | 2.7 | 15.2 | 83 | 3 | 3.6 |  | 0.8 | 10.2 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Grade 2 or 3 <br> Related | 82 | 3 | 3.7 | 0.8 | 10.3 | 83 | 1 | 1.2 |  | 0.0 | 6.5 | 26 | 2 | 7.7 | 0.9 | 25.1 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 3 <br> Related | 82 | 2 | 2.4 | 0.3 | 8.5 | 83 | 0 | 0.0 |  | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 |  | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Myalgia | All | 82 | 40 | 48.8 | 37.6 | 60.1 | 83 | 9 | 10 |  | 5.1 | 19.6 | 26 | 9 | 34.6 | 17.2 | 55.7 | 248 | 8 | 33.3 | 15.6 | 55.3 |
|  | Grade 2 or 3 | 82 | 13 | 15.9 | 8.7 | 25.6 | 83 | 6 | 7.2 |  | 2.7 | 15.1 | 26 | 7 | 26.9 | 11.6 | 47.8 | 24 | - | 12.5 | 2.7 | 32.4 |
|  | Grade 3 | 82 | 6 | 7.3 | 2.7 | 15.2 | 83 | 1 | 1.2 |  | 0.0 | 6.5 | 26 | 2 | 7.7 | 0.9 | 25.1 | 24 | 2 | 8.3 | 1.0 | 27.0 |
|  | Related | 82 | 20 | 24.4 | 15.6 | 35.1 | 83 | 2 | 2.4 |  | 0.3 | 8.4 | 26 | 4 | 15.4 | 4.4 | 34.9 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Grade 2 or 3 <br> Related | 82 | 10 | 12.2 | 6.0 | 21.3 | 83 | 2 | 2.4 |  | 0.3 | 8.4 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |

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|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 3 Related | 82 | 6 | 7.3 | 2.7 | 15.2 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Shivering | All | 82 | 18 | 22.0 | 13.6 | 32.5 | 83 | 7 | 8.4 | 3.5 | 16.6 | 26 | 8 | 30.8 | 14.3 | 51.8 | 24 | 6 | 25.0 | 9.8 | 46.7 |
|  | Grade 2 or 3 | 82 | 5 | 6.1 | 2.0 | 13.7 | 83 | 5 | 6.0 | 2.0 | 13.5 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Grade 3 | 82 | 3 | 3.7 | 0.8 | 10.3 | 83 | 2 | 2.4 | 0.3 | 8.4 | 26 | 2 | 7.7 | 0.9 | 25.1 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Related | 82 | 10 | 12.2 | 6.0 | 21.3 | 83 | 3 | 3.6 | 0.8 | 10.2 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 1 | 4.2 | 0.1 | 21.1 |
|  | Grade 2 or 3 <br> Related | 82 | 5 | 6.1 | 2.0 | 13.7 | 83 | 2 | 2.4 | 0.3 | 8.4 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 3 Related | 82 | 3 | 3.7 | 0.8 | 10.3 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 82 | 13 | 15.9 | 8.7 | 25.6 | 83 | 2 | 2.4 | 0.3 | 8.4 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 2 | 8.3 | 1.0 | 27.0 |
|  | $\geq 37.5$ | 82 | 13 | 15.9 | 8.7 | 25.6 | 83 | 2 | 2.4 | 0.3 | 8.4 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 |  | 8.3 | 1.0 | 27.0 |
|  | >38.0 | 82 | 2 | 2.4 | 0.3 | 8.5 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | $>38.5$ | 82 | 1 | 1.2 | 0.0 | 6.6 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | - | 0.0 | 0.0 | 14.2 |
|  | >39.0 | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | - | 0.0 | 0.0 | 14.2 |
|  | >39.5 | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | >40.0 | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Related | 82 | 11 | 13.4 | 6.9 | 22.7 | 83 | 1 | 1.2 | 0.0 | 6.5 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | $\begin{array}{\|l\|} \hline>38.0 \\ \text { Related } \\ \hline \end{array}$ | 82 | 2 | 2.4 | 0.3 | 8.5 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | $\begin{aligned} & >39.0 \\ & \text { Related } \end{aligned}$ | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 69 | 38 | 55.1 | 42.6 | 67.1 | 81 | 42 | 51.9 | 40.5 | 63.1 | 24 |  | 66.7 | 44.7 | 84.4 | 22 | 14 | 63.6 | 40.7 | 82.8 |
|  | Grade 2 or 3 | 69 | 19 | 27.5 | 17.5 | 39.6 | 81 | 21 | 25.9 | 16.8 | 36.9 | 24 | 8 | 33.3 | 15.6 | 55.3 | 22 | 8 | 36.4 | 17.2 | 59.3 |
|  | Grade 3 | 69 | 5 | 7.2 | 2.4 | 16.1 | 81 | 5 | 6.2 | 2.0 | 13.8 | 24 | 4 | 16.7 | 4.7 | 37.4 | 22 | 1 | 4.5 | 0.1 | 22.8 |
|  | Related | 69 | 5 | 7.2 | 2.4 | 16.1 | 81 | 8 | 9.9 | 4.4 | 18.5 | 24 |  | 4.2 | 0.1 | 21.1 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Grade 2 or 3 <br> Related | 69 | 2 | 2.9 | 0.4 | 10.1 | 81 | 4 | 4.9 | 1.4 | 12.2 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Grade 3 Related | 69 | 0 | 0.0 | 0.0 | 5.2 | 81 | 1 | 1.2 | 0.0 | 6.7 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Medical advice | 69 | 1 | 1.4 | 0.0 | 7.8 | 81 | 1 | 1.2 | 0.0 | 6.7 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
| Gastrointestinal symptoms | All | 69 | 27 | 39.1 | 27.6 | 51.6 | 81 | 28 | 34.6 | 24.3 | 46.0 | 24 | 11 | 45.8 | 25.6 | 67.2 | 22 | 10 | 45.5 | 24.4 | 67.8 |
|  | Grade 2 or 3 | 69 | 14 | 20.3 | 11.6 | 31.7 | 81 | 9 | 11.1 | 5.2 | 20.0 | 24 | 5 | 20.8 | 7.1 | 42.2 | 22 | 6 | 27.3 | 10.7 | 50.2 |
|  | Grade 3 | 69 | 4 | 5.8 | 1.6 | 14.2 | 81 | 1 | 1.2 | 0.0 | 6.7 | 24 |  | 4.2 | 0.1 | 21.1 | 22 | 2 | 9.1 | 1.1 | 29.2 |
|  | Related | 69 | 5 | 7.2 | 2.4 | 16.1 | 81 | 2 | 2.5 | 0.3 | 8.6 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Grade 2 or 3 <br> Related | 69 | 2 | 2.9 | 0.4 | 10.1 | 81 | 2 | 2.5 | 0.3 | 8.6 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |

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|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  |  |  |  | 95 \% CI |  | 95 \% CI |  |  |  |  |  |  |  | 95 \% Cl |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 3 Related | 69 | 1 | 1.4 | 0.0 | 7.8 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Medical advice | 69 | 1 | 1.4 | 0.0 | 7.8 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
| Headache | All | 69 | 20 | 29.0 | 18.7 | 41.2 | 81 | 17 | 21.0 | 12.7 | 31.5 | 24 | 9 | 37.5 | 18.8 | 59.4 | 22 | 7 | 31.8 | 13.9 | 54.9 |
|  | Grade 2 or 3 | 69 | 10 | 14.5 | 7.2 | 25.0 | 81 | 5 | 6.2 | 2.0 | 13.8 | 24 | 4 | 16.7 | 4.7 | 37.4 | 22 | 2 | 9.1 | 1.1 | 29.2 |
|  | Grade 3 | 69 | 2 | 2.9 | 0.4 | 10.1 | 81 | 2 | 2.5 | 0.3 | 8.6 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Related | 69 | 5 | 7.2 | 2.4 | 16.1 | 81 | 2 | 2.5 | 0.3 | 8.6 | 24 | 2 | 8.3 | 1.0 | 27.0 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Grade 2 or 3 <br> Related | 69 | 3 | 4.3 | 0.9 | 12.2 | 81 | 1 | 1.2 | 0.0 | 6.7 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Grade 3 Related | 69 | 0 | 0.0 | 0.0 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Medical advice | 69 | 1 | 1.4 | 0.0 | 7.8 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
| Myalgia | All | 69 | 22 | 31.9 | 21.2 | 44.2 | 81 | 16 | 19.8 | 11.7 | 30.1 | 24 | 8 | 33.3 | 15.6 | 55.3 | 22 | 6 | 27.3 | 10.7 | 50.2 |
|  | Grade 2 or 3 | 69 | 11 | 15.9 | 8.2 | 26.7 | 81 | 8 | 9.9 | 4.4 | 18.5 | 24 | 3 | 12.5 | 2.7 | 32.4 | 22 | 4 | 18.2 | 5.2 | 40.3 |
|  | Grade 3 | 69 | 1 | 1.4 | 0.0 | 7.8 | 81 | 1 | 1.2 | 0.0 | 6.7 | 24 | 2 | 8.3 | 1.0 | 27.0 | 22 |  | 0.0 | 0.0 | 15.4 |
|  | Related | 69 | 10 | 14.5 | 7.2 | 25.0 | 81 | 3 | 3.7 | 0.8 | 10.4 | 24 | 3 | 12.5 | 2.7 | 32.4 | 22 |  | 4.5 | 0.1 | 22.8 |
|  | Grade 2 or 3 <br> Related | 69 | 5 | 7.2 | 2.4 | 16.1 | 81 | 1 | 1.2 | 0.0 | 6.7 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 1 | 4.5 | 0.1 | 22.8 |
|  | Grade 3 Related | 69 | 0 | 0.0 | 0.0 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Medical advice | 69 | 0 | 0.0 | 0.0 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
| Shivering | All | 69 | 12 | 17.4 | 9.3 | 28.4 | 81 | 11 | 13.6 | 7.0 | 23.0 | 24 |  | 25.0 | 9.8 | 46.7 | 22 |  | 27.3 | 10.7 | 50.2 |
|  | Grade 2 or 3 | 69 | 5 | 7.2 | 2.4 | 16.1 | 81 | 1 | 1.2 | 0.0 | 6.7 | 24 | 4 | 16.7 | 4.7 | 37.4 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Grade 3 | 69 | 1 | 1.4 | 0.0 | 7.8 | 81 | 1 | 1.2 | 0.0 | 6.7 | 24 |  | 4.2 | 0.1 | 21.1 | 22 |  | 0.0 | 0.0 | 15.4 |
|  | Related | 69 | 5 | 7.2 | 2.4 | 16.1 | 81 | 3 | 3.7 | 0.8 | 10.4 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 1 | 4.5 | 0.1 | 22.8 |
|  | Grade 2 or 3 <br> Related | 69 | 2 | 2.9 | 0.4 | 10.1 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 1 | 4.2 | 0.1 | 21.1 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Grade 3 <br> Related | 69 | 1 | 1.4 | 0.0 | 7.8 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Medical advice | 69 | 0 | 0.0 | 0.0 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 69 | 3 | 4.3 | 0.9 | 12.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 5 | 20.8 | 7.1 | 42.2 | 22 | 1 | 4.5 | 0.1 | 22.8 |
|  | $\geq 37.5$ | 69 | 3 | 4.3 | 0.9 | 12.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 5 | 20.8 | 7.1 | 42.2 | 22 | 1 | 4.5 | 0.1 | 22.8 |
|  | >38.0 | 69 | 1 | 1.4 | 0.0 | 7.8 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 |  | 4.5 | 0.1 | 22.8 |
|  | >38.5 | 69 | 0 | 0.0 | 0.0 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | $>39.0$ | 69 | 0 | 0.0 | 0.0 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | $>39.5$ | 69 | 0 | 0.0 | 0.0 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | >40.0 | 69 | 0 | 0.0 | 0.0 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | Related | 69 | 2 | 2.9 | 0.4 | 10.1 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 2 | 8.3 | 1.0 | 27.0 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | $\begin{array}{\|l\|} \hline>38.0 \\ \text { Related } \end{array}$ | 69 | 1 | 1.4 | 0.0 | 7.8 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
|  | $\begin{aligned} & >39.0 \\ & \text { Related } \end{aligned}$ | 69 | 0 | 0.0 | 0.0 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |


|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Medical advice | 69 | 0 | 0.0 | 0.0 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 0 | 0.0 | 0.0 | 14.2 | 22 | 0 | 0.0 | 0.0 | 15.4 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 151 | 73 | 48.3 | 40.1 | 56.6 | 164 | 70 | 42.7 | 35.0 | 50.6 | 50 | 34 | 68.0 | 53.3 | 80.5 | 46 | 28 | 60.9 | 45.4 | 74.9 |
|  | Grade 2 or 3 | 151 | 36 | 23.8 | 17.3 | 31.4 | 164 | 29 | 17.7 | 12.2 | 24.4 | 50 | 20 | 40.0 | 26.4 | 54.8 | 46 | 15 | 32.6 | 19.5 | 48.0 |
|  | Grade 3 | 151 | 10 | 6.6 | 3.2 | 11.8 | 164 | 6 | 3.7 | 1.4 | 7.8 | 50 | 9 | 18.0 | 8.6 | 31.4 | 46 | 3 | 6.5 | 1.4 | 17.9 |
|  | Related | 151 | 17 | 11.3 | 6.7 | 17.4 | 164 | 18 | 11.0 | 6.6 | 16.8 | 50 | 2 | 4.0 | 0.5 | 13.7 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Grade 2 or 3 <br> Related | 151 | 9 | 6.0 | 2.8 | 11.0 | 164 | 8 | 4.9 | 2.1 | 9.4 | 50 | 1 | 2.0 | 0.1 | 10.6 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Grade 3 Related | 151 | 3 | 2.0 | 0.4 | 5.7 | 164 | 1 | 0.6 | 0.0 | 3.4 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Medical advice | 151 | 1 | 0.7 | 0.0 | 3.6 | 164 | 1 | 0.6 | 0.0 | 3.4 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
| Gastrointestinal symptoms | All | 151 | 43 | 28.5 | 21.4 | 36.4 | 164 | 36 | 22.0 | 15.9 | 29.1 | 50 | 27 | 54.0 | 39.3 | 68.2 | 46 | 23 | 50.0 | 34.9 | 65.1 |
|  | Grade 2 or 3 | 151 | 20 | 13.2 | 8.3 | 19.7 | 164 | 13 | 7.9 | 4.3 | 13.2 | 50 | 13 | 26.0 | 14.6 | 40.3 | 46 | 13 | 28.3 | 16.0 | 43.5 |
|  | Grade 3 | 151 | 5 | 3.3 | 1.1 | 7.6 | 164 | 4 | 2.4 | 0.7 | 6.1 | 50 | 2 | 4.0 | 0.5 | 13.7 | 46 | 4 | 8.7 | 2.4 | 20.8 |
|  | Related | 151 | 11 | 17.3 | 3.7 | 12.7 | 164 | 4 | 2.4 | 0.7 | 6.1 | 50 | 4 | 8.0 | 2.2 | 19.2 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Grade 2 or 3 <br> Related | 151 | 3 | 2.0 | 0.4 | 5.7 | 164 | 3 | 1.8 | 0.4 | 5.3 | 50 | 1 | 2.0 | 0.1 | 10.6 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Grade 3 Related | 151 | 1 | 0.7 | 0.0 | 3.6 | 164 | 1 | 0.6 | 0.0 | 3.4 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Medical advice | 151 | 1 | 0.7 | 0.0 | 3.6 | 164 | 1 | 0.6 | 0.0 | 3.4 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 1 | 2.2 | 0.1 | 11.5 |
| Headache | All | 151 | 36 | 23.8 | 17.3 | 31.4 | 164 | 28 | 17.1 | 11.7 | 23.7 | 50 | 19 | 38.0 | 24.7 | 52.8 | 46 | 19 | 41.3 | 27.0 | 56.8 |
|  | Grade 2 or 3 | 151 | 19 | 12.6 | 7.7 | 19.0 | 164 | 8 | 4.9 | 2.1 | 9.4 | 50 | 8 | 16.0 | 7.2 | 29.1 | 46 | 6 | 13.0 | 4.9 | 26.3 |
|  | Grade 3 | 151 | 5 | 3.3 | 1.1 | 7.6 | 164 | 2 | 1.2 | 0.1 | 4.3 | 50 | 1 | 2.0 | 0.1 | 10.6 | 46 | 1 | 2.2 | 0.1 | 11.5 |
|  | Related | 151 | 11 | 17.3 | 3.7 | 12.7 | 164 | 5 | 3.0 | 1.0 | 7.0 | 50 | 5 | 10.0 | 3.3 | 21.8 | 46 | 1 | 2.2 | 0.1 | 11.5 |
|  | Grade 2 or 3 <br> Related | 151 | 6 | 4.0 | 1.5 | 8.4 | 164 | 2 | 1.2 | 0.1 | 4.3 | 50 | 3 | 6.0 | 1.3 | 16.5 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Grade 3 Related | 151 | 2 | 1.3 | 0.2 | 4.7 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Medical advice | 151 | 1 | 0.7 | 0.0 | 3.6 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
| Myalgia | All | 151 | 62 | 41.1 | 33.1 | 49.3 | 164 | 25 | 15.2 | 10.1 | 21.7 | 50 | 17 | 34.0 | 21.2 | 48.8 | 46 | 14 | 30.4 | 17.7 | 45.8 |
|  | Grade 2 or 3 | 151 | 24 | 15.9 | 10.5 | 22.7 | 164 | 14 | 8.5 | 4.7 | 13.9 | 50 | 10 | 20.0 | 10.0 | 33.7 | 46 | 7 | 15.2 | 6.3 | 28.9 |
|  | Grade 3 | 151 | 7 | 4.6 | 1.9 | 9.3 | 164 | 2 | 1.2 | 0.1 | 4.3 | 50 | 4 | 8.0 | 2.2 | 19.2 | 46 | 2 | 4.3 | 0.5 | 14.8 |
|  | Related | 151 | 30 | 19.9 | 13.8 | 27.1 | 164 | 5 | 3.0 | 1.0 | 7.0 | 50 | 7 | 14.0 | 5.8 | 26.7 | 46 | 2 | 4.3 | 0.5 | 14.8 |
|  | Grade 2 or 3 <br> Related | 151 | 15 | 9.9 | 5.7 | 15.9 | 164 | 3 | 1.8 | 0.4 | 5.3 | 50 | 4 | 8.0 | 2.2 | 19.2 | 46 | 1 | 2.2 | 0.1 | 11.5 |
|  | Grade 3 Related | 151 | 6 | 4.0 | 1.5 | 8.4 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 1 | 2.0 | 0.1 | 10.6 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Medical advice | 151 | 0 | 0.0 | 0.0 | 2.4 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
| Shivering | All | 151 | 30 | 19.9 | 13.8 | 27.1 | 164 | 18 | 11.0 | 6.6 | 16.8 | 50 | 14 | 28.0 | 16.2 | 42.5 | 46 | 12 | 26.1 | 14.3 | 41.1 |

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|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 2 or 3 | 151 | 10 | 6.6 | 3.2 | 11.8 | 164 | 6 | 3.7 | 1.4 | 7.8 | 50 | 7 | 14.0 | 5.8 | 26.7 | 46 | 1 | 2.2 | 0.1 | 11.5 |
|  | Grade 3 | 1514 | 4 | 2.6 | 0.7 | 6.6 | 164 | 3 | 1.8 | 0.4 | 5.3 | 50 | 3 | 6.0 | 1.3 | 16.5 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Related | 151 | 15 | 9.9 | 5.7 | 15.9 | 164 |  | 3.7 | 1.4 | 7.8 | 50 | 2 | 4.0 | 0.5 | 13.7 | 46 | 2 | 4.3 | 0.5 | 14.8 |
|  | Grade 2 or 3 <br> Related | 1517 | 7 | 4.6 | 1.9 | 9.3 | 164 | 2 | 1.2 | 0.1 | 4.3 | 50 | 2 | 4.0 | 0.5 | 13.7 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Grade 3 <br> Related | 1514 | 4 | 2.6 | 0.7 | 6.6 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 1 | 2.0 | 0.1 | 10.6 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Medical advice | 1510 | 0 | 0.0 | 0.0 | 2.4 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 151 | 16 | 10.6 | 6.2 | 16.6 | 164 | 2 | 1.2 | 0.1 | 4.3 | 50 | 5 | 10.0 | 3.3 | 21.8 | 46 | 3 | 6.5 | 1.4 | 17.9 |
|  | $\geq 37.5$ | 151 | 16 | 10.6 | 6.2 | 16.6 | 164 | 2 | 1.2 | 0.1 | 4.3 | 50 | 5 | 10.0 | 3.3 | 21.8 | 46 | 3 | 6.5 | 1.4 | 17.9 |
|  | $>38.0$ | 1513 | 3 | 2.0 | 0.4 | 5.7 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 1 | 2.2 | 0.1 | 11.5 |
|  | $>38.5$ | 1511 | 1 | 0.7 | 0.0 | 3.6 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | $>39.0$ | 1510 | 0 | 0.0 | 0.0 | 2.4 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | $>39.5$ | 1510 | 0 | 0.0 | 0.0 | 2.4 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | >40.0 | 1510 | 0 | 0.0 | 0.0 | 2.4 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Related | 151 | 13 | 8.6 | 4.7 | 14.3 | 164 | 1 | 0.6 | 0.0 | 3.4 | 50 | 2 | 4.0 | 0.5 | 13.7 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | $\begin{array}{\|l\|} \hline>38.0 \\ \text { Related } \\ \hline \end{array}$ | 1513 | 3 | 2.0 | 0.4 | 5.7 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | $\begin{aligned} & >39.0 \\ & \text { Related } \end{aligned}$ | 1510 | 0 | 0.0 | 0.0 | 2.4 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 0 | 0.0 | 0.0 | 7.7 |
|  | Medical advice | 1510 | 0 | 0.0 | 0.0 | 2.4 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 0 | 0.0 | 0.0 | 7.1 | 46 | 1 | 2.2 | 0.1 | 11.5 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 82 | 53 | 64.6 | 53.3 | 74.9 | 83 | 50 | 60.2 | 48.9 | 70.8 | 26 | 21 | 80.8 | 60.6 | 93.4 | 24 | 16 | 66.7 | 44.7 | 84.4 |
|  | Grade 2 or 3 | 82 | 29 | 35.4 | 25.1 | 46.7 | 83 | 26 | 31.3 | 21.6 | 42.4 | 26 | 14 | 53.8 | 33.4 | 73.4 | 24 | 10 | 41.7 | 22.1 | 63.4 |
|  | Grade 3 | 82 | 10 | 12.2 | 6.0 | 21.3 | 83 | 5 | 6.0 | 2.0 | 13.5 | 26 | 6 | 23.1 | 9.0 | 43.6 | 24 | 3 | 12.5 | 2.7 | 32.4 |
|  | Related | 82 | 15 | 18.3 | 10.6 | 28.4 | 83 | 14 | 16.9 | 9.5 | 26.7 | 26 | 2 | 7.7 | 0.9 | 25.1 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 2 or 3 <br> Related | 82 | 9 | 11.0 | 5.1 | 19.8 | 83 | 8 | 9.6 | 4.3 | 18.1 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 3 <br> Related | 82 | 3 | 3.7 | 0.8 | 10.3 | 83 | 1 | 1.2 | 0.0 | 6.5 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 1 | 1.2 | 0.0 | 6.6 | 83 | 1 | 1.2 | 0.0 | 6.5 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Gastrointestinal symptoms | All | 82 | 30 | 36.6 | 26.2 | 48.0 | 83 | 33 | 39.8 | 29.2 | 51.1 | 26 | 18 | 69.2 | 48.2 | 85.7 | 24 | 15 | 62.5 | 40.6 | 81.2 |
|  | Grade 2 or 3 | 82 | 16 | 19.5 | 11.6 | 29.7 | 83 | 11 | 13.3 | 6.8 | 22.5 | 26 | 8 | 30.8 | 14.3 | 51.8 | 24 | 10 | 41.7 | 22.1 | 63.4 |
|  | Grade 3 | 82 | 5 | 6.1 | 2.0 | 13.7 | 83 | 4 | 4.8 | 1.3 | 11.9 | 26 |  | 3.8 | 0.1 | 19.6 | 24 | 3 | 12.5 | 2.7 | 32.4 |
|  | Related | 82 | 7 | 8.5 | 3.5 | 16.8 | 83 | 3 | 3.6 | 0.8 | 10.2 | 26 | 4 | 15.4 | 4.4 | 34.9 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 2 or 3 <br> Related | 82 | 2 | 2.4 | 0.3 | 8.5 | 83 | 3 | 3.6 | 0.8 | 10.2 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Grade 3 Related | 82 | 1 | 1.2 | 0.0 | 6.6 | 83 | 1 | 1.2 | 0.0 | 6.5 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 1 | 1.2 | 0.0 | 6.6 | 83 | 1 | 1.2 | 0.0 | 6.5 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 1 | 4.2 | 0.1 | 21.1 |
| Headache | All | 82 | 28 | 34.1 | 24.0 | 45.4 | 83 | 24 | 28.9 | 19.5 | 39.9 | 26 | 13 | 50.0 | 29.9 | 70.1 | 24 | 14 | 58.3 | 36.6 | 77.9 |

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|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  |  |  |  | 95 \% CI |  | 95 \% Cl |  |  |  |  |  |  |  | 95 \% Cl |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N |  | \% | LL | UL |
|  | Grade 2 or 3 | 82 | 15 | 18.3 | 10.6 | 28.4 | 83 | 8 | 9.6 | 4.3 | 18.1 | 26 | 6 | 23.1 | 9.0 | 43.6 | 245 |  | 20.8 | 7.1 | 42.2 |
|  | Grade 3 | 82 | 5 | 6.1 | 2.0 | 13.7 | 83 | 2 | 2.4 | 0.3 | 8.4 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 |  | 4.2 | 0.1 | 21.1 |
|  | Related | 82 | 10 | 12.2 | 6.0 | 21.3 | 83 | 5 | 6.0 | 2.0 | 13.5 | 26 | 5 | 19.2 | 6.6 | 39.4 | 24 |  | 4.2 | 0.1 | 21.1 |
|  | Grade 2 or 3 <br> Related | 82 | 5 | 6.1 | 2.0 | 13.7 | 83 | 2 | 2.4 | 0.3 | 8.4 | 26 | 3 | 11.5 | 2.4 | 30.2 | 240 |  | 0.0 | 0.0 | 14.2 |
|  | Grade 3 <br> Related | 82 | 2 | 2.4 | 0.3 | 8.5 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 240 |  | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 1 | 1.2 | 0.0 | 6.6 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 240 |  | 0.0 | 0.0 | 14.2 |
| Myalgia | All | 82 | 48 | 58.5 | 47.1 | 69.3 | 83 | 21 | 25.3 | 16.4 | 36.0 | 26 | 10 | 38.5 | 20.2 | 59.4 | 24 |  | 37.5 | 18.8 | 59.4 |
|  | Grade 2 or 3 | 82 | 21 | 25.6 | 16.6 | 36.4 | 83 | 13 | 15.7 | 8.6 | 25.3 | 26 | 8 | 30.8 | 14.3 | 51.8 | 245 |  | 20.8 | 7.1 | 42.2 |
|  | Grade 3 | 82 | 7 | 8.5 | 3.5 | 16.8 | 83 | 2 | 2.4 | 0.3 | 8.4 | 26 | 4 | 15.4 | 4.4 | 34.9 | 242 |  | 8.3 | 1.0 | 27.0 |
|  | Related | 82 | 24 | 29.3 | 19.7 | 40.4 | 83 | 4 | 4.8 | 1.3 | 11.9 | 26 | 5 | 19.2 | 6.6 | 39.4 | 24 |  | 4.2 | 0.1 | 21.1 |
|  | Grade 2 or 3 <br> Related | 82 | 13 | 15.9 | 8.7 | 25.6 | 83 | 3 | 3.6 | 0.8 | 10.2 | 26 | 3 | 11.5 | 2.4 | 30.2 | 24 |  | 4.2 | 0.1 | 21.1 |
|  | Grade 3 <br> Related | 82 | 6 | 7.3 | 2.7 | 15.2 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 |  | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 |  | 0.0 | 0.0 | 14.2 |
| Shivering | All | 82 | 27 | 32.9 | 22.9 | 44.2 | 83 | 16 | 19.3 | 11.4 | 29.4 | 26 | 10 | 38.5 | 20.2 | 59.4 | 24 |  | 37.5 | 18.8 | 59.4 |
|  | Grade 2 or 3 | 82 | 9 | 11.0 | 5.1 | 19.8 | 83 | 6 | 7.2 | 2.7 | 15.1 | 26 | 4 | 15.4 | 4.4 | 34.9 | 24 |  | 4.2 | 0.1 | 21.1 |
|  | Grade 3 | 82 | 3 | 3.7 | 0.8 | 10.3 | 83 | 3 | 3.6 | 0.8 | 10.2 | 26 | 2 | 7.7 | 0.9 | 25.1 | 24 |  | 0.0 | 0.0 | 14.2 |
|  | Related | 82 | 14 | 17.1 | 9.7 | 27.0 | 83 | 4 | 4.8 | 1.3 | 11.9 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 |  | 4.2 | 0.1 | 21.1 |
|  | Grade 2 or 3 <br> Related | 82 | 6 | 7.3 | 2.7 | 15.2 | 83 | 2 | 2.4 | 0.3 | 8.4 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 |  | 0.0 | 0.0 | 14.2 |
|  | Grade 3 <br> Related | 82 | 3 | 3.7 | 0.8 | 10.3 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 |  | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 240 |  | 0.0 | 0.0 | 14.2 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 82 | 15 | 18.3 | 10.6 | 28.4 | 83 | 2 | 2.4 | 0.3 | 8.4 | 26 | 5 | 19.2 | 6.6 | 39.4 | 24 |  | 12.5 | 2.7 | 32.4 |
|  | $\geq 37.5$ | 82 | 15 | 18.3 | 10.6 | 28.4 | 83 | 2 | 2.4 | 0.3 | 8.4 | 26 | 5 | 19.2 | 6.6 | 39.4 | 24 |  | 12.5 | 2.7 | 32.4 |
|  | >38.0 | 82 | 3 | 3.7 | 0.8 | 10.3 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 |  | 4.2 | 0.1 | 21.1 |
|  | $>38.5$ | 82 | 1 | 1.2 | 0.0 | 6.6 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 |  | 0.0 | 0.0 | 14.2 |
|  | >39.0 | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 |  | 0.0 | 0.0 | 14.2 |
|  | $>39.5$ | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 |  | 0.0 | 0.0 | 14.2 |
|  | >40.0 | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 |  | 0.0 | 0.0 | 14.2 |
|  | Related | 82 | 12 | 14.6 | 7.8 | 24.2 | 83 | 1 | 1.2 | 0.0 | 6.5 | 26 | 2 | 7.7 | 0.9 | 25.1 | 24 |  | 0.0 | 0.0 | 14.2 |
|  | $\begin{aligned} & \hline>38.0 \\ & \text { Related } \end{aligned}$ | 82 | 3 | 3.7 | 0.8 | 10.3 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 240 |  | 0.0 | 0.0 | 14.2 |
|  | $>39.0$ <br> Related | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 240 |  | 0.0 | 0.0 | 14.2 |
|  | Medical advice | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 |  | 4.2 | 0.1 | 21.1 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group

## CONFIDENTIAL

Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit
$\left(^{*}\right)=$ Temperature is measured by oral, axillary or tympanic routes
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for oral, axillary or tympanic route

Table 8.141 Number and percentage of subjects who reported temperature by half degree measured via oral route during the 7-day (Days 0-6) post-vaccination period following each dose (no conversion) by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  | Placebo |  |  |  | HZ/su |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% Cl |  |  |  | 95 \% CI |  |  |  | 95 \% CI |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type | N | n \% | LL | UL | N | n \% | LL |  | N | n \% | \% LL | L UL |  | n \% |  |  | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 82 | 44.9 | 1.3 | 312.0 | 83 | 11.2 | 0.0 | 6.5 | 260 | 00.0 | 0.00 .0 | 0.0 13.2 | 240 | 00. | 0.0 | 0.0 | O 14.2 |
|  | $\geq 35.5$ | 82 | 44.9 | 1.3 | 312.08 | 83 | 11.2 | 0.0 | 6.5 | 260 | 00.0 | 0.00 .0 | 0.013 .2 | 240 | 00. | 0.0 | 0.0 | 014.2 |
|  | >36.0 | 82 | 44.9 | 1.3 | 312.08 | 83 | 11.2 | 0.0 | 6.5 | 260 | 00.0 | 0.00 .0 | 0.013 .2 | 240 | 00. | 0.0 | 0.0 | 014.2 |
|  | >36.5 | 82 | 44.9 | 1.3 | 312.08 | 83 | 11.2 | 0.0 | 6.5 | 260 | 00.0 | 0.00 .0 | 0.013 .2 | 240 | 00. | 0.0 | 0.0 | 014.2 |
|  | >37.0 | 82 | 44.9 | 1.3 | 312.0 | 83 | 11.2 | 0.0 | 6.5 | 260 | 00.0 | 0.00 .0 | 0.013 .2 | 240 | 00. | 0.0 | 0.0 | 014.2 |
|  | >37.5 | 82 | 11.2 | 0.0 | 06.6 | 83 | 11.2 | 0.0 | 6.5 | 260 | 00.0 | 0.00 .0 | 0.013 .2 | 240 | 00. | 0.0 | 0.0 | 014.2 |
|  | >38.0 | 82 | 00.0 | 0.0 | 0 4.4 | 83 | 00.0 | 0.0 | 4.3 | 260 | 00.0 | 0.00 .0 | 0.013 .2 | 240 | 00. | 0.0 | 0.0 | . 14.2 |
|  | >38.5 | 82 | 00.0 | 0.0 | 04.4 | 83 | 00.0 | 0.0 | 4.3 | 260 | 00.0 | 0.00 .0 | 0.013 .2 | 240 | 00. | 0.0 | 0.0 | 014.2 |
|  | >39.0 | 82 | 00.0 | 0.0 | 04.4 | 83 | 00.0 | 0.0 | 4.3 | 260 | 00.0 | 0.00 .0 | 0.013 .2 | 240 | 00. | 0.0 | 0.0 | 014.2 |
|  | >39.5 | 82 | 00.0 | 0.0 | 04.4 | 83 | 00.0 | 0.0 | 4.3 | 260 | 00.0 | 0.00 .0 | 0.013 .2 | 240 | 00. | 0.0 | 0.0 | 014.2 |
|  | >40.0 | 82 | 00.0 | 0.0 | 04.4 | 83 | 00.0 | 0.0 | 4.3 | 260 | 00.0 | 0.00 .0 | 0.013 .2 | 240 | 00. | 0.0 | 0.0 | 014.2 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 69 | 22.9 | 0.4 | 410.1 1 | 81 | 00.0 | 0.0 | 4.5 | 241 | 14.2 | 4.20 .1 | 0.121 .1 | 220 | 0 | 0.0 | 0.0 | 015.4 |
|  | $\geq 35.5$ | 69 | 22.9 | 0.4 | . 410.18 | 81 | 00.0 | 0.0 | 4.5 | 241 | 14.2 | 4.20 .1 | 0.121 .1 | 220 | 00. | 0.0 | 0.0 | 015.4 |
|  | >36.0 | 69 | 22.9 | 0.4 | 410.181 | 81 | 00.0 | 0.0 | 4.5 | 241 | 14.2 | 4.20 .1 | 0.121 .1 | 220 | 00. | 0.0 | 0.0 | 015.4 |
|  | >36.5 | 69 | 22.9 | 0.4 | . 410.181 | 81 | 00.0 | 0.0 | 4.5 | 241 | 14.2 | 4.20 .1 | 0.121 .1 | 220 | 00. | 0.0 | 0.0 | . 15.4 |
|  | >37.0 | 69 | 22.9 | 0.4 | . 410.181 | 81 | 00.0 | 0.0 | 4.5 | 241 | 14.2 | 4.20 .1 | 0.121 .1 | 220 | 00. | 0.0 | 0.0 | . 15.4 |
|  | >37.5 | 69 | 22.9 | 0.4 | . 10.181 | 81 | 00.0 | 0.0 | 4.5 | 241 | 14.2 | 4.20 .1 | 0.121 .1 | 220 | 00. | 0.0 | 0.0 | O 15.4 |
|  | $>38.0$ | 69 | 11.4 | 0.0 | . 7.8 | 81 | 00.0 | 0.0 | 4.5 | 240 | 00.0 | 0.00 .0 | 0.014 .2 | 220 | 00. | 0.0 | 0.0 | 015.4 |
|  | >38.5 | 69 | 00.0 | 0.0 | 05.2 | 81 | 00.0 | 0.0 | 4.5 | 240 | 00.0 | 0.00 .0 | 0.014 .2 | 220 | 00. | 0.0 | 0.0 | 015.4 |
|  | >39.0 | 69 | 00.0 | 0.0 | 05.2 | 81 | 00.0 | 0.0 | 4.5 | 240 | 00.0 | 0.00 .0 | 0.014 .2 | 220 | 00. | 0.0 | 0.0 | O 15.4 |
|  | >39.5 | 69 | 00.0 | 0.0 | 05.2 | 81 | 00.0 | 0.0 | 4.5 | 240 | 00.0 | 0.00 .0 | 0.014 .2 | 220 | 00. | 0.0 | 0.0 | 015.4 |
|  | >40.0 | 69 | 00.0 | 0.0 | 05.2 | 81 | 00.0 | 0.0 | 4.5 | 240 | 00.0 | 0.00 .0 | 0.014 .2 | 220 | 00. | 0.0 | 0.0 | 015.4 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 151 | 64.0 | 1.5 | 5 8.4 | 164 | 10.6 | 0.0 | 3.4 | 50 1 | 12.0 | $2.0 \mid 0.1$ | .110.6 | 46 | 010. | 0.0 | 0.0 | 0.7 .7 |
|  | $\geq 35.5$ | 151 | 64.0 | 1.5 | 58.4 | 164 | 10.6 | 0.0 | 3.4 | 501 | 12.0 | 2.00 .1 | 0.110 .6 | 460 | 00. | 0.0 | 0.0 | 07.7 |
|  | >36.0 | 151 | 64.0 | 1.5 | 158.4 | 164 | 10.6 | 0.0 | 3.4 | 501 | 12.0 | 2.00 .1 | 0.110 .6 | 460 | 00. | 0.0 | 0.0 | 07.7 |
|  | >36.5 | 151 | 64.0 | 1.5 | 18.4 | 164 | 10.6 | 0.0 | 3.4 | 501 | 12.0 | 2.00 .1 | 0.110 .6 | 460 | 00. | 0.0 | 0.0 | . 7.7 |
|  | >37.0 | 151 | 64.0 | 1.5 | 158.4 | 164 | 10.6 | 0.0 | 3.4 | 501 | 12.0 | 2.00 .1 | 0.110 .6 | 46 | 00. | 0.0 | 0.0 | . 7.7 |
|  | >37.5 | 151 | 32.0 | 0.4 | . 5.7 | 164 | 10.6 | 0.0 | 3.4 | 501 | 12.0 | 2.00 .1 | 0.110 .6 | 460 | 00. | 0.0 | 0.0 | . 7.7 |
|  | >38.0 | 151 | 10.7 | 0.0 | 03.6 | 164 | 00.0 | 0.0 | 2.2 | 500 | 00.0 | 0.00 .0 | 0.07 .1 | 460 | 00. | 0.0 | 0.0 | 07.7 |
|  | >38.5 | 151 | 00.0 | 0.0 | 02.4 | 164 | 00.0 | 0.0 | 2.2 | 500 | 00.0 | 0.00 .0 | 0.07.1 | 460 | 00. | 0.0 | 0.0 | . 7.7 |
|  | >39.0 | 151 | 00.0 | 0.0 | 02.4 | 164 | 00.0 | 0.0 | 2.2 | 500 | 00.0 | 0.00 .0 | 0.0 7.1 | 460 | 00. | 0.0 | 0.0 | 07.7 |
|  | >39.5 | 151 | 00.0 | 0.0 | 02.4 | 164 | 00.0 | 0.0 | 2.2 | 500 | 00.0 | 0.00 .0 | 0.07 .1 | 460 | 00. | 0.0 | 0.0 | 07.7 |
|  | >40.0 | 151 | 00.0 | 0.0 | 02.4 | 164 | 00.0 | 0.0 | 2.2 | 500 | 00.0 | 0.00 .0 | 0.07 .1 | 460 | 00. | 0.0 |  | O 7.7 |

## Overall/subject

 $\geq 35.58256 .12 .013 .783111 .20 .0 |$|  | 6.5 | 26 | 1 | 3.8 | 0.1 | 19.6 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | $\begin{array}{lllllllllllllllllllllllllll}>36.0 & 82 & 5 & 6.1 & 2.0 & 13.7 & 83 & 1 & 1.2 & 0.0 & 6.5 & 26 & 1 & 3.8 & 0.1 & 19.6 & 24 & 0 & 0.0 & 0.0 & 14.2 \\ >\end{array}$ $\begin{array}{llllllllllllllllllllllll}>36.5 & 82 & 5 & 6.1 & 2.0 & 13.7 & 83 & 1 & 1.2 & 0.0 & 6.5 & 26 & 1 & 3.8 & 0.1 & 19.6 & 24 & 0 & 0.0 & 0.0 & 14.2 \\ >37.0\end{array}$

 $\begin{array}{lllllllllllllllllllllll}>37.5 & 82 & 2 & 2.4 & 0.3 & 8.5 & 83 & 1 & 1.2 & 0.0 & 6.5 & 26 & 1 & 3.8 & 0.1 & 19.6 & 24 & 0 & 0.0 & 0.0 & 14.2 \\ >38.0 & 82 & 1 & 1.2 & 0.0 & 6\end{array}$ $\begin{array}{lllllllllllllllllllllll}>38.0 & 82 & 1 & 1.2 & 0.0 & 6.6 & 83 & 0 & 0.0 & 0.0 & 4.3 & 26 & 0 & 0.0 & 0.0 & 13.2 & 24 & 0 & 0.0 & 0.0 & 14.2 \\ >\end{array}$

 $\left.$| $>39.0$ | 82 | 0 | 0.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | 0.0 \right\rvert\, 0.014 .2

|  |  | PreChemo |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  | Placebo |  |  |  | HZ/su |  |  |  | Placebo |  |  |  |  |
|  |  |  |  | $95 \% \mathrm{Cl}$ |  |  |  | \% Cl |  |  |  | 5 \% CI |  |  |  |  | \% Cl |
| Symptom | Type | N | n\% | LL UL | N | n\% | LL | UL | N | n\% | LL | L UL |  | n \% | \% | LL | UL |
|  | >39.5 | 82 | 00.0 | 00.0 4.4 | 83 | 00.0 | 0.0 | 04.3 | 26 | 00.0 | 00.0 | 013.2 | 24 | 00. | 0.0 | 0.0 | 14.2 |
|  | $>40.0$ | 82 | 00.0 | 0.0.04.4 | 83 | 00.0 | 0.0 | 04.3 | 26 | 00.0 | 00.0 | 013.2 | 24 | 00. | 0.0 |  | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
n/\% = number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for oral route

Table 8.142 Number and percentage of subjects who reported temperature by half degree measured via axillary route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  | Placebo |  |  |  |
|  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  | 95 \% CI |  |  |  |
| Symptom | Type | N | n | \% | LL U | UL | N |  | \% | LL | UL |  | n \% | LL | UL |  | n \% |  | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 82 | 9 | 11.0 | 5.11 | 19.8 | 83 | 1 | 1.2 | 0.0 | 6.5 | 260 | 00.0 | 0.0 | . 13.2 | 242 | 28.3 |  | 027.0 |
|  | $\geq 35.5$ | 82 | 9 | 11.0 | 5.11 | 19.8 | 83 | 1 | 1.2 | 0.0 | 6.5 | 260 | 00.0 | 0.0 | 13.2 | 242 | 28.3 | 1.0 | 027.0 |
|  | $>36.0$ | 82 | 9 | 11.0 | 5.11 | 19.8 | 83 | 1 | 1.2 | 0.0 | 6.5 | 260 | 00.0 | 0.0 | 13.2 | 242 | 28.3 | 1.0 | 027.0 |
|  | >36.5 | 82 | 9 | 11.0 | 5.11 | 19.8 | 83 | 1 | 1.2 | 0.0 | 6.5 | 260 | 00.0 | 0.0 | 13.2 | 24 | 28.3 | 1.0 | 027.0 |
|  | >37.0 | 82 | 9 | 11.0 | 5.11 | 19.8 | 83 | 1 | 1.2 | 0.0 | 6.5 | 260 | 00.0 | 0.0 | 13.2 | 242 | 28.3 | 1.0 | 027.0 |
|  | $>37.5$ | 82 | 7 | 8.5 | 3.51 | 16.8 | 83 | 1 | 1.2 | 0.0 | 6.5 | 260 | 00.0 | 0.0 | 0 13.2 | 242 | 28.3 | 1.0 | 027.0 |
|  | $>38.0$ | 82 | 2 | 2.4 | 0.38 | 8.5 | 83 | 0 | 0.0 | 0.0 | 4.3 | 260 | 00.0 | 0.0 | 0. 13.2 | 240 | 00.0 | 0.0 | 014.2 |
|  | $>38.5$ | 82 | 1 | 1.2 | 0.06 | 6.6 | 83 | 0 | 0.0 | 0.0 | 4.3 | 260 | 00.0 | 0.0 | 13.2 | 24 | 00.0 | 0.0 | 014.2 |
|  | $>39.0$ | 82 | 0 | 0.0 | 0.04 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 260 | 00.0 | 0.0 | 13.2 | 240 | 00.0 | 0.0 | 014.2 |
|  | $>39.5$ | 82 | 0 | 0.0 | 0.04 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 260 | 00.0 | 0.0 | 13.2 | 240 | 00.0 | 0.0 | 014.2 |
|  | $>40.0$ | 82 | 0 | 0.0 | 0.04 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 260 | 00.0 | 0.0 | 13.2 | 240 | 00.0 |  | 014.2 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 69 | 1 | 1.4 | 0.07 | 7.8 | 81 | 0 | 0.0 | 0.0 | 4.5 | 243 | 312.5 | 2.7 | 32.4 | 221 | 14.5 | 0.1 | 122.8 |
|  | $\geq 35.5$ | 69 | 1 | 1.4 | 0.07 | 7.8 | 81 | 0 | 0.0 | 0.0 | 4.5 | 243 | 312.5 | 2.7 | 732.4 | 221 | 14.5 | 0.1 | 122.8 |
|  | $>36.0$ | 69 | 1 | 1.4 | 0.07 | 7.8 | 81 | 0 | 0.0 | 0.0 | 4.5 | 243 | 312.5 | 2.7 | 732.4 | 22 | 14.5 | 0.1 | 122.8 |
|  | >36.5 | 69 | 1 | 1.4 | 0.07 | 7.8 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 312.5 | 2.7 | 732.4 | 22 | 14.5 |  | 122.8 |
|  | $>37.0$ | 69 | 1 | 1.4 | 0.07 | 7.8 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 312.5 | 2.7 | 732.4 | 22 | 14.5 | 0.1 | 122.8 |
|  | $>37.5$ | 69 | 0 | 0.0 | 0.05 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 241 | 14.2 | 0.1 | 121.1 | 221 | 14.5 | 0.1 | 122.8 |
|  | $>38.0$ | 69 | 0 | 0.0 | 0.05 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 00.0 | 0.0 | 14.2 | 22 | 14.5 | 0.1 | 122.8 |
|  | $>38.5$ | 69 | 0 | 0.0 | 0.05 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 00.0 | 0.0 | . 14.2 | 220 | 00.0 | 0.0 | 015.4 |
|  | $>39.0$ | 69 | 0 | 0.0 | 0.05 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 240 | 00.0 | 0.0 | 0 14.2 | 220 | 00.0 | 0.0 | 015.4 |
|  | $>39.5$ | 69 | 0 | 0.0 | 0.05 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 24 | 00.0 | 0.0 | 0 14.2 | 220 | 00.0 | 0.0 | 015.4 |
|  | $>40.0$ | 69 | 0 | 0.0 | 0.05 | 5.2 | 81 | 0 | 0.0 | 0.0 | 4.5 | 240 | 00.0 | 0.0 | 14.2 | 220 | 00.0 |  | 015.4 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 151 | 10 | 6.6 | 3.21 | 11.8 | 164 | 110 | 0.6 | 0.0 | 3.4 | 50 | 36.0 | 1.3 | 16.5 | 4613 | 36.5 | 1.4 | 417.9 |
|  | $\geq 35.5$ | 151 | 10 | 6.6 | 3.21 | 11.8 | 164 | 1 | 0.6 | 0.0 | 3.4 | 50 | 36.0 | 1.3 | 316.5 | 463 | 36.5 | 1.4 | 417.9 |
|  | $>36.0$ | 151 | 10 | 6.6 | 3.21 | 11.8 | 164 | 1 | 0.6 | 0.0 | 3.4 | 50 | 36.0 | 1.3 | 316.5 | 463 | 36.5 | 1.4 | 417.9 |
|  | >36.5 | 151 | 10 | 6.6 | 3.21 | 11.8 | 164 | 1 | 0.6 | 0.0 | 3.4 | 50 | 36.0 | 1.3 | 316.5 | 46 | 36.5 | 1.4 | 417.9 |
|  | $>37.0$ | 151 | 10 | 6.6 | 3.21 | 11.8 | 164 | 1 | 0.6 | 0.0 | 3.4 | 50 | 36.0 | 1.3 | 316.5 | 463 | 36.5 | 1.4 | 417.9 |
|  | $>37.5$ | 151 | 7 | 4.6 | 1.99 | 9.3 | 164 | 1 | 0.6 | 0.0 | 3.4 | 501 | 12.0 | 0.1 | 110.6 | 46 | 36.5 | 1.4 | 417.9 |
|  | $>38.0$ | 151 | 2 | 1.3 | 0.24 | 4.7 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 00.0 | 0.0 | 7.1 | 46 | 12.2 | 0.1 | 111.5 |
|  | >38.5 | 151 | 1 | 0.7 | 0.03 | 3.6 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 00.0 | 0.0 | 7.1 | 460 | 00.0 | 0.0 | 07.7 |
|  | >39.0 | 151 | 0 | 0.0 | 0.02 | 2.4 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 00.0 | 0.0 | 7.1 | 460 | 00.0 | 0.0 | 07.7 |
|  | >39.5 | 151 | 0 | 0.0 | 0.02 | 2.4 | 164 | 0 | 0.0 | 0.0 | 2.2 | 50 | 00.0 | 0.0 | 7.1 | 460 | 00.0 | 0.0 | 07.7 |
|  | >40.0 | 151 | 0 | 0.0 | 0.02 | 2.4 | 164 | 0 | 0.0 | 0.0 | 2.2 | 501 | 00.0 | 0.0 | 7.1 | 460 | 00.0 |  | 07.7 |

## Overall/subject

 \begin{tabular}{llllllllllllllllllllll}
$\geq 35.5$ \& 82 \& 10 \& 12.2 \& 6.0 \& 21.3 \& 83 \& 1 \& 1.2 \& 0.0 \& 6.5 \& 26 \& 3 \& 11.5 \& 2.4 \& 30.2 \& 24 \& 3 \& 12.5 \& 2.7 \& 32.4 <br>
\hline

 

$\gg 36.0$ \& 82 \& 10 \& 12.2 \& 6.0 \& 21.3 \& 83 \& 1 \& 1.2 \& 0.0 \& 6.5 \& 26 \& 3 \& 11.5 \& 2.4 \& 30.2 \& 24 \& 3 \& 12.5 \& 2.7 \& 32.4 <br>
\hline

 

$>36.5$ \& 82 \& 10 \& 12.2 \& 6.0 \& 21.3 \& 83 \& 1 \& 1.2 \& 0.0 \& 6.5 \& 26 \& 3 \& 11.5 \& 2.4 \& 30.2 \& 24 \& 3

 12.52 .732 .4 

$>37.0$ \& 82 \& 10 \& 12.2 \& 6.0 \& 21.3 \& 83 \& 1 \& 1.2 \& 0.0 \& 6.5 \& 26 \& 11.5 \& 2.4 \& 30.2 \& 24 \& 3 \& 12.5 \& 2.7 <br>
32.4 <br>
\hline
\end{tabular}

 $\begin{array}{llllllllllllllllllllll}>38.0 & 82 & 2 & 2.4 & 0.3 & 8.5 & 83 & 0 & 0.0 & 0.0 & 4.3 & 26 & 0 & 0.0 & 0.0 & 13.2 & 24 & 1 & 4.2 & 0.1 & 21.1\end{array}$ | $>38.5$ | 82 | 1 | 1.2 | 0.0 | 6.6 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |




Table 8.143 Number and percentage of subjects who reported temperature by half degree measured via tympanic route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  | PreChemo |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  | Placebo |  |  |  |
|  |  | 95 \% Cl |  |  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  | 95 \% Cl |  |  |  |
| Symptom | Type | N | n \% | LL | UL | N | n \% | \% LL | LL UL | UL | N | n \% | \% LL | UL | N | n \% | LL |  |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 82 | 00.0 | 0.0 | 4.4 | 83 |  | 0.00 .0 | 0.04 | 4.3 | 26 | 00.0 | . 00.0 | 13.2 | 240 | 00.0 | 0.0 | 14.2 |
|  | $\geq 35.5$ | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 00.0 | . 00.0 | 13.2 | 240 | 00.0 | 0.0 | 14.2 |
|  | $>36.0$ | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 00.0 | . 0.0 | 13.2 | 240 | 00.0 | 0.0 | . 14.2 |
|  | >36.5 | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.0 0.0 | 0.04 | 4.3 | 26 | 00.0 | . 00.0 | 13.2 | 240 | 00.0 | 0.0 | 14.2 |
|  | >37.0 | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 00.0 | . 00.0 | 13.2 | 240 | 00.0 | 0.0 | 14.2 |
|  | $>37.5$ | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 00.0 | . 00.0 | 13.2 | 240 | 00.0 | 0.0 | 14.2 |
|  | >38.0 | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 00.0 | . 00.0 | 13.2 | 240 | 00.0 | 0.0 | 14.2 |
|  | $>38.5$ | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 00.0 | . 0.0 | 13.2 | 240 | 00.0 | 0.0 | 14.2 |
|  | $>39.0$ | 82 | 00.0 | 0.0 | 4.4 | 83 |  | 0.0 0.0 | 0.04 | 4.3 | 26 | 00.0 | . 00.0 | 13.2 | 240 | 00.0 | 0.0 | . 14.2 |
|  | >39.5 | 82 | 00.0 | 0.0 | 4.4 | 83 |  | 0.0 0.0 | 0.04 | 4.3 | 26 | 00.0 | . 00.0 | 13.2 | 240 | 00.0 | 0.0 | . 14.2 |
|  | >40.0 | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 00.0 | . 00.0 | 13.2 | 240 | 00.0 | 0.0 | 14.2 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 69 | 00.0 | 0.0 | 5.2 | 81 | 00.0 | 0.00 .0 | 0.04 | 4.5 | 24 | 14.2 | . 20.1 | 21.1 | 22 | 00.0 | 0.0 | 15.4 |
|  | $\geq 35.5$ | 69 | 00.0 | 0.0 | 5.2 | 81 | 00.0 | 0.0 0.0 | 0.04 | 4.5 | 24 | 14.2 | . 0.1 | 21.1 | 220 | 00.0 | 0.0 | 15.4 |
|  | >36.0 | 69 | 00.0 | 0.0 | 5.2 | 81 | 00.0 | 0.0 0.0 | 0.04 | 4.5 | 24 | 14.2 | . 0.1 | 21.1 | 220 | 00.0 | 0.0 | 15.4 |
|  | >36.5 | 69 | 00.0 | 0.0 | 5.2 | 81 | 00.0 | 0.00 .0 | 0.04 | 4.5 | 24 | 14.2 | . 0.1 | 21.1 | 220 | 00.0 | 0.0 | 15.4 |
|  | >37.0 | 69 | 00.0 | 0.0 | 5.2 | 81 | 00.0 | 0.00 .0 | 0.04 | 4.5 | 24 | 14.2 | . 0.1 | 21.1 | 220 | 00.0 | 0.0 | 15.4 |
|  | $>37.5$ | 69 | 00.0 | 0.0 | 5.2 | 81 | 00.0 | 0.00 .0 | 0.04 | 4.5 | 24 | 00.0 | . 00.0 | 14.2 | 220 | 00.0 | 0.0 | . 15.4 |
|  | $>38.0$ | 69 | 00.0 | 0.0 | 5.2 | 81 | 00.0 | 0.0 0.0 | 0.04 | 4.5 | 24 | 00.0 | . 00.0 | 14.2 | 220 | 00.0 | 0.0 | . 15.4 |
|  | >38.5 | 69 | 00.0 | 0.0 | 5.2 | 81 | 00.0 | 0.00 .0 | 0.04 | 4.5 | 24 | 00.0 | . 00.0 | 14.2 | 220 | 00.0 | 0.0 | . 15.4 |
|  | >39.0 | 69 | 00.0 | 0.0 | 5.2 | 81 | 00.0 | 0.00 .0 | 0.04 | 4.5 | 24 | 00.0 | . 00.0 | 14.2 | 220 | 00.0 | 0.0 | . 15.4 |
|  | $>39.5$ | 69 | 00.0 | 0.0 | 5.2 | 81 | 00.0 | 0.00 .0 | 0.04 | 4.5 | 24 | 00.0 | . 00.0 | 14.2 | 220 | 00.0 | 0.0 | . 15.4 |
|  | >40.0 | 69 | 00.0 | 0.0 | 5.2 | 81 |  | 0.00 .0 | 0.04 | 4.5 | 24 | 00.0 | . 00.0 | 14.2 | 220 | 00.0 | . 0 | 15.4 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 151 | 00.0 | 0.0 | 2.4 | 164 | 00.0 | 0.0 0.0 | 0.02 | 2.2 | 50 | 12.0 | . 00.1 | 10.6 | 460 | 00.0 | 0.0 | 7.7 |
|  | $\geq 35.5$ | 151 | 00.0 | 0.0 | 2.4 | 164 | 00.0 | 0.00 .0 | 0.02 | 2.2 | 50 | 12.0 | 2.00 .1 | 10.6 | 460 | 00.0 | 0.0 | 7.7 |
|  | >36.0 | 151 | 00.0 | 0.0 | 2.4 | 164 | 00.0 | 0.0 0.0 | 0.02 | 2.2 | 50 | 12.0 | 2.0 .1 | 10.6 | 460 | 00.0 | 0.0 | 7.7 |
|  | >36.5 | 151 | 00.0 | 0.0 | 2.4 | 164 | 00.0 | 0.00 .0 | 0.02 | 2.2 | 50 | 12.0 | 2.00 .1 | 10.6 | 460 | 00.0 | 0.0 | 7.7 |
|  | $>37.0$ | 151 | 00.0 | 0.0 | 2.4 | 164 | 00.0 | 0.0 0.0 | 0.02 | 2.2 | 50 | 12.0 | . 00.1 | 10.6 | 460 | 00.0 | 0.0 | 7.7 |
|  | >37.5 | 151 | 00.0 | 0.0 | 2.4 | 164 |  | 0.00 .0 | 0.02 | 2.2 | 50 | 00.0 | . 0.0 | 7.1 | 460 | 00.0 | 0.0 | 7.7 |
|  | >38.0 | 151 | 00.0 | 0.0 | 2.4 | 164 |  | 0.00 .0 | 0.02 | 2.2 | 50 | 00.0 | . 0.0 | 7.1 | 460 | 00.0 | 0.0 | 7.7 |
|  | >38.5 | 151 | 00.0 | 0.0 | 2.4 | 164 | 00.0 | 0.00 .0 | 0.02 | 2.2 | 50 | 00.0 | . 00.0 | 7.1 | 460 | 00.0 | 0.0 | 7.7 |
|  | >39.0 | 151 | 00.0 | 0.0 | 2.4 | 164 | 00.0 | 0.00 .0 | 0.02 | 2.2 | 50 | 00.0 | . 00.0 | 7.1 | 460 | 00.0 | 0.0 | O7.7 |
|  | >39.5 | 151 | 00.0 | 0.0 | 2.4 | 164 |  | 0.00 .0 | 0.02 | 2.2 | 50 | 00.0 | 0.00 | 7.1 | 460 | 00.0 | 0.0 | O 7.7 |
|  | >40.0 | 151 | 00.0 | 0.0 | 2.4 | 164 | 00.0 | 0.00 .0 | 0.0 | 2.2 | 50 | 00.0 | . 00.0 | 7.1 | 460 | 00.0 | 0.0 | O 7.7 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 13.8 | 3 80.1 | 19.6 | 240 | 00.0 | 0.0 | . 14.2 |
|  | $\geq 35.5$ | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 13.8 | 3 0.1 | 19.6 | 240 | 00.0 | 0.0 | . 14.2 |
|  | $>36.0$ | 82 | 00.0 | 0.0 | 4.4 | 83 |  | 0.0 0.0 | 0.04 | 4.3 | 26 | 13.8 | 3 80.1 | 19.6 | 240 | 00.0 | 0.0 | . 14.2 |
|  | >36.5 | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 13.8 | 3 0.1 | 19.6 | 240 | 00.0 | 0.0 | . 14.2 |
|  | >37.0 | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 13.8 | 3 80.1 | 19.6 | 240 | 00.0 | 0.0 | . 14.2 |
|  | $>37.5$ | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 00.0 | . 00.0 | 13.2 | 240 | 00.0 | 0.0 | . 14.2 |
|  | $>38.0$ | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.0 0.0 | 0.04 | 4.3 | 26 | 00.0 | . 0.0 | 13.2 | 240 | 00.0 | 0.0 | . 14.2 |
|  | >38.5 | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 00.0 | . 00.0 | 13.2 | 240 | 00.0 | 0.0 | . 14.2 |
|  | >39.0 | 82 | 00.0 | 0.0 | 4.4 | 83 | 00.0 | 0.00 .0 | 0.04 | 4.3 | 26 | 00.0 | . 00.0 | 13.2 | 240 | 00.0 | 0.0 | . 14.2 |


|  |  | PreChemo |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type | N | n \% | LL | UL | N |  | \% | LL | UL | N |  | \% | LL | UL | N |  | \% | LL | UL |
|  | >39.5 | 82 | 00.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |
|  | $>40.0$ | 82 | 00.0 | 0.0 | 4.4 | 83 | 0 | 0.0 | 0.0 | 4.3 | 26 | 0 | 0.0 | 0.0 | 13.2 | 24 | 0 | 0.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
95\%CI = Exact 95\% confidence interval; LL = lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for tympanic route
Table 8.144 Number and percentage of subjects who reported temperature by half degree measured via rectal route during the 7-day (Days 0-6) post-vaccination period following each dose (no conversion) by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

No records exist in this table

Table 8.145 Number of days with grade 3 local symptoms during the solicited post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Pain | Dose 1 | PreChemo | HZ/su | 7 | 1.1 | 1.0 | 1.0 | 1.0 | 1.0 | 2.0 |
|  | Dose 2 | PreChemo | HZ/su | 3 | 2.3 | 1.0 | 1.0 | 3.0 | 3.0 | 3.0 |
|  |  | OnChemo | HZ/su | 1 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
|  | Overall/dose | PreChemo | HZ/su | 10 | 1.5 | 1.0 | 1.0 | 1.0 | 2.0 | 3.0 |
|  |  | OnChemo | HZ/su | 1 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
| Redness | Dose 1 | PreChemo | HZ/su | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | PreChemo | HZ/su | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of doses with the symptom
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.146 Number of days with grade 3 general symptoms during the solicited post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Fatigue | Dose 1 | PreChemo | HZ/su | 5 | 1.8 | 1.0 | 1.0 | 1.0 | 2.0 | 4.0 |
|  |  |  | Placebo | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  | OnChemo | HZ/su | 5 | 2.4 | 1.0 | 2.0 | 2.0 | 3.0 | 4.0 |
|  |  |  | Placebo | 2 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  | Dose 2 | PreChemo | HZ/su | 5 | 2.6 | 1.0 | 1.0 | 2.0 | 2.0 | 7.0 |
|  |  |  | Placebo | 5 | 2.0 | 1.0 | 1.0 | 1.0 | 3.0 | 4.0 |
|  |  | OnChemo | HZ/su | 4 | 4.0 | 2.0 | 2.5 | 3.5 | 5.5 | 7.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | PreChemo | HZ/su | 10 | 2.2 | 1.0 | 1.0 | 1.5 | 2.0 | 7.0 |
|  |  |  | Placebo | 6 | 2.0 | 1.0 | 1.0 | 1.5 | 3.0 | 4.0 |
|  |  | OnChemo | HZ/su | 9 | 3.1 | 1.0 | 2.0 | 3.0 | 4.0 | 7.0 |
|  |  |  | Placebo | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
| Gastrointestinal symptoms | Dose 1 | PreChemo | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  |  | OnChemo | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
|  | Dose 2 | PreChemo | HZ/su | 4 | 2.3 | 1.0 | 1.5 | 2.0 | 3.0 | 4.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | OnChemo | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 2.5 | 1.0 | 1.0 | 2.5 | 4.0 | 4.0 |
|  | Overall/dose | PreChemo | HZ/su | 5 | 2.2 | 1.0 | 2.0 | 2.0 | 2.0 | 4.0 |
|  |  |  | Placebo | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
|  |  | OnChemo | HZ/su | 2 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 4 | 2.8 | 1.0 | 2.0 | 3.0 | 3.5 | 4.0 |
| Headache | Dose 1 | PreChemo | HZ/su | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  |  | OnChemo | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Dose 2 | PreChemo | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | OnChemo | HZ/su | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | PreChemo | HZ/su | 5 | 1.6 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | OnChemo | HZ/su | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Myalgia | Dose 1 | PreChemo | HZ/su | 6 | 2.2 | 1.0 | 1.0 | 1.5 | 2.0 | 6.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | OnChemo | HZ/su | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  |  | Placebo | 2 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
|  | Dose 2 | PreChemo | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 1 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 |
|  |  | OnChemo | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  | Overall/dose | PreChemo | HZ/su | 7 | 2.1 | 1.0 | 1.0 | 2.0 | 2.0 | 6.0 |
|  |  |  | Placebo | 2 | 3.0 | 1.0 | 1.0 | 3.0 | 5.0 | 5.0 |
|  |  | OnChemo | HZ/su | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
|  |  |  | Placebo | 2 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
| Shivering | Dose 1 | PreChemo | HZ/su | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | OnChemo | HZ/su | 2 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  | Dose 2 | PreChemo | HZ/su | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | OnChemo | HZ/su | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | PreChemo | HZ/su | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |


| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  |  |  | Placebo | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  | OnChemo | HZ/su | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |  |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.147 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=88$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=24 \end{gathered}$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 72 | 83.7 | 74.2 | 90.8 | 79 | 89.8 | 81.5 | 95.2 | 26 | 96.3 | 81.0 | 99.9 | 22 | 91.7 | 73.0 | 99.0 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 4 | 4.7 | 1.3 | 11.5 | 5 | 5.7 | 1.9 | 12.8 | 1 | 3.7 | 0.1 | 19.0 | 1 | 4.2 | 0.1 | 21.1 |
|  | Febrile neutropenia (10016288) | 2 | 2.3 | 0.3 | 8.1 | 1 | 1.1 | 0.0 | 6.2 | 2 | 7.4 | 0.9 | 24.3 | 1 | 4.2 | 0.1 | 21.1 |
|  | Iron deficiency anaemia (10022972) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Leukocytosis (10024378) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Leukopenia (10024384) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lymphopenia (10025327) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neutropenia (10029354) | 10 | 11.6 | 5.7 | 20.3 | 12 | 13.6 | 7.2 | 22.6 | 1 | 3.7 | 0.1 | 19.0 | 3 | 12.5 | 2.7 | 32.4 |
|  | Thrombocytopenia (10043554) | 4 | 4.7 | 1.3 | 11.5 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Cardiac disorders (10007541) | Palpitations (10033557) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Tachycardia (10043071) | 2 | 2.3 | 0.3 | 8.1 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Tinnitus (10043882) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 2 | 8.3 | 1.0 | 27.0 |
| Eye disorders (10015919) | Eye discharge (10015915) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Eye irritation (10015946) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Eye swelling (10015967) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lacrimation increased (10023644) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 2 | 7.4 | 0.9 | 24.3 | 1 | 4.2 | 0.1 | 21.1 |
|  | Myopia (10028651) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Visual acuity reduced (10047531) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Abdominal pain (10000081) | 2 | 2.3 | 0.3 | 8.1 | 1 | 1.1 | 0.0 | 6.2 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Abdominal pain upper (10000087) | 3 | 3.5 | 0.7 | 9.9 | 3 | 3.4 | 0.7 | 9.6 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Aerophagia (10052813) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Aphthous ulcer (10002959) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Constipation (10010774) | 11 | 12.8 | 6.6 | 21.7 | 10 | 11.4 | 5.6 | 19.9 | 5 | 18.5 | 6.3 | 38.1 | 2 | 8.3 | 1.0 | 27.0 |
|  | Diarrhoea (10012735) | 7 | 8.1 | 3.3 | 16.1 | 7 | 8.0 | 3.3 | 15.7 | 1 | 3.7 | 0.1 | 19.0 | 3 | 12.5 | 2.7 | 32.4 |

## CONFIDENTIAL

116427 (ZOSTER-028)
Report Final


## CONFIDENTIAL

116427 (ZOSTER-028)
Report Final

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=88$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | Placebo$N=24$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Generalised oedema (10018092) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Inflammation (10061218) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Influenza like illness (10022004) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Injection site pruritus (10022093) | 2 | 2.3 | 0.3 | 8.1 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Malaise (10025482) | 3 | 3.5 | 0.7 | 9.9 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Mucosal dryness (10028111) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Mucosal inflammation (10028116) | 6 | 7.0 | 2.6 | 14.6 | 5 | 5.7 | 1.9 | 12.8 | 4 | 14.8 | 4.2 | 33.7 | 1 | 4.2 | 0.1 | 21.1 |
|  | Oedema peripheral (10030124) | 3 | 3.5 | 0.7 | 9.9 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pain (10033371) | 2 | 2.3 | 0.3 | 8.1 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Peripheral swelling (10048959) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pyrexia (10037660) | 2 | 2.3 | 0.3 | 8.1 | 4 | 4.5 | 1.3 | 11.2 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Temperature intolerance (10057040) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hepatic steatosis (10019708) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hepatomegaly (10019842) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hyperbilirubinaemia (10020578) | 0 | 0.0 | 0.0 | 4.2 |  | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypersensitivity (10020751) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Seasonal allergy (10048908) | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Bacterial infection (10060945) | 2 | 2.3 | 0.3 | 8.1 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Bronchitis (10006451) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.3 | 0.3 | 8.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Erysipelas (10015145) | 1 | 1.2 | 0.0 | 6.3 | - | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Folliculitis (10016936) |  | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Gastroenteritis (10017888) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=88$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=97 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |  |
|  |  | 95\% Cl |  |  |  | N=88 |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Gingivitis (10018292) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Herpes zoster (10019974) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Infection (10021789) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Influenza (10022000) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 |  | 0.0 | 0.0 | 14.2 |
|  | Nasopharyngitis (10028810) | 2 | 2.3 | 0.3 | 8.1 | 1 | 1.1 | 0.0 | 6.2 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neutropenic sepsis (10049151) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oral fungal infection (10061324) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oral herpes (10067152) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Oral infection (10048685) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pneumonia (10035664) | 2 | 2.3 | 0.3 | 8.1 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Post procedural infection (10067268) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 1 | 4.2 | 0.1 | 21.1 |
|  | Respiratory tract infection (10062352) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 |  | 0.0 | 0.0 | 14.2 |
|  | Sepsis (10040047) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Sinusitis (10040753) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | O | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | - | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Upper respiratory tract infection (10046306) | 3 | 3.5 | 0.7 | 9.9 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urinary tract infection (10046571) | 0 | 0.0 | 0.0 | 4.2 | 3 | 3.4 | 0.7 | 9.6 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Injury, poisoning and procedural complications (10022117) | Arthropod bite (10003399) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Gastrostomy failure (10050056) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | - | 0.0 | 0.0 | 14.2 |
|  | Ligament sprain (10024453) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Post procedural complication (10058046) | 2 | 2.3 | 0.3 | 8.1 | 2 | 2.3 | 0.3 | 8.0 | - | 0.0 | 0.0 | 12.8 | 2 | 8.3 | 1.0 | 27.0 |
|  | Post procedural diarrhoea (10057585) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | - | 0.0 | 0.0 | 14.2 |
|  | Radiation skin injury (10063562) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 2 | 8.3 | 1.0 | 27.0 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | - | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Investigations (10022891) | Blood iron decreased (10005619) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=8 \end{aligned}$ |  |  |  | Placebo$N=88$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |  |
|  |  | 95\% CI |  |  |  | - $95 \%$ CI |  |  |  | 95\% Cl |  |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Headache (10019211) | 3 | 3.5 | 0.7 | 9.9 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Hepatic encephalopathy (10019660) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypoaesthesia (10020937) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Motor dysfunction (10061296) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Muscle contractions involuntary (10028293) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neuropathy peripheral (10029331) | 2 | 2.3 | 0.3 | 8.1 | 3 | 3.4 | 0.7 | 9.6 | 3 | 11.1 | 2.4 | 29.2 | 1 | 4.2 | 0.1 | 21.1 |
|  | Neurotoxicity (10029350) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Paraesthesia (10033775) | 3 | 3.5 | 0.7 | 9.9 | 3 | 3.4 | 0.7 | 9.6 | 2 | 7.4 | 0.9 | 24.3 | 1 | 4.2 | 0.1 | 21.1 |
|  | Paresis (10033985) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Peripheral sensory neuropathy (10034620) | 2 | 2.3 | 0.3 | 8.1 | 3 | 3.4 | 0.7 | 9.6 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Syncope (10042772) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Tremor (10044565) | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.3 | 0.3 | 8.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
| Psychiatric disorders (10037175) | Aggression (10001488) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Anxiety (10002855) | 4 | 4.7 | 1.3 | 11.5 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Depression (10012378) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Insomnia (10022437) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 3 | 11.1 | 2.4 | 29.2 | 2 | 8.3 | 1.0 | 27.0 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Bladder spasm (10048994) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Chronic kidney disease (10064848) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Dysuria (10013990) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Renal impairment (10062237) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urinary retention (10046555) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Reproductive system and breast disorders (10038604) | Oedema genital (10030104) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Asthma (10003553) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Catarrh (10007774) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Cough (10011224) | 3 | 3.5 | 0.7 | 9.9 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Dysaesthesia pharynx (10062665) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
|  | Dysphonia (10013952) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Dyspnoea (10013968) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |

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|  |  | PreChemo |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=88$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=97 \end{aligned}$ |  |  | Placebo$N=24$ |  |  |  |
|  |  | 95\% CI |  |  |  | N=88 |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Epistaxis (10015090) | 1 | 1.2 | 0.0 | 6.3 | 4 | 4.5 | 1.3 | 11.2 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Haemoptysis (10018964) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hiccups (10020039) | 1 | 1.2 | 0.0 | 6.3 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Nasal congestion (10028735) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oropharyngeal discomfort (10068318) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oropharyngeal pain (10068319) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pulmonary embolism (10037377) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 16 | 18.6 | 11.0 | 28.4 | 17 | 719.3 | 11.7 | 29.1 | 5 | 18.5 | 6.3 | 38.1 | 6 | 25.0 | 9.8 | 46.7 |
|  | Dermatitis (10012431) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Dry skin (10013786) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Erythema (10015150) | 4 | 4.7 | 1.3 | 11.5 | 1 | 1.1 | 0.0 | 6.2 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Nail dystrophy (10028698) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Onychalgia (10064251) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Palmar-plantar erythrodysaesthesia syndrome (10033553) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pruritus (10037087) | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 | 2 | 8.3 | 1.0 | 27.0 |
|  | Pruritus generalised (10052576) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Rash (10037844) | 1 | 1.2 | 0.0 | 6.3 | 3 | 3.4 | 0.7 | 9.6 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Rash macular (10037867) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | - | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Scar pain (10049002) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | - | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Swelling face (10042682) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urticaria (10046735) | 2 | 2.3 | 0.3 | 8.1 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Social circumstances (10041244) | Menopause (10027308) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | - | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Haematoma (10018852) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hot flush (10060800) | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.3 | 0.3 | 8.0 | O | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypotension (10021097) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |

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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ N=88 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=24 \end{gathered}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Lymphocele (10048642) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Phlebitis (10034879) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Thrombosis (10043607) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Vascular pain (10047095) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.148 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30 -day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=158 \end{aligned}$ |  |  |  | Placebo$N=172$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | Placebo$N=47$ |  |  |  |
|  |  | 95\% CI |  |  |  | N $95 \% \mathrm{Cl}$ |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL | n ${ }^{\text {\% }}$ | \% | LL | UL |
| At least one symptom |  | 109 | 69.0 | 61.2 | 76.1 | 129 | 75.0 | 67.8 | 81.3 | 40 | 78.4 | 64.7 | 88.7 | 34 | 72.3 | 57.4 | 84.4 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 4 | 2.5 | 0.7 | 6.4 | 5 | 2.9 | 1.0 | 6.7 | 1 | 2.0 | 0.0 | 10.4 | 1 | 2.1 | 0.1 | 11.3 |
|  | Febrile neutropenia (10016288) | 2 | 1.3 | 0.2 | 4.5 | 1 | 0.6 | 0.0 | 3.2 | 2 | 3.9 | 0.5 | 13.5 | 2 | 4.3 | 0.5 | 14.5 |
|  | Iron deficiency anaemia (10022972) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Leukocytosis (10024378) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Leukopenia (10024384) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Lymphopenia (10025327) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Neutropenia (10029354) | 11 | 7.0 | 3.5 | 12.1 | 13 | 7.6 | 4.1 | 12.6 | 1 | 2.0 | 0.0 | 10.4 | 4 | 8.5 | 2.4 | 20.4 |
|  | Thrombocytopenia (10043554) | 4 | 2.5 | 0.7 | 6.4 | 3 | 1.7 | 0.4 | 5.0 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
| Cardiac disorders (10007541) | Palpitations (10033557) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Tachycardia (10043071) | 2 | 1.3 | 0.2 | 4.5 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Congenital, familial and genetic disorders (10010331) Ear and labyrinth disorders (10013993) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | - | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Neurosensory hypoacusis (10067587) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | - | 0.0 | 0.0 | 7.5 |
|  | Tinnitus (10043882) | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 2 | 4.3 | 0.5 | 14.5 |
| Eye disorders (10015919) | Eye discharge (10015915) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 |  | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Eye irritation (10015946) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Eye swelling (10015967) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Lacrimation increased (10023644) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 2 | 3.9 | 0.5 | 13.5 | 1 | 2.1 | 0.1 | 11.3 |
|  | Myopia (10028651) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Visual acuity reduced (10047531) | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Abdominal pain (10000081) | 2 | 1.3 | 0.2 | 4.5 | 1 | 0.6 | 0.0 | 3.2 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Abdominal pain upper (10000087) | 3 | 1.9 | 0.4 | 5.4 | 3 | 1.7 | 0.4 | 5.0 | 2 | 3.9 | 0.5 | 13.5 | 0 | 0.0 | 0.0 | 7.5 |
|  | Aerophagia (10052813) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | - | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Aphthous ulcer (10002959) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 |  | 0.0 | 0.0 | 7.0 | - | 0.0 | 0.0 | 7.5 |
|  | Constipation (10010774) | 13 | 8.2 | 4.5 | 13.7 | 10 | 5.8 | 2.8 | 10.4 | 5 | 9.8 | 3.3 | 21.4 | 2 | 4.3 | 0.5 | 14.5 |
|  | Diarrhoea (10012735) | 9 | 5.7 | 2.6 | 10.5 | 7 | 4.1 | 1.7 | 8.2 | 1 | 2.0 | 0.0 | 10.4 | 3 | 6.4 | 1.3 | 17.5 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=158 \end{aligned}$ |  |  |  | Placebo$N=172$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | Placebo$N=47$ |  |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Gastroenteritis (10017888) | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.2 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Gingivitis (10018292) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Herpes zoster (10019974) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Infection (10021789) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Influenza (10022000) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Nasopharyngitis (10028810) | 2 | 1.3 | 0.2 | 4.5 | 1 | 0.6 | 0.0 | 3.2 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Neutropenic sepsis (10049151) | 1 | 0.6 | 0.0 | 3.5 | 2 | 1.2 | 0.1 | 4.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oral fungal infection (10061324) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oral herpes (10067152) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oral infection (10048685) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Pneumonia (10035664) | 2 | 1.3 | 0.2 | 4.5 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Post procedural infection (10067268) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 1 | 2.1 | 0.1 | 11.3 |
|  | Respiratory tract infection (10062352) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Sepsis (10040047) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Sinusitis (10040753) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Upper respiratory tract infection (10046306) | 3 | 1.9 | 0.4 | 5.4 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Urinary tract infection (10046571) | 0 | 0.0 | 0.0 | 2.3 | 3 | 1.7 | 0.4 | 5.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Injury, poisoning and procedural complications (10022117) | Arthropod bite (10003399) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Gastrostomy failure (10050056) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Ligament sprain (10024453) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Post procedural complication (10058046) | 2 | 1.3 | 0.2 | 4.5 | 2 | 1.2 | 0.1 | 4.1 | 0 | 0.0 | 0.0 | 7.0 | 2 | 4.3 | 0.5 | 14.5 |
|  | Post procedural diarrhoea (10057585) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 2 | 3.9 | 0.5 | 13.5 | 0 | 0.0 | 0.0 | 7.5 |
|  | Radiation skin injury (10063562) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 2 | 4.3 | 0.5 | 14.5 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=158 \end{aligned}$ |  |  |  | Placebo$N=172$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | Placebo$N=47$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | - $95 \%$ Cl |  |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| Investigations (10022891) | Blood iron decreased (10005619) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Body temperature fluctuation (10063488) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Haemoglobin decreased (10018884) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Platelet count decreased (10035528) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Weight decreased (10047895) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Weight increased (10047899) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) | 9 | 5.7 | 2.6 | 10.5 | 3 | 1.7 | 0.4 | 5.0 | 2 | 3.9 | 0.5 | 13.5 | 2 | 4.3 | 0.5 | 14.5 |
|  | Hypercholesterolaemia (10020603) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hyperglycaemia (10020635) | 2 | 1.3 | 0.2 | 4.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hypocalcaemia (10020947) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Iron deficiency (10022970) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 3 | 1.9 | 0.4 | 5.4 | 3 | 1.7 | 0.4 | 5.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Back pain (10003988) | 2 | 1.3 | 0.2 | 4.5 | 2 | 1.2 | 0.1 | 4.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Bone pain (10006002) | 3 | 1.9 | 0.4 | 5.4 | 2 | 1.2 | 0.1 | 4.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Groin pain (10018735) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Muscle contracture (10062575) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Muscle spasms (10028334) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Musculoskeletal discomfort (10053156) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Musculoskeletal pain (10028391) | 2 | 1.3 | 0.2 | 4.5 | 2 | 1.2 | 0.1 | 4.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Myalgia (10028411) | 4 | 2.5 | 0.7 | 6.4 | 5 | 2.9 | 1.0 | 6.7 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Neck pain (10028836) | 2 | 1.3 | 0.2 | 4.5 | 1 | 0.6 | 0.0 | 3.2 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Pain in extremity (10033425) | 2 | 1.3 | 0.2 | 4.5 | 2 | 1.2 | 0.1 | 4.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Prostate cancer (10060862) | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 3 | 1.9 | 0.4 | 5.4 | 3 | 1.7 | 0.4 | 5.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Dizziness postural (10013578) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Dysaesthesia (10013886) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=158 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=172 \end{aligned}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=47 \end{gathered}$ |  |  |  |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Dysgeusia (10013911) | 0 | 0.0 | 0.0 | 2.3 | 4 | 2.3 | 0.6 | 5.8 | 1 | 2.0 | 0.0 | 10.4 | 2 | 4.3 | 0.5 | 14.5 |
|  | Headache (10019211) | 4 | 2.5 | 0.7 | 6.4 | 2 | 1.2 | 0.1 | 4.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Hepatic encephalopathy (10019660) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hypoaesthesia (10020937) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Motor dysfunction (10061296) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Muscle contractions involuntary (10028293) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Neuropathy peripheral (10029331) | 2 | 1.3 | 0.2 | 4.5 | 4 | 2.3 | 0.6 | 5.8 | 3 | 5.9 | 1.2 | 16.2 | 1 | 2.1 | 0.1 | 11.3 |
|  | Neurotoxicity (10029350) | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Paraesthesia (10033775) | 5 | 3.2 | 1.0 | 7.2 | 4 | 2.3 | 0.6 | 5.8 | 2 | 3.9 | 0.5 | 13.5 | 1 | 2.1 | 0.1 | 11.3 |
|  | Paresis (10033985) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Peripheral sensory neuropathy (10034620) | 2 | 1.3 | 0.2 | 4.5 | 3 | 1.7 | 0.4 | 5.0 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Syncope (10042772) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Tremor (10044565) | 0 | 0.0 | 0.0 | 2.3 | 3 | 1.7 | 0.4 | 5.0 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
| Psychiatric disorders (10037175) | Aggression (10001488) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Anxiety (10002855) | 6 | 3.8 | 1.4 | 8.1 | 2 | 1.2 | 0.1 | 4.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Depression (10012378) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Insomnia (10022437) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 3 | 5.9 | 1.2 | 16.2 | 2 | 4.3 | 0.5 | 14.5 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Bladder spasm (10048994) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Chronic kidney disease (10064848) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Dysuria (10013990) | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Renal impairment (10062237) | 2 | 1.3 | 0.2 | 4.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Urinary retention (10046555) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
| Reproductive system and breast disorders (10038604) | Oedema genital (10030104) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Respiratory, thoracic and mediastinal disorders(10038738) | Asthma (10003553) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Catarrh (10007774) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Cough (10011224) | 3 | 1.9 | 0.4 | 5.4 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Dysaesthesia pharynx (10062665) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=158 \end{aligned}$ |  |  |  | Placebo$N=172$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | Placebo$N=47$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Dysphonia (10013952) | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Dyspnoea (10013968) | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.2 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Epistaxis (10015090) | 1 | 0.6 | 0.0 | 3.5 | 4 | 2.3 | 0.6 | 5.8 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Haemoptysis (10018964) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hiccups (10020039) | 1 | 0.6 | 0.0 | 3.5 | 3 | 1.7 | 0.4 | 5.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Nasal congestion (10028735) | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oropharyngeal discomfort (10068318) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oropharyngeal pain (10068319) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Pulmonary embolism (10037377) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 16 | 10.1 | 5.9 | 15.9 | 17 | 9.9 | 5.9 | 15.4 | 5 | 9.8 | 3.3 | 21.4 | 6 | 12.8 | 4.8 | 25.7 |
|  | Dermatitis (10012431) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Dry skin (10013786) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Erythema (10015150) | 5 | 3.2 | 1.0 | 7.2 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Nail dystrophy (10028698) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Onychalgia (10064251) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Palmar-plantar erythrodysaesthesia syndrome (10033553) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Pruritus (10037087) | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.1 | 0 | 0.0 | 0.0 | 7.0 | 2 | 4.3 | 0.5 | 14.5 |
|  | Pruritus generalised (10052576) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Rash (10037844) | 1 | 0.6 | 0.0 | 3.5 | 3 | 1.7 | 0.4 | 5.0 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Rash macular (10037867) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Scar pain (10049002) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Swelling face (10042682) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Urticaria (10046735) | 2 | 1.3 | 0.2 | 4.5 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Social circumstances (10041244) | Menopause (10027308) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Haematoma (10018852) | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |

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PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.149 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30 -day (Days $0-29$ ) post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)


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|  |  | PreChemo |  |  |  |  |  | OnChemo |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  | $\begin{gathered} \text { Placebo } \\ N=88 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | Placebo$N=24$ |  |  |
|  |  | 95\% CI |  |  | 95\% CI |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL UL | n \% | LL | UL |  | \% | LL | UL | n \% | LL | UL |
|  | Renal impairment (10062237) | 1 | 1.2 | 0.06 .3 | 00.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Pleural effusion (10035598) | 0 | 0.0 | 0.04 .2 | 11.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Pulmonary embolism (10037377) | 1 | 1.2 | 0.06 .3 | 00.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 1 | 1.2 | 0.06 .3 | 00.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | . 21.1 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.04 .2 | 11.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Vascular disorders (10047065) | Lymphocele (10048642) | 0 | 0.0 | 0.04 .2 | 00.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 14.2 |  | 21.1 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \%$ CI $=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.150 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30 -day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)


|  |  | PreChemo |  |  |  |  |  |  | OnChemo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=158 \end{aligned}$ |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=172 \end{aligned}$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  | Placebo$N=47$ |  |  |
|  |  |  | 95\% CI |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  |  |  | 95\% CI |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL UL |  | \% | LL | UL |  | \% | LL UL | n \% |  | UL |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.02 .3 |  | 0.6 | 0.0 | ) 3.2 | 0 | 0.0 | 0.07 .0 | 00.0 | 0.0 | 7.5 |
|  | Renal impairment (10062237) | 2 | 1.3 | 0.24 .5 | 0 | 0.0 | 0.0 | 2.1 |  | 0.0 | 0.07 .0 | 00.0 | 0.0 | 0.7.5 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Pleural effusion (10035598) | 0 | 0.0 | 0.02 .3 | 1 | 0.6 | 0.0 | ) 3.2 | 0 | 0.0 | 0.07 .0 | 00.0 | 0.0 | 0.7.5 |
|  | Pulmonary embolism (10037377) | 1 | 0.6 | 0.03 .5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.07 .0 | 00.0 | 0.0 | 7.5 |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 1 | 0.6 | 0.03 .5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.07 .0 | 12.1 | 0.1 | 111.3 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.02 .3 |  | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.07 .0 | 00.0 | 0.0 | 0.0.5 |
| Vascular disorders (10047065) | Lymphocele (10048642) | 0 | 0.0 | 0.02.3 |  | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.07 .0 | 12.1 |  | 111.3 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
n/\% = number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.151 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) postvaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  | PreChemo |  |  |  |  |  |  | OnChemo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  | Placebo$N=88$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | Placebo$N=24$ |  |  |
|  |  |  | 95\% CI |  | 95\% CI |  |  |  | 95\% Cl |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL UL | n $\%$ | \% LL | LL U | UL | n \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 10 | 11.6 | 5.720 .3 |  | 8.03. | 3.31 | 15.7 | 00. | 0.0 | 12.8 | 28.3 | 1.0 | 1.027.0 |
| Blood and lymphatic system disorders (10005329) | Neutropenia (10029354) | 0 | 0.0 | 0.04 .2 |  | 0.00. | 0.04 | 4.1 | 00. | 0.0 | 12.8 | 14.2 | 0.1 | . 121.1 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 1.2 | 0.06 .3 |  | 1.10. | 0.06 | 6.2 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0. 14.2 |
| Gastrointestinal disorders (10017947) | Swollen tongue (10042727) | 1 | 1.2 | 0.06 .3 |  | 0.00. | 0.04 | 4.1 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0. 14.2 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 2 | 2.3 | 0.38 .1 |  | 1.10. | 0.06 | 6.2 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0. 14.2 |
|  | Axillary pain (10048750) | 0 | 0.0 | 0.04 .2 |  | 1.10. | 0.06 | 6.2 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0. 14.2 |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.04 .2 |  | 1.10. | 0.06 | 6.2 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0 14.2 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.04 .2 |  | 0.00. | 0.04 | 4.1 | 00. | 0.0 | 12.8 | 14.2 | 0.1 | . 121.1 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.04 .2 |  | 1.10. | 0.06 | 6.2 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0 14.2 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.04 .2 |  | 1.10. | 0.06 | 6.2 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | . 14.2 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.04.2 |  | 2.30. | 0.38 | 8.0 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0. 14.2 |
|  | Injection site pruritus (10022093) | 2 | 2.3 | 0.38 .1 |  | 0.00. | 0.04 | 4.1 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | . 14.2 |
|  | Malaise (10025482) | 1 | 1.2 | 0.06 .3 | 00.0 | 0.00. | 0.04 | 4.1 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0. 14.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.04 .2 |  | 1.10. | 0.06 | 6.2 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | . 14.2 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 1 | 1.2 | 0.06 .3 |  | 0.00. | 0.04 | 4.1 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0 14.2 |
|  | Oral herpes (10067152) | 1 | 1.2 | 0.06 .3 |  | 0.00. | 0.04 | 4.1 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | . 14.2 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.04 .2 |  | 1.10. | 0.06 | 6.2 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0 14.2 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 1 | 1.2 | 0.06 .3 |  | 1.10. | 0.06 | 6.2 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | . 14.2 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 0 | 0.0 | 0.04 .2 |  | 1.10. | 0.06 | 6.2 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0. 14.2 |
|  | Muscle contractions involuntary (10028293) |  | 1.2 | 0.06 .3 |  | 0.00. | 0.04 | 4.1 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0. 14.2 |
| Skin and subcutaneous tissue disorders (10040785) | Erythema (10015150) | 1 | 1.2 | 0.06 .3 |  | 0.00 | 0.04 | 4.1 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0. 14.2 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.04 .2 |  | 1.10. | 0.06 | 6.2 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 0. 14.2 |
|  | Urticaria (10046735) | 0 | 0.0 | 0.04 .2 | 11. | 1.10. | 0.06 | 6.2 | 00. | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group

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At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.152 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  | PreChemo |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=158 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=172 \end{aligned}$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  | Placebo$N=47$ |  |  |
|  |  | 95\% CI |  |  |  |  | 95\% Cl |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL |  | \% | LL | UL | JL | n \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 11 | 7.0 | 3.5 | 12.1 | 9 | 5.2 | 2.4 | 49.7 | 9 7 | 00.0 | 00.0 | 7.0 | 24.3 | 0.5 | 14.5 |
| Blood and lymphatic system disorders (10005329) | Neutropenia (10029354) | 0 | 0.0 | 0.0 | 02.3 | 0 | 0.0 | 0.0 | 02. | 2.10 | 00.0 | 00.0 | 7.0 | 12.1 | 0.1 | 11.3 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 0.6 | 0.0 | 0 3.5 |  | 0.6 | 0.0 |  | 32 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| Gastrointestinal disorders (10017947) | Swollen tongue (10042727) | 1 | 0.6 | 0.0 | O 3.5 | 0 | 0.0 | 0.0 | 02. | . 10 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 2 | 1.3 | 0.2 | 24.5 |  | 0.6 | 0.0 |  | . 20 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Axillary pain (10048750) | 0 | 0.0 | 0.0 | 0 2.3 |  | 1.2 | 0.1 |  | . 10 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.0 | 0 2.3 |  | 0.6 | 0.0 |  | 32 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 0 2.3 | 0 | 0.0 | 0.0 |  | 2.1 | 00.0 | 00.0 | 7.0 | 12.1 |  | 11.3 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.0 | 02.3 |  | 0.6 | 0.0 |  | 32 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 0 2.3 |  | 0.6 | 0.0 |  | . 20 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.0 | 02.3 | 2 | 1.2 | 0.1 |  | . 10 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Injection site pruritus (10022093) | 2 | 1.3 | 0.2 | 24.5 | 0 | 0.0 | 0.0 |  | 2.1 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Malaise (10025482) | 2 | 1.3 | 0.2 | 24.5 | 0 | 0.0 | 0.0 |  | 2.1 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | . 7.5 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | . 2.3 |  | 0.6 | 0.0 |  | 3.2 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 1 | 0.6 | 0.0 | O 3.5 |  | 0.0 | 0.0 |  | 2.10 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Oral herpes (10067152) | 1 | 0.6 | 0.0 | . 3.5 | 0 | 0.0 | 0.0 |  | 2.1 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | O2.3 |  | 0.6 | 0.0 |  | 32 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 1 | 0.6 | 0.0 | . 3.5 |  | 0.6 | 0.0 |  | 32 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 0 | 0.0 | 0.0 | O2.3 |  | 0.6 | 0.0 |  | 3.2 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Muscle contractions involuntary (10028293) | 1 | 0.6 | 0.0 | O 3.5 | 0 | 0.0 | 0.0 |  | 2.1 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
| Skin and subcutaneous tissue disorders (10040785) | Erythema (10015150) | 1 | 0.6 | 0.0 | O 3.5 | 0 | 0.0 | 0.0 |  | 2.1 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 | 7.5 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | . 2.3 |  | 0.6 | 0.0 |  | 3.2 | 00.0 | 00.0 | 7.0 | 00.0 |  | 7.5 |
|  | Urticaria (10046735) | 0 | 0.0 | 0.0 | 2.3 |  | 0.6 | 0.0 | 03. | 32 | 00.0 | 00.0 | 7.0 | 00.0 | 0.0 |  |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group

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At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
$95 \% \mathrm{CI}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.153 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30 -day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  | PreChemo |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  | Placebo$N=88$ |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |  |
|  |  | $\begin{gathered} 95 \% \\ \mathrm{CI} \end{gathered}$ |  | $\begin{gathered} 95 \% \\ \mathrm{CI} \end{gathered}$ |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n ${ }^{\text {\% }}$ | LL UL | n \% | LL | UL |  | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 11.2 | 0.06 .3 | 00.0 | 0.0 | 4.1 |  | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 11.2 | 0.06 .3 | 00.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit
Table 8.154 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

|  |  | PreChemo |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \text { HZ/su } \\ & \mathrm{N}=158 \end{aligned}$ |  |  |  | Placebo$N=172$ |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | Placebo$N=47$ |  |  |  |
|  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{CI} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n $\%$ | LL | UL | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |
| At least one symptom |  | 10.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 10.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.155 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  |  |  |  | PreC | hem |  |  |  |  |  |  | OnChe | mo |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =86 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { icebo } \\ & =88 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =27 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { ceebc } \\ & =24 \end{aligned}$ |  |
|  |  |  |  | 95\% | Cl |  |  | 95\% | CI |  |  | 95\% | \% CI |  |  |  | \% CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |
| At least one symptom |  | 19 | 22.1 | 13.9 | 32.3 | 27 | 30.7 | 21.3 | 41.4 | 12 | 44.4 | 25.5 | 64.7 | 5 | 20.8 | 7.1 | 42.2 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 2 | 2.3 | 0.3 | 8.1 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
|  | Febrile neutropenia (10016288) | 2 | 2.3 | 0.3 | 8.1 | 1 | 1.1 | 0.0 | 6.2 | 2 | 7.4 | 0.9 | 24.3 |  | 4.2 | 0.1 | 21.1 |
|  | Neutropenia (10029354) | 2 | 2.3 | 0.3 | 8.1 | 3 | 3.4 | 0.7 | 9.6 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Abdominal pain (10000081) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Abdominal pain upper (10000087) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Constipation (10010774) | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
|  | Diarrhoea (10012735) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Dyspepsia (10013946) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Dysphagia (10013950) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Gastrooesophageal reflux disease (10017885) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
|  | Nausea (10028813) | 3 | 3.5 | 0.7 | 9.9 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Stomatitis (10042128) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Swollen tongue (10042727) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Vomiting (10047700) | 1 | 1.2 | 0.0 | 6.3 | 3 | 3.4 | 0.7 | 9.6 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 2 | 2.3 | 0.3 | 8.1 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=88$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |
|  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% Cl |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |
|  | Mucosal inflammation (10028116) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pyrexia (10037660) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hepatomegaly (10019842) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Gastroenteritis (10017888) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 |  | 0.0 | 0.0 | 14.2 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Nasopharyngitis (10028810) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Neutropenic sepsis (10049151) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Post procedural infection (10067268) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Respiratory tract infection (10062352) | - | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Sepsis (10040047) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Upper respiratory tract infection (10046306) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Platelet count decreased (10035528) |  | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) |  | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Musculoskeletal and connective tissue disorders (10028395) | Back pain (10003988) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

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PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.156 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=158 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=172 \end{aligned}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=47 \end{aligned}$ |  |  |
|  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  | 95\% Cl |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |
| At least one symptom |  | 23 | 14.6 | 9.5 | 21.0 | 34 | 19.8 | 14.1 | 26.5 | 13 | 25.5 | 14.3 | 39.6 | 7 | 14.9 | 6.2 | 28.3 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 2 | 1.3 | 0.2 | 4.5 | 2 | 1.2 | 0.1 | 4.1 | 0 | 0.0 | 0.0 | 7.0 |  | 2.1 | 0.1 | 11.3 |
|  | Febrile neutropenia (10016288) | 2 | 1.3 | 0.2 | 4.5 | 1 | 0.6 | 0.0 | 3.2 | 2 | 3.9 | 0.5 | 13.5 | 2 | 4.3 | 0.5 | 14.5 |
|  | Neutropenia (10029354) | 3 | 1.9 | 0.4 | 5.4 | 3 | 1.7 | 0.4 | 5.0 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 |  | 2.1 | 0.1 | 11.3 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 |  | 0.0 | 0.0 | 7.5 |
|  | Abdominal pain (10000081) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Abdominal pain upper (10000087) | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Constipation (10010774) | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.1 | 0 | 0.0 | 0.0 | 7.0 |  | 2.1 | 0.1 | 11.3 |
|  | Diarrhoea (10012735) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Dyspepsia (10013946) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Dysphagia (10013950) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Gastrooesophageal reflux disease (10017885) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 |  | 2.1 | 0.1 | 11.3 |
|  | Nausea (10028813) | 3 | 1.9 | 0.4 | 5.4 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Stomatitis (10042128) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Swollen tongue (10042727) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | - | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Vomiting (10047700) | 1 | 0.6 | 0.0 | 3.5 | 3 | 1.7 | 0.4 | 5.0 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 2 | 1.3 | 0.2 | 4.5 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Mucosal inflammation (10028116) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 |  | 7.5 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=158 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=179 \end{aligned}$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  | Placebo$N=47$ |  |  |  |
|  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  | 95\% Cl |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |
|  | Pyrexia (10037660) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 |  | 2.1 | 0.1 | 11.3 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hepatomegaly (10019842) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Gastroenteritis (10017888) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 |  | 2.1 | 0.1 | 11.3 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Nasopharyngitis (10028810) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 |  | 0.0 | 0.0 | 7.5 |
|  | Neutropenic sepsis (10049151) | 1 | 0.6 | 0.0 | 3.5 | 2 | 1.2 | 0.1 | 4.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Post procedural infection (10067268) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Respiratory tract infection (10062352) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Sepsis (10040047) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Upper respiratory tract infection (10046306) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Platelet count decreased (10035528) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) | 1 | 0.6 | 0.0 | ) 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Musculoskeletal and connective tissue disorders (10028395) | Back pain (10003988) | 0 | 0.0 |  | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Muscle spasms (10028334) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |

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|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=158 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=172 \end{aligned}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=51 \end{aligned}$ |  |  |  | Placebo$N=47$ |  |  |  |
|  |  | 95\% Cl |  |  |  |  |  | 95\% CI |  | 95\% CI |  |  |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |
|  | Neck pain (10028836) | 0 | 0.0 | 0.02 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Pain in extremity (10033425) | 2 | 1.3 | 0.24 | 4.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 0.6 | 0.03 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Prostate cancer (10060862) | 1 | 0.6 | 0.03 | 3.5 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 1 | 0.6 | 0.03 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Headache (10019211) | 0 | 0.0 | 0.02 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Hepatic encephalopathy (10019660) | 1 | 0.6 | 0.03 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Motor dysfunction (10061296) | 0 | 0.0 | 0.02 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Neuropathy peripheral (10029331) | 1 | 0.6 | 0.03 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Paraesthesia (10033775) | 0 | 0.0 | 0.02 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Seizure (10039906) | 0 | 0.0 | 0.02 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Syncope (10042772) | 0 | 0.0 | 0.02 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
| Psychiatric disorders (10037175) | Anxiety (10002855) | 0 | 0.0 | 0.02 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.02 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 1 | 2.1 | 0.1 | 11.3 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.02 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Cough (10011224) | 0 | 0.0 | 0.02 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Epistaxis (10015090) | 0 | 0.0 | 0.02 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Hiccups (10020039) | 0 | 0.0 | 0.02 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.02 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Pulmonary embolism (10037377) | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Skin and subcutaneous tissue disorders (10040785) | Erythema (10015150) | 0 | 0.0 | 0.02 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.02 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.02 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
|  | Scar pain (10049002) | 0 | 0.0 | 0.02 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.02 | 2.3 | 1 | 0.6 | 0.0 | 3.2 | 0 | 0.0 | 0.0 | 7.0 |  | 0.0 | 0.0 | 7.5 |
|  | Urticaria (10046735) | 1 | 0.6 | 0.03 | 3.5 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | 0 | 0.0 | 0.0 | 7.5 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.02 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 0 | 0.0 | 0.0 | 7.0 | , | 2.1 | 0.1 | 11.3 |
|  | Thrombosis (10043607) | 0 | 0.0 | 0.02 | 2.3 | 0 | 0.0 | 0.0 | 2.1 | 1 | 2.0 | 0.0 | 10.4 | 0 | 0.0 | 0.0 | 7.5 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)

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$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; $\mathrm{LL}=$ Lower Limit, UL = Upper Limit

Table 8.157 Global Summary of unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :---: | :---: | :---: | :---: | :---: |
|  | PreChemo |  |  |  |  |  |  |  |  | OnChemo | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |  |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 72 | 79 | 26 | 22 | 98 | 101 |  |  |  |  |  |
| Number of doses followed by at least one unsolicited symptom | 109 | 129 | 40 | 34 | 149 | 163 |  |  |  |  |  |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 299 | 304 | 107 | 84 | 406 | 388 |  |  |  |  |  |
| Number of unsolicited symptoms reported** | 312 | 315 | 109 | 85 | 421 | 400 |  |  |  |  |  |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.158 Global Summary of grade 3 unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  | PreChemo |  | OnChemo |  | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su |
|  | Placebo |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 13 | 9 | 5 | 6 | 18 |
| Number of doses followed by at least one unsolicited symptom | 16 | 9 | 6 | 6 | 22 |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 17 | 14 | 6 | 8 | 23 |
| Number of unsolicited symptoms reported** | 17 | 14 | 6 | 8 | 22 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.159 Global Summary of unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  | PreChemo |  | OnChemo |  | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su |
|  | Placebo |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 10 | 7 | 0 | 2 | 10 |
| Number of doses followed by at least one unsolicited symptom | 11 | 9 | 0 | 2 | 11 |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term | 13 | 15 | 0 | 2 | 13 |
| Number of unsolicited symptoms reported** | 13 | 15 | 0 | 2 | 13 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.160 Global Summary of grade 3 unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | PreChemo |  | OnChemo |  | All |  |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |
| Number of subjects with at least one unsolicited symptom reported | 1 | 0 | 0 | 0 | 1 | 0 |
| Number of doses followed by at least one unsolicited symptom | 1 | 0 | 0 | 0 | 1 | 0 |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 1 | 0 | 0 | 0 | 1 | 0 |
| Number of unsolicited symptoms reported** | 1 | 0 | 0 | 0 | 1 | 0 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.161 Global Summary of unsolicited signs and symptoms reported with medically attended visit, within the 30 -day (Days $0-29$ ) postvaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :---: | :---: | :---: | :---: | :---: |
|  | PreChemo |  |  |  |  |  |  |  | OnChemo | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su |  |  |  |  |  |
|  | Placebo |  |  |  |  |  |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 19 | 27 | 12 | 5 | 31 |  |  |  |  |  |
| 32 |  |  |  |  |  |  |  |  |  |  |
| Number of doses followed by at least one unsolicited symptom | 23 | 34 | 13 | 7 | 36 |  |  |  |  |  |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 40 | 48 | 20 | 12 | 60 |  |  |  |  |  |
| Number of unsolicited symptoms reported** | 40 | 48 | 20 | 12 | 60 |  |  |  |  |  |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.162 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to 30 days post last vaccination by PreChemo/OnChemo groups (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

No records exist in this table

Table 8.163 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from 30 days post last vaccination up to the study end by PreChemo/OnChemo groups (ATP cohort for safety up to the study end)

|  |  | PreChemo |  |  |  |  | OnChemo |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \text { HZ/su } \\ & \mathrm{N}=86 \end{aligned}$ |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=88 \end{gathered}$ |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=24 \end{gathered}$ |  |  |
|  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  | $\begin{array}{r} 95^{\circ} \\ \mathrm{Cl} \end{array}$ | $5 \%$ |  |  | 95\% | CI |  |  | \% Cl |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL UL | n \% | LL | UL | n \% | \% L | LL | UL | n \% | LL | UL |
| At least one symptom |  | 00.0 | 0.04 .2 | 00.0 | 0.0 | 4.1 | 0 | . 0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 00.0 | 0.04 .2 | 00.0 | 0.0 | 4.1 | 0 | . 0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.164 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to the study end by PreChemo/OnChemo groups (ATP cohort for safety up to the study end)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=88$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | Placebo$N=24$ |  |  |
|  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) |  | \% | LL | UL |  | \% | LL | UL | n $\%$ | LL | UL | n \% | LL | UL |
| At least one symptom |  | 0 | 0.0 | 0.0 | 4.2 |  | 0.0 | 0.0 | 4.1 | 00 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 00 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit
Table 8.165 Global Summary of serious adverse events reported from the first vaccination up to 30 days post last vaccination by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :---: | :---: | :---: | :---: |
|  | PreChemo |  |  |  |  |  |  |  | OnChemo | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 9 | 9 | 7 | 4 | 16 | 13 |  |  |  |  |
| Number of doses followed by at least one unsolicited symptom | 9 | 10 | 8 | 5 | 17 | 15 |  |  |  |  |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 9 | 15 | 10 | 8 | 19 | 23 |  |  |  |  |
| Number of unsolicited symptoms reported** | 9 | 15 | 10 | 8 | 19 | 23 |  |  |  |  |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.166 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from the first vaccination up to 30 days post last vaccination by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=88$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | Placebo$N=24$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% Cl |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) |  | \% | LL | UL | n \% | LL | UL |  | \% | LL | UL |  | \% | LL | UL |
| At least one symptom |  | 9 | 10.5 | 4.9 | 18.9 | 910.2 | 4.8 | 818.5 | 7 | 25.9 | 11.1 | 46.3 | 4 | 16.7 | 4.7 | 37.4 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 0 | 0.0 | 0.0 | 4.2 | 22.3 | 0.3 | 38.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Febrile neutropenia (10016288) | 2 | 2.3 | 0.3 | 8.1 | 11.1 | 0.0 | 06.2 | 2 | 7.4 | 0.9 | 24.3 | 1 | 4.2 | 0.1 | 21.1 |
|  | Neutropenia (10029354) | 0 | 0.0 | 0.0 | 4.2 | 11.1 | 0.0 | 06.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 4.2 | 00.0 | 0.0 | 0 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Gastrointestinal disorders (10017947) | Constipation (10010774) | 0 | 0.0 | 0.0 | 4.2 | 00.0 | 0.0 | . 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| General disorders and administration site conditions (10018065) | Mucosal inflammation (10028116) | 0 | 0.0 | 0.0 | 4.2 | 00.0 | 0.0 | 04.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 4.2 | 00.0 | 0.0 | 0 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 4.2 | 11.1 | 0.0 | 06.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 0 | 0.0 | 0.0 | 4.2 | 00.0 | 0.0 | 0 4.1 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hepatitis c (10019744) | 0 | 0.0 | 0.0 | 4.2 | 00.0 | 0.0 | 04.1 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 4.2 | 00.0 | 0.0 | 04.1 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 4.2 | 11.1 | 0.0 | 0.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 4.2 | 00.0 | 0.0 | 0.4 .1 |  | 3.7 | 0.1 | 19.0 |  | 0.0 | 0.0 | 14.2 |
|  | Nasopharyngitis (10028810) | 1 | 1.2 | 0.0 | 6.3 | 00.0 | 0.0 | 04.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neutropenic sepsis (10049151) | 1 | 1.2 | 0.0 | 6.3 | 11.1 | 0.0 | 06.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Respiratory tract infection (10062352) | 0 | 0.0 | 0.0 | 4.2 | 00.0 | 0.0 | 0 4.1 |  | 3.7 | 0.1 | 19.0 |  | 0.0 | 0.0 | 14.2 |
|  | Sepsis (10040047) | 1 | 1.2 | 0.0 | 6.3 | 00.0 | 0.0 | 04.1 |  | 3.7 | 0.1 | 19.0 |  | 0.0 | 0.0 | 14.2 |
|  | Urinary tract infection (10046571) | 1 | 1.2 | 0.0 | 6.3 | 00.0 | 0.0 | . 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 4.2 | 11.1 | 0.0 | .06.2 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 0 | 0.0 | 0.0 | 4.2 | 00.0 | 0.0 | 04.1 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 1 | 1.2 | 0.0 | 6.3 | 00.0 | 0.0 | 04.1 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Prostate cancer (10060862) | 0 | 0.0 | 0.0 | 4.2 | 11.1 | 0.0 | 06.2 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
| Nervous system disorders (10029205) | Hepatic encephalopathy (10019660) | 1 | 1.2 | 0.0 | 6.3 | 00.0 | 0.0 | 04.1 | , | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 4.2 | 11.1 | 0.0 | 06.2 |  | 3.7 | 0.1 | 19.0 |  | 0.0 | 0.0 | 14.2 |

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|  |  | PreChemo |  |  |  | OnChemo |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  | Placebo$N=88$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  | Placebo$N=24$ |  |  |
|  |  | 95\% CI |  | 95\% CI |  | 95\% CI |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL UL | n \% | LL UL | n \% | LL | UL | n \% | LL | UL |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 00.0 | 0.04 .2 | 11.1 | 0.06.2 | 00.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
|  | Hydronephrosis (10020524) | 00.0 | 0.04 .2 | 11.1 | 0.06 .2 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Pleural effusion (10035598) | 00.0 | 0.04 .2 | 11.1 | 0.06 .2 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | ) 14.2 |
|  | Pulmonary embolism (10037377) | 11.2 | 0.06 .3 | 00.0 | 0.04 .1 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Skin and subcutaneous tissue disorders (10040785) | Skin haemorrhage (10064265) | 00.0 | 0.04.2 | 11.1 | 0.06 .2 | 00.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Vascular disorders (10047065) | Thrombosis (10043607) | 00.0 | 0.04.2 | 00.0 | 0.04 .1 | 13.7 | 0.1 | 19.0 | 00.0 |  | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.167 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, from the first vaccination up to 30 days post last vaccination by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

No records exist in this table

Table 8.168 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from 30 days post last vaccination up to the study end by PreChemo/OnChemo groups (ATP cohort for safety up to the study end)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=88$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=24 \end{gathered}$ |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  | 95\% Cl |  |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |  | \% | LL | UL |
| At least one symptom |  | 22 | 25.6 | 16.8 | 36.1 | 24 | 27.3 | 18.3 | 37.8 | 8 | 29.6 | 13.8 | 50.2 | 6 | 25.0 | 9.8 | 46.7 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 2 | 2.3 | 0.3 | 8.1 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Febrile neutropenia (10016288) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 2 | 7.4 | 0.9 | 24.3 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neutropenia (10029354) | 1 | 1.2 | 0.0 | 6.3 | 3 | 3.4 | 0.7 | 9.6 | 1 | 3.7 | 0.1 | 19.0 |  | 0.0 | 0.0 | 14.2 |
|  | Pancytopenia (10033661) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | - | 0.0 | 0.0 | 14.2 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Cardiac disorders (10007541) | Cardiac arrest (10007515) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Cardiac failure (10007554) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Cardiac failure congestive (10007559) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Myocardial infarction (10028596) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
| Gastrointestinal disorders (10017947) | Constipation (10010774) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Diarrhoea (10012735) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Dysphagia (10013950) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Enteritis (10014866) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Mouth ulceration (10028034) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Nausea (10028813) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Odynophagia (10030094) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oesophagitis (10030216) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| General disorders and administration site conditions (10018065) | Death (10011906) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Mucosal inflammation (10028116) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 |  | 0.0 | 0.0 | 14.2 |
| Hepatobiliary disorders (10019805) | Cholangitis acute (10008605) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Infections and infestations (10021881) | Anal abscess (10048946) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Bacteraemia (10003997) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |

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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=88$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=24 \end{gathered}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  | 95\% Cl |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL | n | \% | LL | UL |
|  | Clostridium bacteraemia (10058852) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Clostridium difficile infection (10054236) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Device related sepsis (10069802) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Diverticulitis (10013538) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Epiglottitis (10015030) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Gastroenteritis (10017888) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lung infection (10061229) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neutropenic sepsis (10049151) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oral candidiasis (10030963) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pleural infection (10061351) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pneumonia (10035664) | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.3 | 0.3 | 8.0 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Respiratory tract infection (10062352) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Sepsis (10040047) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Staphylococcal infection (10058080) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Upper respiratory tract infection (10046306) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Injury, poisoning and procedural complications (10022117) | Lumbar vertebral fracture (10049947) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Metabolism and nutrition disorders (10027433) | Diabetic ketoacidosis (10012671) | 2 | 2.3 | 0.3 | 8.1 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypokalaemia (10021015) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hyponatraemia (10021036) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 | O | 0.0 | 0.0 | 14.2 |
|  | Malnutrition (10061273) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Musculoskeletal chest pain (10050819) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Bladder cancer (10005003) | 2 | 2.3 | 0.3 | 8.1 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Breast cancer recurrent (10006198) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Cholangiocarcinoma (10008593) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Colon cancer (10009944) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Colorectal cancer (10061451) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Colorectal cancer metastatic (10052358) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Head and neck cancer (10067821) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Liposarcoma (10024627) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=88$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% Cl |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |  | \% | LL | UL |
|  | Lung neoplasm malignant (10058467) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Malignant melanoma (10025650) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Metastases to central nervous system (10059282) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Metastases to liver (10027457) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Non-small cell lung cancer (10061873) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Ovarian cancer (10033128) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Prostate cancer (10060862) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Rectal cancer metastatic (10055097) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Squamous cell carcinoma of lung (10041826) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Tongue neoplasm malignant stage unspecified (10043966) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Tumour haemorrhage (10049750) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Uterine leiomyosarcoma (10046799) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Bronchial obstruction (10006440) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pleural effusion (10035598) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pulmonary embolism (10037377) | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Respiratory failure (10038695) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Surgical and medical procedures (10042613) | Abdominal hernia repair (10060802) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Vascular disorders (10047065) | Superior vena cava occlusion (10058988) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%$ = number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.169 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, from 30 days post last vaccination up to the study end by PreChemo/OnChemo groups (ATP cohort for safety up to the study end)

No records exist in this table

Table 8.170 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to the study end by PreChemo/OnChemo groups (ATP cohort for safety up to the study end)

|  |  | PreChemo |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=88 \\ \hline \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | Placebo$N=24$ |  |  |
|  |  | 95\% CI |  |  |  | - 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% Cl |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | - | \% | LL | UL | n | \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 27 | 31.4 | 21.8 | 42.3 | 33 | 37.5 | 27.4 | 48.5 | 9 | 33.3 | 16.5 | 54.0 | 833.3 | 15.6 | 55.3 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 2 | 2.3 | 0.3 | 8.1 | 3 | 3.4 | 0.7 | 9.6 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Febrile neutropenia (10016288) | 3 | 3.5 | 0.7 | 9.9 | 1 | 1.1 | 0.0 | 6.2 | 3 | 11.1 | 2.4 | 29.2 | 14.2 | 0.1 | 21.1 |
|  | Neutropenia (10029354) | 1 | 1.2 | 0.0 | 6.3 | 4 | 4.5 | 1.3 | 11.2 | 1 | 3.7 | 0.1 | 19.0 | 00.0 | 0.0 | 14.2 |
|  | Pancytopenia (10033661) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 00.0 | 0.0 | 14.2 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
| Cardiac disorders (10007541) | Cardiac arrest (10007515) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Cardiac failure (10007554) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Cardiac failure congestive (10007559) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Myocardial infarction (10028596) |  | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
| Gastrointestinal disorders (10017947) | Constipation (10010774) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 14.2 | 0.1 | 21.1 |
|  | Diarrhoea (10012735) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 00.0 | 0.0 | 14.2 |
|  | Dysphagia (10013950) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Enteritis (10014866) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Mouth ulceration (10028034) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Nausea (10028813) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Odynophagia (10030094) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Oesophagitis (10030216) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| General disorders and administration site conditions (10018065) | Death (10011906) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 |  | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Mucosal inflammation (10028116) | 0 | 0.0 | 0.0 | 4.2 | - | 0.0 | 0.0 | 4.1 | 2 | 7.4 | 0.9 | 24.3 | 00.0 | 0.0 | 14.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 14.2 | 0.1 | 21.1 |
| Hepatobiliary disorders (10019805) | Cholangitis acute (10008605) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 4.2 |  | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
| Infections and infestations (10021881) | Anal abscess (10048946) | 0 | 0.0 | 0.0 | 4.2 | - | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |
|  | Bacteraemia (10003997) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 00.0 | 0.0 | 14.2 |

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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & N=88 \end{aligned}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ N=24 \end{gathered}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% Cl |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |  | \% | LL | UL |
|  | Candida infection (10074170) | - | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Clostridium bacteraemia (10058852) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Clostridium difficile infection (10054236) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Device related sepsis (10069802) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Diverticulitis (10013538) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Epiglottitis (10015030) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Gastroenteritis (10017888) |  | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hepatitis c (10019744) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lung infection (10061229) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Nasopharyngitis (10028810) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Neutropenic sepsis (10049151) | 1 | 1.2 | 0.0 | 6.3 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Oral candidiasis (10030963) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pleural infection (10061351) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pneumonia (10035664) | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.3 | 0.3 | 8.0 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Respiratory tract infection (10062352) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Sepsis (10040047) | 2 | 2.3 | 0.3 | 8.1 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 | 1 | 4.2 | 0.1 | 21.1 |
|  | Staphylococcal infection (10058080) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Upper respiratory tract infection (10046306) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urinary tract infection (10046571) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Lumbar vertebral fracture (10049947) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
| Metabolism and nutrition disorders (10027433) | Diabetic ketoacidosis (10012671) | 2 | 2.3 | 0.3 | 8.1 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hypokalaemia (10021015) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Hyponatraemia (10021036) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Malnutrition (10061273) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Musculoskeletal chest pain (10050819) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 |  | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |

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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | $\begin{aligned} & \text { Z/su } \\ & \text { I }=86 \end{aligned}$ |  |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Z} / \mathrm{su} \\ & \mathrm{~V}=2 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { aceb } \\ & \mathrm{V}=2 \end{aligned}$ |  |
|  |  |  |  |  | CI |  |  |  | Cl |  |  |  | \% CI |  |  |  | CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL |  | \% | LL | UL |  | \% | LL | UL |
| Neoplasms benign, malignant and unspecified (incl cysts and | Adenocarcinoma of colon (10001167) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Bladder cancer (10005003) | 2 | 2.3 | 0.3 | 8.1 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Breast cancer recurrent (10006198) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Cholangiocarcinoma (10008593) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Colon cancer (10009944) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 |  | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Colorectal cancer (10061451) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Colorectal cancer metastatic (10052358) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Head and neck cancer (10067821) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 1 | 4.2 | 0.1 | 21.1 |
|  | Liposarcoma (10024627) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 |  | 0.0 | 0.0 | 12.8 |  | 0.0 | 0.0 | 14.2 |
|  | Lung neoplasm malignant (10058467) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Malignant melanoma (10025650) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Metastases to central nervous system (10059282) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Metastases to liver (10027457) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Non-small cell lung cancer (10061873) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Ovarian cancer (10033128) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Prostate cancer (10060862) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 |  | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Rectal cancer metastatic (10055097) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Squamous cell carcinoma of lung (10041826) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Tongue neoplasm malignant stage unspecified (10043966) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Tumour haemorrhage (10049750) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 |  | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
|  | Uterine leiomyosarcoma (10046799) | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
| Nervous system disorders (10029205) | Hepatic encephalopathy (10019660) | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.1 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 1 | 3.7 | 0.1 | 19.0 | 0 | 0.0 | 0.0 | 14.2 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 |  | 4.2 | 0.1 | 21.1 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Bronchial obstruction (10006440) | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.1 | 0.0 | 6.2 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pleural effusion (10035598) | 1 | 1.2 | 0.0 | 6.3 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |
|  | Pulmonary embolism (10037377) | 1 | 1.2 | 0.0 | 6.3 | 2 | 2.3 | 0.3 | 8.0 | 0 | 0.0 | 0.0 | 12.8 | 0 | 0.0 | 0.0 | 14.2 |

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PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.171 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, from first vaccination up to the study end by PreChemo/OnChemo groups (ATP cohort for safety up to the study end)

No records exist in this table

Table 8.172 Global Summary of potential immune mediated diseases reported from the first vaccination up to 30 days post last vaccination by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

No records exist in this table

Table 8.173 Number and percentage of subjects with fatal outcome reported up to the study end by PreChemo/OnChemo groups (ATP cohort for safety up to the study end)

|  | PreChemo |  | OnChemo |  |
| :---: | :---: | :---: | :---: | :---: |
|  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ | Placebo $N=88$ | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=27 \end{aligned}$ | Placebo $N=24$ |
| Characteristics | n \% | n \% | n \% | n \% |
| Fatalities | 910.5 | 1011.4 | 311.1 | 14.2 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once

Table 8.174 Percentage of subjects with concomitant medication during the 30day (Day 0-29) post vaccination period by PreChemo/OnChemo groups (ATP cohort for safety up to 30 days post last vaccination)

|  | PreChemo |  |  |  |  |  |  |  |  |  | OnChemo |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  | 95\% CI |  |  |  |  |  |  |  | 95\% CI |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  |
|  | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 86 | 82 | 95.3 | 88.5 | 98.7 | 88 | 82 | 93.2 | 85.7 | 97.5 | 27 | 26 | 96.3 | 81.0 | 99.9 | 24 | 24 | 100 | 85.8 | 100 |
| Steroids to prevent chemotherapy nausea and vomiting | 86 | 75 | 87.2 | 78.3 | 93.4 | 88 | 74 | 84.1 | 74.8 | 91.0 | 27 | 23 | 85.2 | 66.3 | 95.8 | 24 | 21 | 87.5 | 67.6 | 97.3 |
| Any in anticipation of study vaccine reaction | 86 | 0 | 0.0 | 0.0 | 4.2 | 88 | 0 | 0.0 | 0.0 | 4.1 | 27 | 0 | 0.0 | 0.0 | 12.8 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Any chronic use | 86 | 4 | 4.7 | 1.3 | 11.5 | 88 | 4 | 4.5 | 1.3 | 11.2 | 27 | 0 | 0.0 | 0.0 | 12.8 | 24 | 3 | 12.5 | 2.7 | 32.4 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 72 | 65 | 90.3 | 81.0 | 96.0 | 84 | 73 | 86.9 | 77.8 | 93.3 | 24 | 21 | 87.5 | 67.6 | 97.3 | 23 | 18 | 78.3 | 56.3 | 92.5 |
| Steroids to prevent chemotherapy nausea and vomiting | 72 | 58 | 80.6 | 69.5 | 88.9 | 84 | 62 | 73.8 | 63.1 | 82.8 | 24 | 20 | 83.3 | 62.6 | 95.3 | 23 | 17 | 73.9 | 51.6 | 89.8 |
| Any in anticipation of study vaccine reaction | 72 | 0 | 0.0 | 0.0 | 5.0 | 84 | 0 | 0.0 | 0.0 | 4.3 | 24 | 0 | 0.0 | 0.0 | 14.2 | 23 | 0 | 0.0 | 0.0 | 14.8 |
| Any chronic use | 72 | 1 | 1.4 | 0.0 | 7.5 | 84 | 6 | 7.1 | 2.7 | 14.9 | 24 | 1 | 4.2 | 0.1 | 21.1 | 23 | 1 | 4.3 | 0.1 | 21.9 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 158 | 147 | 93.0 | 87.9 | 96.5 | 172 | 155 | 90.1 | 84.6 | 94.1 | 51 | 47 | 92.2 | 81.1 | 97.8 | 47 | 42 | 89.4 | 76.9 | 96.5 |
| Steroids to prevent chemotherapy nausea and vomiting | 158 | 133 | 84.2 | 77.5 | 89.5 | 172 | 136 | 79.1 | 72.2 | 84.9 | 51 | 43 | 84.3 | 71.4 | 93.0 | 47 | 38 | 80.9 | 66.7 | 90.9 |
| Any in anticipation of study vaccine reaction | 158 | 0 | 0.0 | 0.0 | 2.3 | 172 | 0 | 0.0 | 0.0 | 2.1 | 51 | 0 | 0.0 | 0.0 | 7.0 | 47 | 0 | 0.0 | 0.0 | 7.5 |
| Any chronic use | 158 | 5 | 3.2 | 1.0 | 7.2 | 172 | 10 | 5.8 | 2.8 | 10.4 | 51 | 1 | 2.0 | 0.0 | 10.4 | 47 | 4 | 8.5 | 2.4 | 20.4 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 86 | 83 | 96.5 | 90.1 | 99.3 | 88 | 86 | 97.7 | 92.0 | 99.7 | 27 | 26 | 96.3 | 81.0 | 99.9 | 24 | 24 | 100 | 85.8 | 100 |
| Steroids to prevent chemotherapy nausea and vomiting | 86 | 76 | 88.4 | 79.7 | 94.3 | 88 | 77 | 87.5 | 78.7 | 93.6 | 27 | 24 | 88.9 | 70.8 | 97.6 | 24 | 21 | 87.5 | 67.6 | 97.3 |
| Any in anticipation of study vaccine reaction | 86 | 0 | 0.0 | 0.0 | 4.2 | 88 | 0 | 0.0 | 0.0 | 4.1 | 27 | 0 | 0.0 | 0.0 | 12.8 | 24 | 0 | 0.0 | 0.0 | 14.2 |
| Any chronic use | 86 | 5 | 5.8 | 1.9 | 13.0 | 88 | 8 | 9.1 | 4.0 | 17.1 | 27 | 1 | 3.7 | 0.1 | 19.0 | 24 | 4 | 16.7 | 4.7 | 37.4 |

PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or -1 day)
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one administered dose
$n / \%=$ number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.175 Number and percentage of subjects who received vaccine dose(s) by age strata (Total Vaccinated Cohort)

|  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  | Placebo$N=30$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=85 \end{aligned}$ |  | $\begin{aligned} & \hline \text { HZ/su } \\ & \mathrm{N}=117 \\ & \hline \end{aligned}$ |  | Placebo$N=115$ |  |
| Total number of doses received | n | \% | n | \% | n | \% | n | \% | n | \% | n | \% |
| 1 | 2 | 6.5 | 0 | 0.0 | 15 | 517.4 | 5 | 5.9 | 17 | 14.5 | , | 4.3 |
| 2 | 29 | 93.5 | 30 | 100 | 71 | 182.6 | 80 | 94.1 | 100 | 85.5 | 110 | 95.7 |
| Any | 31 | 100 | 30 | 100 | 86 | 6100 | 85 | 100 | 117 | 100 | 115 | 100 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in each group or in total included in the considered cohort $\mathrm{n} / \%=$ number/percentage of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least one dose
Table 8.176 Compliance in returning symptom sheets by age strata (Total Vaccinated Cohort)
$\left.\begin{array}{|l|l|l|l|l|l|l|l|l|}\hline \text { Dose } & \text { Sub-group } & \text { Group } & \begin{array}{l}\text { Number } \\ \text { of } \\ \text { doses }\end{array} & \begin{array}{l}\text { Doses } \\ \text { NOT } \\ \text { according to } \\ \text { protocol }\end{array} & \begin{array}{l}\text { Number } \\ \text { of } \\ \text { general SS }\end{array} & \begin{array}{l}\text { Compliance } \\ \% \\ \text { general SS }\end{array} & \begin{array}{l}\text { Number } \\ \text { of } \\ \text { local SS }\end{array} & \begin{array}{l}\text { Compliance } \\ \%\end{array} \\ \text { local SS }\end{array}\right]$

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
SS = Symptom screens/sheets used for the collection of local and general solicited AEs
Compliance \% = (number of doses with symptom screen/sheet return / number of administered doses) X 100

Table 8.177 Incidence and nature of symptoms (solicited and unsolicited) reported during the 7 -day (Days $0-6$ ) post-vaccination period following each dose and overall by age strata (Total Vaccinated Cohort)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | 18-49ys | HZ/su | 31 | 30 | 96.8 | 83.3 | 99.9 | 31 | 24 | 77.4 | 58.9 | 90.4 | 31 | 27 | 87.1 | 70.2 | 96.4 |
|  |  | Placebo | 30 | 17 | 56.7 | 37.4 | 74.5 | 30 | 16 | 53.3 | 34.3 | 71.7 | 30 | 4 | 13.3 | 3.8 | 30.7 |
|  | $\geq 50 y s$ | HZ/su | 86 | 76 | 88.4 | 79.7 | 94.3 | 86 | 60 | 69.8 | 58.9 | 79.2 | 86 | 61 | 70.9 | 60.1 | 80.2 |
|  |  | Placebo | 85 | 41 | 48.2 | 37.3 | 59.3 | 85 | 41 | 48.2 | 37.3 | 59.3 | 85 | 0 | 0.0 | 0.0 | 4.2 |
| Dose 2 | 18-49ys | HZ/su | 29 | 25 | 86.2 | 68.3 | 96.1 | 29 | 23 | 79.3 | 60.3 | 92.0 | 29 | 21 | 72.4 | 52.8 | 87.3 |
|  |  | Placebo | 30 | 24 | 80.0 | 61.4 | 92.3 | 30 | 24 | 80.0 | 61.4 | 92.3 | 30 | 4 | 13.3 | 3.8 | 30.7 |
|  | $\geq 50 y s$ | HZ/su | 71 | 57 | 80.3 | 69.1 | 88.8 | 71 | 53 | 74.6 | 62.9 | 84.2 | 71 | 35 | 49.3 | 37.2 | 61.4 |
|  |  | Placebo | 80 | 60 | 75.0 | 64.1 | 84.0 | 80 | 60 | 75.0 | 64.1 | 84.0 | 80 | 2 | 2.5 | 0.3 | 8.7 |
| Overall/dose | 18-49ys | HZ/su | 60 | 55 | 91.7 | 81.6 | 97.2 | 60 | 47 | 78.3 | 65.8 | 87.9 | 60 | 48 | 80.0 | 67.7 | 89.2 |
|  |  | Placebo | 60 | 41 | 68.3 | 55.0 | 79.7 | 60 | 40 | 66.7 | 53.3 | 78.3 | 60 | 8 | 13.3 | 5.9 | 24.6 |
|  | $\geq 50 y s$ | HZ/su | 157 | 133 | 84.7 | 78.1 | 90.0 | 157 | 113 | 72.0 | 64.3 | 78.8 | 157 | 96 | 61.1 | 53.1 | 68.8 |
|  |  | Placebo | 165 | 101 | 61.2 | 53.3 | 68.7 | 165 | 101 | 61.2 | 53.3 | 68.7 | 165 | 2 | 1.2 | 0.1 | 4.3 |
| Overall/subject | 18-49ys | HZ/su | 31 | 31 | 100 | 88.8 | 100 | 31 | 28 | 90.3 | 74.2 | 98.0 | 31 | 29 | 93.5 | 78.6 | 99.2 |
|  |  | Placebo | 30 | 25 | 83.3 | 65.3 | 94.4 | 30 | 25 | 83.3 | 65.3 | 94.4 | 30 | 7 | 23.3 | 9.9 | 42.3 |
|  | $\geq 50 y s$ | HZ/su | 86 | 78 | 90.7 | 82.5 | 95.9 | 86 | 71 | 82.6 | 72.9 | 89.9 | 86 | 65 | 75.6 | 65.1 | 84.2 |
|  |  | Placebo | 85 | 67 | 78.8 | 68.6 | 86.9 | 85 | 67 | 78.8 | 68.6 | 86.9 | 85 | 2 | 2.4 | 0.3 | 8.2 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of administered doses
$n / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

## Table 8.178 Incidence and nature of grade 3 symptoms (solicited and unsolicited) reported during the 7 -day (Days 0-6) post-vaccination period following each dose and overall by age strata (Total Vaccinated Cohort)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  |  |  |  |  | 95\% Cl |  | 95\% CI |  |  |  |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N |  |  | LL | UL |
| Dose 1 | 18-49ys | HZ/su | 31 | 7 | 22.6 | 9.6 | 41.1 | 31 | 6 | 19.4 | 7.5 | 37.5 | 31 | 4 | 12.9 | 3.6 | 29.8 |
|  |  | Placebo | 30 | 4 | 13.3 | 3.8 | 30.7 | 30 | 4 | 13.3 | 3.8 | 30.7 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 86 | 15 | 17.4 | 10.1 | 27.1 | 86 | 11 | 112.8 | 6.6 | 21.7 | 86 | 6 | 7.0 | 2.6 | 14.6 |
|  |  | Placebo | 85 | 9 | 10.6 | 5.0 | 19.2 | 85 | 9 | 10.6 | 5.0 | 19.2 | 85 | 0 | 0.0 | 0.0 | 4.2 |
| Dose 2 | 18-49ys | HZ/su | 29 | 7 | 24.1 | 10.3 | 43.5 | 29 | 6 | 20.7 | 8.0 | 39.7 | 29 | 1 | 3.4 | 0.1 | 17.8 |
|  |  | Placebo | 30 | 7 | 23.3 | 9.9 | 42.3 | 30 | 7 | 23.3 | 9.9 | 42.3 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 71 | 12 | 16.9 | 9.0 | 27.7 | 71 | 12 | 216.9 | 9.0 | 27.7 | 71 | 3 | 4.2 | 0.9 | 11.9 |
|  |  | Placebo | 80 | 5 | 6.3 | 2.1 | 14.0 | 80 | 5 | 6.3 | 2.1 | 14.0 | 80 | 0 | 0.0 | 0.0 | 4.5 |
| Overall/dose | 18-49ys | HZ/su | 60 | 14 | 23.3 | 13.4 | 36.0 | 60 | 12 | 220.0 | 10.8 | 32.3 | 60 | 5 | 8.3 | 2.8 | 18.4 |
|  |  | Placebo | 60 | 11 | 18.3 | 9.5 | 30.4 | 60 | 11 | 118.3 | 9.5 | 30.4 | 60 | 0 | 0.0 | 0.0 | 6.0 |
|  | $\geq 50 y s$ | HZ/su | 157 | 27 | 17.2 | 11.6 | 24.0 | 157 | 23 | 314.6 | 9.5 | 21.2 | 157 | 9 | 5.7 | 2.7 | 10.6 |
|  |  | Placebo | 165 | 14 | 8.5 | 4.7 | 13.8 | 165 | 14 | 48.5 | 4.7 | 13.8 | 165 | 0 | 0.0 | 0.0 | 2.2 |
| Overall/subject | 18-49ys | HZ/su | 31 | 11 | 35.5 | 19.2 | 54.6 | 31 | 10 | 032.3 | 16.7 | 51.4 | 31 | 4 | 12.9 | 3.6 | 29.8 |
|  |  | Placebo | 30 | 8 | 26.7 | 12.3 | 45.9 | 30 | 8 | 26.7 | 12.3 | 45.9 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 86 | 20 | 23.3 | 14.8 | 33.6 | 86 | 18 | 820.9 | 12.9 | 31.0 | 86 | 9 | 10.5 | 4.9 | 18.9 |
|  |  | Placebo | 85 | 13 | 15.3 | 8.4 | 24.7 | 85 | 13 | 315.3 | 8.4 | 24.7 | 85 | 0 | 0.0 | 0.0 | 4.2 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of administered doses
$n / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered 95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.179 Incidence and nature of symptoms (solicited only) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (Total Vaccinated Cohort)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | 18-49ys | HZ/su | 31 | 30 | 96.8 | 83.3 | 99.9 | 31 | 23 | 74.2 | 55.4 | 88.1 | 31 | 27 | 87.1 | 70.2 | 96.4 |
|  |  | Placebo | 30 | 16 | 53.3 | 34.3 | 71.7 | 30 | 15 | 50.0 | 31.3 | 68.7 | 30 | 3 | 10.0 | 2.1 | 26.5 |
|  | $\geq 50 y s$ | HZ/su | 81 | 74 | 91.4 | 83.0 | 96.5 | 81 | 57 | 70.4 | 59.2 | 80.0 | 81 | 61 | 75.3 | 64.5 | 84.2 |
|  |  | Placebo | 80 | 37 | 46.3 | 35.0 | 57.8 | 80 | 37 | 46.3 | 35.0 | 57.8 | 80 | 0 | 0.0 | 0.0 | 4.5 |
| Dose 2 | 18-49ys | HZ/su | 29 | 25 | 86.2 | 68.3 | 96.1 | 29 | 22 | 75.9 | 56.5 | 89.7 | 29 | 21 | 72.4 | 52.8 | 87.3 |
|  |  | Placebo | 29 | 20 | 69.0 | 49.2 | 84.7 | 29 | 20 | 69.0 | 49.2 | 84.7 | 29 | 4 | 13.8 | 3.9 | 31.7 |
|  | $\geq 50 y s$ | HZ/su | 69 | 50 | 72.5 | 60.4 | 82.5 | 68 | 45 | 66.2 | 53.7 | 77.2 | 69 | 35 | 50.7 | 38.4 | 63.0 |
|  |  | Placebo | 76 | 40 | 52.6 | 40.8 | 64.2 | 75 | 40 | 53.3 | 41.4 | 64.9 | 76 | 1 | 1.3 | 0.0 | 7.1 |
| Overall/dose | 18-49ys | HZ/su | 60 | 55 | 91.7 | 81.6 | 97.2 | 60 | 45 | 75.0 | 62.1 | 85.3 | 60 | 48 | 80.0 | 67.7 | 89.2 |
|  |  | Placebo | 59 | 36 | 61.0 | 47.4 | 73.5 | 59 | 35 | 59.3 | 45.7 | 71.9 | 59 | 7 | 11.9 | 4.9 | 22.9 |
|  | $\geq 50 y s$ | HZ/su | 150 | 124 | 82.7 | 75.6 | 88.4 | 149 | 102 | 68.5 | 60.3 | 75.8 | 150 | 96 | 64.0 | 55.8 | 71.7 |
|  |  | Placebo | 156 | 77 | 49.4 | 41.3 | 57.5 | 155 | 77 | 49.7 | 41.6 | 57.8 | 156 |  | 0.6 | 0.0 | 3.5 |
| Overall/subject | 18-49ys | HZ/su | 31 | 31 | 100 | 88.8 | 100 | 31 | 27 | 87.1 | 70.2 | 96.4 | 31 | 29 | 93.5 | 78.6 | 99.2 |
|  |  | Placebo | 30 | 22 | 73.3 | 54.1 | 87.7 | 30 | 22 | 73.3 | 54.1 | 87.7 | 30 | - | 20.0 | 7.7 | 38.6 |
|  | $\geq 50 y s$ | HZ/su | 81 | 76 | 93.8 | 86.2 | 98.0 | 81 | 64 | 79.0 | 68.5 | 87.3 | 81 | 65 | 80.2 | 69.9 | 88.3 |
|  |  | Placebo | 80 | 51 | 63.8 | 52.2 | 74.2 | 80 | 51 | 63.8 | 52.2 | 74.2 | 80 | 1 | 1.3 | 0.0 | 6.8 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.180 Incidence and nature of grade 3 symptoms (solicited only) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (Total Vaccinated Cohort)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N |  | \% | LL | UL |
| Dose 1 | 18-49ys | HZ/su | 31 | 7 | 22.6 | 9.6 | 41.1 | 31 | 6 | 19.4 | 7.5 | 37.5 | 31 | 4 | 12.9 | 3.6 | 29.8 |
|  |  | Placebo | 30 | 4 | 13.3 | 3.8 | 30.7 | 30 | 4 | 13.3 | 3.8 | 30.7 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 81 | 13 | 16.0 | 8.8 | 25.9 | 81 | 9 | 11.1 | 5.2 | 20.0 | 81 |  | 7.4 | 2.8 | 15.4 |
|  |  | Placebo | 80 | 7 | 8.8 | 3.6 | 17.2 | 80 | 7 | 8.8 | 3.6 | 17.2 | 80 | 0 | 0.0 | 0.0 | 4.5 |
| Dose 2 | 18-49ys | HZ/su | 29 | 7 | 24.1 | 10.3 | 43.5 | 29 | 6 | 20.7 | 8.0 | 39.7 | 29 |  | 3.4 | 0.1 | 17.8 |
|  |  | Placebo | 29 | 6 | 20.7 | 8.0 | 39.7 | 29 | 6 | 20.7 | 8.0 | 39.7 | 29 | 0 | 0.0 | 0.0 | 11.9 |
|  | $\geq 50 y s$ | HZ/su | 69 | 10 | 14.5 | 7.2 | 25.0 | 68 | 10 | 14.7 | 7.3 | 25.4 | 69 | 3 | 4.3 | 0.9 | 12.2 |
|  |  | Placebo | 76 | 4 | 5.3 | 1.5 | 12.9 | 75 | 4 | 5.3 | 1.5 | 13.1 | 76 | 0 | 0.0 | 0.0 | 4.7 |
| Overall/dose | 18-49ys | HZ/su | 60 | 14 | 23.3 | 13.4 | 36.0 | 60 | 12 | 20.0 | 10.8 | 32.3 | 60 | 5 | 8.3 | 2.8 | 18.4 |
|  |  | Placebo | 59 | 10 | 16.9 | 8.4 | 29.0 | 59 | 10 | 16.9 | 8.4 | 29.0 | 59 | 0 | 0.0 | 0.0 | 6.1 |
|  | $\geq 50 y s$ | HZ/su | 150 | 23 | 15.3 | 10.0 | 22.1 | 149 | 19 | 12.8 | 7.9 | 19.2 | 150 | 9 | 6.0 | 2.8 | 11.1 |
|  |  | Placebo | 156 | 11 | 7.1 | 3.6 | 12.3 | 155 | 11 | 11.1 | 3.6 | 12.3 | 156 | 0 | 0.0 | 0.0 | 2.3 |
| Overall/subject | 18-49ys | HZ/su | 31 | 11 | 35.5 | 19.2 | 54.6 | 31 | 10 | 32.3 | 16.7 | 51.4 | 31 | 4 | 12.9 | 3.6 | 29.8 |
|  |  | Placebo | 30 | 7 | 23.3 | 9.9 | 42.3 | 30 | 7 | 23.3 | 9.9 | 42.3 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 81 | 17 | 21.0 | 12.7 | 31.5 | 81 | 15 | 18.5 | 10.8 | 28.7 | 81 | - | 11.1 | 5.2 | 20.0 |
|  |  | Placebo | 80 | 10 | 12.5 | 6.2 | 21.8 | 80 | 10 | 12.5 | 6.2 | 21.8 | 80 |  | 0.0 | 0.0 | 4.5 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.181 Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  |  |  | $\geq 50 \mathrm{ys}$ |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |
|  |  |  |  |  | 95 \% | \% CI |  |  |  | \% Cl |  |  |  | 95 \% | CI |  |  |  | \% Cl |
| Symptom | Type | N | n | \% | LL | UL | N | n \% | LL | UL | N | n | \% | LL | UL | N | n \% |  | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 31 | 26 | 83.9 | 66.3 | 94.5 | 30 | 26.7 | 0.8 | . 22.1 | 81 | 57 | 70.4 | 59.2 | 80.0 | 80 | 00.0 | 0.0 | . 5 |
|  | Grade 2 or 3 | 31 | 11 | 35.5 | 19.2 | 54.6 | 30 | 00.0 | 0.0 | 0.011 .6 | 81 | 16 | 19.8 | 11.7 | 30.1 | 80 | 00.0 | 0.0 | 4.5 |
|  | Grade 3 | 31 | 4 | 12.9 | 3.6 | 29.8 | 30 | 00.0 | 0.0 | . 11.6 | 81 | 4 | 4.9 | 1.4 | 12.2 | 80 | 00.0 | 0.0 | 4.5 |
|  | Medical advice | 31 | 0 | 0.0 | 0.0 | 11.2 | 30 | 00.0 | 0.0 | 0.011 .6 | 81 | 1 | 1.2 | 0.0 | 6.7 | 80 | 00.0 | 0.0 | 4.5 |
| Redness (mm) | All | 31 | 11 | 35.5 | 19.2 | 54.6 | 30 | 00.0 | 0.0 | 0.011 .6 | 81 | 22 | 27.2 | 17.9 | 38.2 | 80 | 00.0 | 0.0 | 4.5 |
|  | $>50$ | 31 | 7 | 22.6 | 9.6 | 41.1 | 30 | 00.0 | 0.0 | . 11.6 | 81 | 11 | 13.6 | 7.0 | 23.0 | 80 | 00.0 | 0.0 | 4.5 |
|  | >100 | 31 | 0 | 0.0 | 0.0 | 11.2 | 30 | 00.0 | 0.0 | . 11.6 | 81 | 2 | 2.5 | 0.3 | 8.6 | 80 | 00.0 | 0.0 | 4.5 |
|  | Medical advice | 31 | 0 | 0.0 | 0.0 | 11.2 | 30 | 00.0 | 0.0 | . 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 00.0 | 0.0 | 4.5 |
| Swelling (mm) | All | 31 | 6 | 19.4 | 7.5 | 37.5 | 30 | 13.3 | 0.1 | 117.2 | 81 | 9 | 11.1 | 5.2 | 20.0 | 80 | 00.0 | 0.0 | 4.5 |
|  | $>50$ | 31 | 3 | 9.7 | 2.0 | 25.8 | 30 | 00.0 | 0.0 | . 11.6 | 81 | 5 | 6.2 | 2.0 | 13.8 | 80 | 00.0 | 0.0 | 4.5 |
|  | >100 | 31 | 0 | 0.0 | 0.0 | 11.2 | 30 | 00.0 | 0.0 | 011.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 00.0 | 0.0 | 4.5 |
|  | Medical advice | 31 | 0 | 0.0 | 0.0 | 11.2 | 30 | 00.0 | 0.0 | 011.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 |  |  |  |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 29 | 19 | 65.5 | 45.7 | 82.1 | 29 | 413.8 | 3.9 | 9 31.7 | 69 | 33 | 47.8 | 35.6 | 60.2 | 76 | 1 |  | 7.1 |
|  | Grade 2 or 3 | 29 | 5 | 17.2 | 5.8 | 35.8 | 29 | 00.0 | 0.0 | 0.011 .9 | 69 | 14 | 20.3 | 11.6 | 31.7 | 76 | 11.3 | 0.0 | 7.1 |
|  | Grade 3 | 29 | 1 | 3.4 | 0.1 | 17.8 | 29 | 00.0 | 0.0 | 0.011 .9 | 69 | 3 | 4.3 | 0.9 | 12.2 | 76 | 00.0 | 0.0 | 4.7 |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 00.0 | 0.0 | 0.011 .9 | 69 | 0 | 0.0 | 0.0 | 5.2 | 76 | 00.0 | 0.0 | 4.7 |
| Redness (mm) | All | 29 | 8 | 27.6 | 12.7 | 47.2 | 29 | 00.0 | 0.0 | 011.9 | 69 | 12 | 17.4 | 9.3 | 28.4 | 76 | 00.0 | 0.0 | 4.7 |
|  | $>50$ | 29 | 3 | 10.3 | 2.2 | 27.4 | 29 | 00.0 | 0.0 | 0.011 .9 | 69 | 5 | 7.2 | 2.4 | 16.1 | 76 | 00.0 | 0.0 | 4.7 |
|  | >100 | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 00.0 | 0.0 | 0.011 .9 | 69 | 0 | 0.0 | 0.0 | 5.2 | 76 | 00.0 | 0.0 | 4.7 |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 00.0 | 0.0 | 011.9 | 69 | 0 | 0.0 | 0.0 | 5.2 | 76 | 00.0 | 0.0 | 4.7 |
| Swelling (mm) | All | 29 | 4 | 13.8 | 3.9 | 31.7 | 29 | 00.0 | 0.0 | . 11.9 | 69 | 4 | 5.8 | 1.6 | 14.2 | 76 | 00.0 | 0.0 | 4.7 |
|  | $>50$ | 29 | 1 | 3.4 | 0.1 | 17.8 | 29 | 00.0 | 0.0 | . 11.9 | 69 | 3 | 4.3 | 0.9 | 12.2 | 76 | 00.0 | 0.0 | 4.7 |
|  | >100 | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 00.0 | 0.0 | . 11.9 | 69 | 0 | 0.0 | 0.0 | 5.2 | 76 | 00.0 | 0.0 | 4.7 |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 00.0 | 0.0 | 11.9 | 69 | 0 | 0.0 | 0.0 | 5.2 | 76 | 00.0 |  | 4.7 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 60 | 45 | 75.0 | 62.1 | 85.3 | 59 | 610.2 | 3.8 | 20.8 | 150 | 90 | 60.0 | 51.7 | 67.9 | 156 | 10.6 | 0.0 | 3.5 |
|  | Grade 2 or 3 | 60 | 16 | 26.7 | 16.1 | 39.7 | 59 | 00.0 | 0.0 | 6.1 | 150 | 30 | 20.0 | 13.9 | 27.3 | 156 | 10.6 | 0.0 | 3.5 |
|  | Grade 3 | 60 | 5 | 8.3 | 2.8 | 18.4 | 59 | 00.0 | 0.0 | 0.1 | 150 | 7 | 4.7 | 1.9 | 9.4 | 156 | 00.0 | 0.0 | 2.3 |
|  | Medical advice | 60 | 0 | 0.0 | 0.0 | 6.0 | 59 | 00.0 | 0.0 | 0.1 | 150 | 1 | 0.7 | 0.0 | 3.7 | 156 | 00.0 | 0.0 | 2.3 |
| Redness (mm) | All | 60 | 19 | 31.7 | 20.3 | 45.0 | 59 | 00.0 | 0.0 | 6.1 | 150 | 34 | 22.7 | 16.2 | 30.2 | 156 | 00.0 | 0.0 | 2.3 |
|  | $>50$ | 60 | 10 | 16.7 | 8.3 | 28.5 | 59 | 00.0 | 0.0 | 6.1 | 150 | 16 | 10.7 | 6.2 | 16.7 | 156 | 00.0 | 0.0 | 2.3 |
|  | >100 | 60 | 0 | 0.0 | 0.0 | 6.0 | 59 | 00.0 | 0.0 | 6.1 | 150 | 2 | 1.3 | 0.2 | 4.7 | 156 | 00.0 | 0.0 | 2.3 |
|  | Medical advice | 60 | 0 | 0.0 | 0.0 | 6.0 | 59 | 00.0 | 0.0 | 6.1 | 150 | 0 | 0.0 | 0.0 | 2.4 | 156 | 00.0 | 0.0 | 2.3 |
| Swelling (mm) | All | 60 | 10 | 16.7 | 8.3 | 28.5 | 59 | 11.7 | 0.0 | 9.1 | 150 | 13 | 8.7 | 4.7 | 14.4 | 156 | 00.0 | 0.0 | 2.3 |
|  | $>50$ | 60 | 4 | 6.7 | 1.8 | 16.2 | 59 | 00.0 | 0.0 | 06.1 | 150 | 8 | 5.3 | 2.3 | 10.2 | 156 | 00.0 | 0.0 | 2.3 |
|  | >100 | 60 | 0 | 0.0 | 0.0 | 6.0 | 59 | 00.0 | 0.0 | 6.1 | 150 | 0 | 0.0 | 0.0 | 2.4 | 156 | 00.0 | 0.0 | 2.3 |
|  | Medical advice | 60 | 0 | 0.0 | 0.0 | 6.0 | 59 | 00.0 | 0.0 | 6.1 | 150 | 0 | 0.0 | 0.0 | 2.4 | 156 | 00.0 | 0.0 | 2.3 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 31 | 28 | 90.3 | 74.2 | 98.0 | 30 | $6 \mid 20.0$ | 7.7 | 738.6 | 81 | 62 | 76.5 | 65.8 | 85.2 | 80 | 11.3 | 0.0 | 6.8 |
|  | Grade 2 or 3 | 31 | 12 | 38.7 | 21.8 | 57.8 | 30 | 00.0 | 0.0 | 11.6 | 81 | 23 | 28.4 | 18.9 | 39.5 | 80 | 11.3 | 0.0 | 6.8 |
|  | Grade 3 | 31 | 4 | 12.9 | 3.6 | 29.8 | 30 | 00.0 | 0.0 | . 11.6 | 81 | 7 | 8.6 | 3.5 | 17.0 | 80 | 00.0 | 0.0 | 4.5 |
|  | Medical advice | 31 | 0 | 0.0 | 0.0 | 11.2 | 30 | 00.0 | 0.0 | . 11.6 | 81 | 1 | 1.2 | 0.0 | 6.7 | 80 | 00.0 | 0.0 | 4.5 |
| Redness (mm) | All | 31 | 14 | 45.2 | 27.3 | 64.0 | 30 | 00.0 | 0.0 | . 11.6 | 81 | 26 | 32.1 | 22.2 | 43.4 | 80 | 00.0 | 0.0 | 4.5 |
|  | $>50$ | 31 | 7 | 22.6 | 9.6 | 41.1 | 30 | 00.0 | 0.0 | . 11.6 | 81 | 12 | 14.8 | 7.9 | 24.4 | 80 | 00.0 | 0.0 | 4.5 |
|  | >100 | 31 | 0 | 0.0 | 0.0 | 11.2 | 30 | 00.0 | 0.0 | . 11.6 | 81 | 2 | 2.5 | 0.3 | 8.6 | 80 | 00.0 |  | 4.5 |
|  | Medical advice | 31 | 0 | 0.0 | 0.0 | 11.2 |  | 00.0 | 0.0 | 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 00.0 |  | 4.5 |



18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; $\mathrm{LL}=$ lower limit, UL = upper limit

116427 (ZOSTER-028)
Report Final
Table 8.182 Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  |  |  |  | $\geq 50 \mathrm{ys}$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N n | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 311 | 17 | 54.8 | 36.0 | 72.7 | 30 | 14 | 46.7 | 28.3 | 65.7 | 81 | 39 | 48.1 | 36.9 | 59.5 | 80 | 30 | 37.5 | 26.9 | 49.0 |
|  | Grade 2 or 3 | 311 | 10 | 32.3 | 16.7 | 51.4 | 30 | 5 | 16.7 | 5.6 | 34.7 | 81 | 20 | 24.7 | 15.8 | 35.5 | 80 | 10 | 12.5 | 6.2 | 21.8 |
|  | Grade 3 | 315 |  | 16.1 | 5.5 | 33.7 | 30 | 2 | 6.7 | 0.8 | 22.1 | 81 | 5 | 6.2 | 2.0 | 13.8 | 80 | 1 | 1.3 | 0.0 | 6.8 |
|  | Related | 318 |  | 25.8 | 11.9 | 44.6 | 305 | 5 | 16.7 | 5.6 | 34.7 | 81 | 7 | 8.6 | 3.5 | 17.0 | 80 | 5 | 6.3 | 2.1 | 14.0 |
|  | Grade 2 or 3 <br> Related | 315 |  | 16.1 | 5.5 | 33.7 | 30 | 1 | 3.3 | 0.1 | 17.2 | 81 | 4 | 4.9 | 1.4 | 12.2 | 80 | 3 | 3.8 | 0.8 | 10.6 |
|  | Grade 3 <br> Related | 312 |  | 6.5 | 0.8 | 21.4 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 1 | 1.2 | 0.0 | 6.7 | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  | Medical advice | 310 |  | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 0 | 0.0 | 0.0 | 4.5 |
| Gastrointestinal symptoms | All | 318 |  | 25.8 | 11.9 | 44.6 | 30 | 6 | 20.0 | 7.7 | 38.6 | 81 | 24 | 29.6 | 20.0 | 40.8 | 80 | 15 | 18.8 | 10.9 | 29.0 |
|  | Grade 2 or 3 | 315 |  | 16.1 | 5.5 | 33.7 | 30 | 4 | 13.3 | 3.8 | 30.7 | 81 | 9 | 11.1 | 5.2 | 20.0 | 80 | 7 | 8.8 | 3.6 | 17.2 |
|  | Grade 3 | 311 |  | 3.2 | 0.1 | 16.7 | 30 | 2 | 6.7 | 0.8 | 22.1 | 81 | 1 | 1.2 | 0.0 | 6.7 | 80 | 3 | 3.8 | 0.8 | 10.6 |
|  | Related | 312 | 2 | 6.5 | 0.8 | 21.4 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 7 | 8.6 | 3.5 | 17.0 | 80 | 2 | 2.5 | 0.3 | 8.7 |
|  | Grade 2 or 3 <br> Related | 311 |  | 3.2 | 0.1 | 16.7 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 1 | 1.2 | 0.0 | 6.7 | 80 | 1 | 1.3 | 0.0 | 6.8 |
|  | Grade 3 <br> Related | 310 |  | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 1 | 1.3 | 0.0 | 6.8 |
|  | Medical advice | 310 |  | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 2 | 2.5 | 0.3 | 8.7 |
| Headache | All | 311 | 10 | 32.3 | 16.7 | 51.4 | 30 | 9 | 30.0 | 14.7 | 49.4 | 81 | 18 | 22.2 | 13.7 | 32.8 | 80 | 15 | 18.8 | 10.9 | 29.0 |
|  | Grade 2 or 3 | 315 |  | 16.1 | 5.5 | 33.7 | 30 | 3 | 10.0 | 2.1 | 26.5 | 81 | 9 | 11.1 | 5.2 | 20.0 | 80 | 5 | 6.3 | 2.1 | 14.0 |
|  | Grade 3 | 311 |  | 3.2 | 0.1 | 16.7 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 2 | 2.5 | 0.3 | 8.6 | 80 | 1 | 1.3 | 0.0 | 6.8 |
|  | Related | 314 |  | 12.9 | 3.6 | 29.8 | 30 | 2 | 6.7 | 0.8 | 22.1 | 81 | 6 | 7.4 | 2.8 | 15.4 | 80 | 2 | 2.5 | 0.3 | 8.7 |
|  | Grade 2 or 3 <br> Related | 312 |  | 6.5 | 0.8 | 21.4 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 4 | 4.9 | 1.4 | 12.2 | 80 | 1 | 1.3 | 0.0 | 6.8 |
|  | Grade 3 <br> Related | 311 |  | 3.2 | 0.1 | 16.7 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 1 | 1.2 | 0.0 | 6.7 | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  | Medical advice | 310 |  | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 0 | 0.0 | 0.0 | 4.5 |
| Myalgia | All | 311 | 15 | 48.4 | 30.2 | 66.9 | 30 | 3 | 10.0 | 2.1 | 26.5 | 81 | 35 | 43.2 | 32.2 | 54.7 | 80 | 14 | 17.5 | 9.9 | 27.6 |
|  | Grade 2 or 3 | 318 |  | 25.8 | 11.9 | 44.6 | 30 | 2 | 6.7 | 0.8 | 22.1 | 81 | 13 | 16.0 | 8.8 | 25.9 | 80 | 7 | 8.8 | 3.6 | 17.2 |
|  | Grade 3 | 314 |  | 12.9 | 3.6 | 29.8 | 30 | 2 | 6.7 | 0.8 | 22.1 | 81 | 4 | 4.9 | 1.4 | 12.2 | 80 | 1 | 1.3 | 0.0 | 6.8 |
|  | Related | 311 | 11 | 35.5 | 19.2 | 54.6 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 14 | 17.3 | 9.8 | 27.3 | 80 | 3 | 3.8 | 0.8 | 10.6 |
|  | Grade 2 or 3 <br> Related | 316 |  | 19.4 | 7.5 | 37.5 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 8 | 9.9 | 4.4 | 18.5 | 80 | 2 | 2.5 | 0.3 | 8.7 |
|  | Grade 3 Related | 313 |  | 9.7 | 2.0 | 25.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 4 | 4.9 | 1.4 | 12.2 | 80 | 0 | 0.0 | 0.0 | 4.5 |


|  |  | 18-49ys |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Medical advice | 310 | 0 | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 0 | 0.0 | 0.0 | 4.5 |
| Shivering | All | 319 | 9 | 29.0 | 14.2 | 48.0 | 30 | 5 | 16.7 | 5.6 | 34.7 | 81 | 18 | 22.2 | 13.7 | 32.8 | 80 | 8 | 10.0 | 4.4 | 18.8 |
|  | Grade 2 or 3 | 313 | 3 | 9.7 | 2.0 | 25.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 6 | 7.4 | 2.8 | 15.4 | 80 | 6 | 7.5 | 2.8 | 15.6 |
|  | Grade 3 | 312 | 2 | 6.5 | 0.8 | 21.4 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 3 | 3.7 | 0.8 | 10.4 | 80 | 2 | 2.5 | 0.3 | 8.7 |
|  | Related | 316 | 6 | 19.4 | 7.5 | 37.5 | 30 | 1 | 3.3 | 0.1 | 17.2 | 81 | 6 | 7.4 | 2.8 | 15.4 | 80 | 3 | 3.8 | 0.8 | 10.6 |
|  | Grade 2 or 3 <br> Related | 313 | 3 | 9.7 | 2.0 | 25.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 4 | 4.9 | 1.4 | 12.2 | 80 | 2 | 2.5 | 0.3 | 8.7 |
|  | Grade 3 Related | 312 | 2 | 6.5 | 0.8 | 21.4 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 2 | 2.5 | 0.3 | 8.6 | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  | Medical advice | 310 | 0 | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 0 | 0.0 | 0.0 | 4.5 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 314 | 4 | 12.9 | 3.6 | 29.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 9 | 11.1 | 5.2 | 20.0 | 80 | 4 | 5.0 | 1.4 | 12.3 |
|  | $\geq 37.5$ | 314 | 4 | 12.9 | 3.6 | 29.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 9 | 11.1 | 5.2 | 20.0 | 80 | 4 | 5.0 | 1.4 | 12.3 |
|  | >38.0 | 310 | 0 | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 2 | 2.5 | 0.3 | 8.6 | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  | $>38.5$ | 310 | 0 | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 1 | 1.2 | 0.0 | 6.7 | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  | >39.0 | 310 | 0 | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  | $>39.5$ | 310 | 0 | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  | >40.0 | 310 | 0 | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  | Related | 314 | 4 | 12.9 | 3.6 | 29.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 7 | 8.6 | 3.5 | 17.0 | 80 | 1 | 1.3 | 0.0 | 6.8 |
|  | $\begin{aligned} & >38.0 \\ & \text { Related } \end{aligned}$ | 310 | 0 | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 2 | 2.5 | 0.3 | 8.6 | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  | $\begin{aligned} & \hline>39.0 \\ & \text { Related } \end{aligned}$ | 310 |  | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  | Medical advice | 310 |  | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 1 | 1.3 | 0.0 | 6.8 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 29 | 18 | 62.1 | 42.3 | 79.3 | 29 | 18 | 62.1 | 42.3 | 79.3 | 68 | 39 | 57.4 | 44.8 | 69.3 | 75 | 39 | 52.0 | 40.2 | 63.7 |
|  | Grade 2 or 3 | 29 | 9 | 31.0 | 15.3 | 50.8 | 29 | 8 | 27.6 | 12.7 | 47.2 | 68 | 19 | 27.9 | 17.7 | 40.1 | 75 | 22 | 29.3 | 19.4 | 41.0 |
|  | Grade 3 | 29 | 4 | 13.8 | 3.9 | 31.7 | 29 | 3 | 10.3 | 2.2 | 27.4 | 68 | 5 | 7.4 | 2.4 | 16.3 | 75 | 3 | 4.0 | 0.8 | 11.2 |
|  | Related | 29 | 3 | 10.3 | 2.2 | 27.4 | 29 | 4 | 13.8 | 3.9 | 31.7 | 68 | 3 | 4.4 | 0.9 | 12.4 | 75 | 4 | 5.3 | 1.5 | 13.1 |
|  | Grade 2 or 3 <br> Related | 29 |  | 3.4 | 0.1 | 17.8 | 29 | 1 | 3.4 | 0.1 | 17.8 | 68 | 1 | 1.5 | 0.0 | 7.9 | 75 | 3 | 4.0 | 0.8 | 11.2 |
|  | Grade 3 Related | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 1 | 3.4 | 0.1 | 17.8 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 1 | 1.5 | 0.0 | 7.9 | 75 | 1 | 1.3 | 0.0 | 7.2 |
| Gastrointestinal symptoms | All | 29 | 16 | 55.2 | 35.7 | 73.6 | 29 | 13 | 44.8 | 26.4 | 64.3 | 68 | 25 | 36.8 | 25.4 | 49.3 | 75 | 26 | 34.7 | 24.0 | 46.5 |
|  | Grade 2 or 3 | 29 | 10 | 34.5 | 17.9 | 54.3 | 29 | 6 | 20.7 | 8.0 | 39.7 | 68 | 11 | 16.2 | 8.4 | 27.1 | 75 | 9 | 12.0 | 5.6 | 21.6 |
|  | Grade 3 | 292 | 2 | 6.9 | 0.8 | 22.8 | 29 | 2 | 6.9 | 0.8 | 22.8 | 68 | 3 | 4.4 | 0.9 | 12.4 | 75 | 1 | 1.3 | 0.0 | 7.2 |
|  | Related | 29 | 3 | 10.3 | 2.2 | 27.4 | 29 | 1 | 3.4 | 0.1 | 17.8 | 68 | 3 | 4.4 | 0.9 | 12.4 | 75 | 1 | 1.3 | 0.0 | 7.2 |
|  | Grade 2 or 3 <br> Related | 29 |  | 3.4 | 0.1 | 17.8 | 29 | 1 | 3.4 | 0.1 | 17.8 | 68 | 1 | 1.5 | 0.0 | 7.9 | 75 | 1 | 1.3 | 0.0 | 7.2 |
|  | Grade 3 <br> Related | 29 |  | 3.4 | 0.1 | 17.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |


|  |  | 18-49ys |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Medical advice | 290 | 0 | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 1 | 1.5 | 0.0 | 7.9 | 75 | 0 | 0.0 | 0.0 | 4.8 |
| Headache | All | 299 | 9 | 31.0 | 15.3 | 50.8 | 29 | 12 | 41.4 | 23.5 | 61.1 | 68 | 20 | 29.4 | 19.0 | 41.7 | 75 | 13 | 17.3 | 9.6 | 27.8 |
|  | Grade 2 or 3 | 294 | 4 | 13.8 | 3.9 | 31.7 | 29 | 3 | 10.3 | 2.2 | 27.4 | 68 | 10 | 14.7 | 7.3 | 25.4 | 75 | 4 | 5.3 | 1.5 | 13.1 |
|  | Grade 3 | 291 | 1 | 3.4 | 0.1 | 17.8 | 29 | 2 | 6.9 | 0.8 | 22.8 | 68 | 2 | 2.9 | 0.4 | 10.2 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | Related | 291 | 1 | 3.4 | 0.1 | 17.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 6 | 8.8 | 3.3 | 18.2 | 75 | 2 | 2.7 | 0.3 | 9.3 |
|  | Grade 2 or 3 <br> Related | 29 | 1 | 3.4 | 0.1 | 17.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 3 | 4.4 | 0.9 | 12.4 | 75 | 1 | 1.3 | 0.0 | 7.2 |
|  | Grade 3 Related | 290 | 0 | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | Medical advice | 29 | 1 | 3.4 | 0.1 | 17.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |
| Myalgia | All | 29 | 11 | 37.9 | 20.7 | 57.7 | 29 | 6 | 20.7 | 8.0 | 39.7 | 68 | 21 | 30.9 | 20.2 | 43.3 | 75 | 17 | 22.7 | 13.8 | 33.8 |
|  | Grade 2 or 3 | 29 | 4 | 13.8 | 3.9 | 31.7 | 29 | 3 | 10.3 | 2.2 | 27.4 | 68 | 11 | 16.2 | 8.4 | 27.1 | 75 | 10 | 13.3 | 6.6 | 23.2 |
|  | Grade 3 | 29 | 1 | 3.4 | 0.1 | 17.8 | 29 | 1 | 3.4 | 0.1 | 17.8 | 68 | 3 | 4.4 | 0.9 | 12.4 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | Related | 29 | 5 | 17.2 | 5.8 | 35.8 | 29 | 1 | 3.4 | 0.1 | 17.8 | 68 | 8 | 11.8 | 5.2 | 21.9 | 75 | 3 | 4.0 | 0.8 | 11.2 |
|  | Grade 2 or 3 <br> Related | 29 | 1 | 3.4 | 0.1 | 17.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 5 | 7.4 | 2.4 | 16.3 | 75 | 2 | 2.7 | 0.3 | 9.3 |
|  | Grade 3 Related | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |
| Shivering | All | 297 | 7 | 24.1 | 10.3 | 43.5 | 29 | 8 | 27.6 | 12.7 | 47.2 | 68 | 13 | 19.1 | 10.6 | 30.5 | 75 | 9 | 12.0 | 5.6 | 21.6 |
|  | Grade 2 or 3 | 29 | 3 | 10.3 | 2.2 | 27.4 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 7 | 10.3 | 4.2 | 20.1 | 75 | 1 | 1.3 | 0.0 | 7.2 |
|  | Grade 3 | 29 | 1 | 3.4 | 0.1 | 17.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 2 | 2.9 | 0.4 | 10.2 | 75 | 1 | 1.3 | 0.0 | 7.2 |
|  | Related | 29 | 1 | 3.4 | 0.1 | 17.8 | 29 | 1 | 3.4 | 0.1 | 17.8 | 68 | 5 | 7.4 | 2.4 | 16.3 | 75 | 3 | 4.0 | 0.8 | 11.2 |
|  | Grade 2 or 3 <br> Related | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 3 | 4.4 | 0.9 | 12.4 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | Grade 3 Related | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 1 | 1.5 | 0.0 | 7.9 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 29 | 4 | 13.8 | 3.9 | 31.7 | 29 | 1 | 3.4 | 0.1 | 17.8 | 68 | 4 | 5.9 | 1.6 | 14.4 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | $\geq 37.5$ | 29 | 4 | 13.8 | 3.9 | 31.7 | 29 | 1 | 3.4 | 0.1 | 17.8 | 68 | 4 | 5.9 | 1.6 | 14.4 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | >38.0 | 29 | 1 | 3.4 | 0.1 | 17.8 | 29 | 1 | 3.4 | 0.1 | 17.8 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | >38.5 | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | $>39.0$ | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | >39.5 | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | >40.0 | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | Related | 29 | 2 | 6.9 | 0.8 | 22.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 2 | 2.9 | 0.4 | 10.2 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | $\begin{array}{\|l\|} \hline>38.0 \\ \text { Related } \end{array}$ | 29 | 1 | 3.4 | 0.1 | 17.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | $>39.0$ <br> Related | 29 | 0 | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |
|  | Medical advice | 29 |  | 0.0 | 0.0 | 11.9 | 29 | 0 | 0.0 | 0.0 | 11.9 | 68 | 0 | 0.0 | 0.0 | 5.3 | 75 | 0 | 0.0 | 0.0 | 4.8 |

116427 (ZOSTER-028)
Report Final

|  |  | 18-49ys |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 60 | 35 | 58.3 | 44.9 | 70.9 | 59 | 32 | 54.2 | 40.8 | 67.3 | 149 | 78 | 52.3 | 44.0 | 60.6 | 155 | 69 | 44.5 | 36.5 | 52.7 |
|  | Grade 2 or 3 | 60 | 19 | 31.7 | 20.3 | 45.0 | 59 | 13 | 22.0 | 12.3 | 34.7 | 149 | 39 | 26.2 | 19.3 | 34.0 | 155 | 32 | 20.6 | 14.6 | 27.9 |
|  | Grade 3 | 60 | 9 | 15.0 | 7.1 | 26.6 | 59 | 5 | 8.5 | 2.8 | 18.7 | 149 | 10 | 6.7 | 3.3 | 12.0 | 155 | 4 | 2.6 | 0.7 | 6.5 |
|  | Related | 60 | 11 | 18.3 | 9.5 | 30.4 | 59 | 9 | 15.3 | 7.2 | 27.0 | 149 | 10 | 6.7 | 3.3 | 12.0 | 155 | 9 | 5.8 | 2.7 | 10.7 |
|  | Grade 2 or 3 <br> Related | 60 |  | 10.0 | 3.8 | 20.5 | 59 | 2 | 3.4 | 0.4 | 11.7 | 149 | 5 | 3.4 | 1.1 | 7.7 | 155 | 6 | 3.9 | 1.4 | 8.2 |
|  | Grade 3 Related | 60 | 2 | 3.3 | 0.4 | 11.5 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 1 | 0.7 | 0.0 | 3.7 | 155 | 0 | 0.0 | 0.0 | 2.4 |
|  | Medical advice | 60 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 1 | 0.7 | 0.0 | 3.7 | 155 | 1 | 0.6 | 0.0 | 3.5 |
| Gastrointestinal symptoms | All | 60 | 24 | 40.0 | 27.6 | 53.5 | 59 | 19 | 32.2 | 20.6 | 45.6 | 149 | 49 | 32.9 | 25.4 | 41.0 | 155 | 41 | 26.5 | 19.7 | 34.1 |
|  | Grade 2 or 3 | 60 | 15 | 25.0 | 14.7 | 37.9 | 59 | 10 | 16.9 | 8.4 | 29.0 | 149 | 20 | 13.4 | 8.4 | 20.0 | 155 | 16 | 10.3 | 6.0 | 16.2 |
|  | Grade 3 | 60 | 3 | 5.0 | 1.0 | 13.9 | 59 | 4 | 6.8 | 1.9 | 16.5 | 149 | 4 | 2.7 | 0.7 | 6.7 | 155 |  | 2.6 | 0.7 | 6.5 |
|  | Related | 605 | 5 | 8.3 | 2.8 | 18.4 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 10 | 6.7 | 3.3 | 12.0 | 155 | 3 | 1.9 | 0.4 | 5.6 |
|  | Grade 2 or 3 <br> Related | 60 | 2 | 3.3 | 0.4 | 11.5 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 2 | 1.3 | 0.2 | 4.8 | 155 | 2 | 1.3 | 0.2 | 4.6 |
|  | Grade 3 Related | 60 |  | 1.7 | 0.0 | 8.9 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 0 | 0.0 | 0.0 | 2.4 | 155 | 1 | 0.6 | 0.0 | 3.5 |
|  | Medical advice | 60 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 1 | 0.7 | 0.0 | 3.7 | 155 | 2 | 1.3 | 0.2 | 4.6 |
| Headache | All | 60 | 19 | 31.7 | 20.3 | 45.0 | 59 | 21 | 35.6 | 23.6 | 49.1 | 149 | 38 | 25.5 | 18.7 | 33.3 | 155 | 28 | 18.1 | 12.4 | 25.0 |
|  | Grade 2 or 3 | 60 | 9 | 15.0 | 7.1 | 26.6 | 59 | 6 | 10.2 | 3.8 | 20.8 | 149 | 19 | 12.8 | 7.9 | 19.2 | 155 | 9 | 5.8 | 2.7 | 10.7 |
|  | Grade 3 | 60 | 2 | 3.3 | 0.4 | 11.5 | 59 | 2 | 3.4 | 0.4 | 11.7 | 149 | 4 | 2.7 | 0.7 | 6.7 | 155 | 1 | 0.6 | 0.0 | 3.5 |
|  | Related | 605 | 5 | 8.3 | 2.8 | 18.4 | 59 | 2 | 3.4 | 0.4 | 11.7 | 149 | 12 | 8.1 | 4.2 | 13.6 | 155 | 4 | 2.6 | 0.7 | 6.5 |
|  | Grade 2 or 3 <br> Related | 60 | 3 | 5.0 | 1.0 | 13.9 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 7 | 4.7 | 1.9 | 9.4 | 155 | 2 | 1.3 | 0.2 | 4.6 |
|  | Grade 3 <br> Related | 60 |  | 1.7 | 0.0 | 8.9 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 1 | 0.7 | 0.0 | 3.7 | 155 | 0 | 0.0 | 0.0 | 2.4 |
|  | Medical advice | 60 |  | 1.7 | 0.0 | 8.9 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 0 | 0.0 | 0.0 | 2.4 | 155 | 0 | 0.0 | 0.0 | 2.4 |
| Myalgia | All | 60 | 26 | 43.3 | 30.6 | 56.8 | 59 | 9 | 15.3 | 7.2 | 27.0 | 149 | 56 | 37.6 | 29.8 | 45.9 | 155 | 31 | 20.0 | 14.0 | 27.2 |
|  | Grade 2 or 3 | 60 | 12 | 20.0 | 10.8 | 32.3 | 59 | 5 | 8.5 | 2.8 | 18.7 | 149 | 24 | 16.1 | 10.6 | 23.0 | 155 | 17 | 11.0 | 6.5 | 17.0 |
|  | Grade 3 | 605 | 5 | 8.3 | 2.8 | 18.4 | 59 | 3 | 5.1 | 1.1 | 14.1 | 149 | 7 | 4.7 | 1.9 | 9.4 | 155 | 1 | 0.6 | 0.0 | 3.5 |
|  | Related | 60 | 16 | 26.7 | 16.1 | 39.7 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 22 | 14.8 | 9.5 | 21.5 | 155 | 6 | 3.9 | 1.4 | 8.2 |
|  | Grade 2 or 3 <br> Related | 60 |  | 11.7 | 4.8 | 22.6 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 13 | 8.7 | 4.7 | 14.5 | 155 | 4 | 2.6 | 0.7 | 6.5 |
|  | Grade 3 Related | 60 |  | 5.0 | 1.0 | 13.9 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 4 | 2.7 | 0.7 | 6.7 | 155 | 0 | 0.0 | 0.0 | 2.4 |
|  | Medical advice | 60 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 0 | 0.0 | 0.0 | 2.4 | 155 | 0 | 0.0 | 0.0 | 2.4 |
| Shivering | All | 60 | 16 | 26.7 | 16.1 | 39.7 | 59 | 13 | 22.0 | 12.3 | 34.7 | 149 | 31 | 20.8 | 14.6 | 28.2 | 155 | 17 | 11.0 | 6.5 | 17.0 |
|  | Grade 2 or 3 | 60 | 6 | 10.0 | 3.8 | 20.5 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 13 | 8.7 | 4.7 | 14.5 | 155 | 7 | 4.5 | 1.8 | 9.1 |


|  |  | 18-49ys |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  | 95 \% CI |  |  |  |  |
| Symptom | Type | N n | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 3 | 603 | 3 | 5.0 | 1.0 | 13.9 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 5 | 3.4 | 1.1 | 7.7 | 155 | 3 | 1.9 | 0.4 | 5.6 |
|  | Related | 607 | 7 | 11.7 | 4.8 | 22.6 | 59 | 2 | 3.4 | 0.4 | 11.7 | 149 | 11 | 7.4 | 3.7 | 12.8 | 155 | 6 | 3.9 | 1.4 | 8.2 |
|  | Grade 2 or 3 <br> Related | 603 | 3 | 5.0 | 1.0 | 13.9 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 7 | 4.7 | 1.9 | 9.4 | 155 | 2 | 1.3 | 0.2 | 4.6 |
|  | Grade 3 Related | 602 | 2 | 3.3 | 0.4 | 11.5 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 3 | 2.0 | 0.4 | 5.8 | 155 | 0 | 0.0 | 0.0 | 2.4 |
|  | Medical advice | 600 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 0 | 0.0 | 0.0 | 2.4 | 155 | 0 | 0.0 | 0.0 | 2.4 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 608 | 8 | 13.3 | 5.9 | 24.6 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 13 | 8.7 | 4.7 | 14.5 | 155 | 4 | 2.6 | 0.7 | 6.5 |
|  | $\geq 37.5$ | 608 | 8 | 13.3 | 5.9 | 24.6 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 13 | 8.7 | 4.7 | 14.5 | 155 | 4 | 2.6 | 0.7 | 6.5 |
|  | >38.0 | 601 | 1 | 1.7 | 0.0 | 8.9 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 2 | 1.3 | 0.2 | 4.8 | 155 | 0 | 0.0 | 0.0 | 2.4 |
|  | $>38.5$ | 600 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 1 | 0.7 | 0.0 | 3.7 | 155 | 0 | 0.0 | 0.0 | 2.4 |
|  | $>39.0$ | 600 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 0 | 0.0 | 0.0 | 2.4 | 155 | 0 | 0.0 | 0.0 | 2.4 |
|  | >39.5 | 600 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 0 | 0.0 | 0.0 | 2.4 | 155 | 0 | 0.0 | 0.0 | 2.4 |
|  | >40.0 | 600 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 0 | 0.0 | 0.0 | 2.4 | 155 | 0 | 0.0 | 0.0 | 2.4 |
|  | Related | 606 |  | 10.0 | 3.8 | 20.5 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 9 | 6.0 | 2.8 | 11.2 | 155 | 1 | 0.6 | 0.0 | 3.5 |
|  | $\begin{array}{\|l\|} \hline>38.0 \\ \text { Related } \end{array}$ | 601 |  | 1.7 | 0.0 | 8.9 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 2 | 1.3 | 0.2 | 4.8 | 155 | 0 | 0.0 | 0.0 | 2.4 |
|  | $>39.0$ <br> Related | 600 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 0 | 0.0 | 0.0 | 2.4 | 155 | 0 | 0.0 | 0.0 | 2.4 |
|  | Medical advice | 600 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 0 | 0.0 | 0.0 | 2.4 | 155 | 1 | 0.6 | 0.0 | 3.5 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 312 | 24 | 77.4 | 58.9 | 90.4 | 30 | 20 | 66.7 | 47.2 | 82.7 | 81 | 54 | 66.7 | 55.3 | 76.8 | 80 | 48 | 60.0 | 48.4 | 70.8 |
|  | Grade 2 or 3 | 311 | 15 | 48.4 | 30.2 | 66.9 | 30 | 11 | 36.7 | 19.9 | 56.1 | 81 | 30 | 37.0 | 26.6 | 48.5 | 80 | 26 | 32.5 | 22.4 | 43.9 |
|  | Grade 3 | 318 | 8 | 25.8 | 11.9 | 44.6 | 30 | 5 | 16.7 | 5.6 | 34.7 | 81 | 8 | 9.9 | 4.4 | 18.5 | 80 | 3 | 3.8 | 0.8 | 10.6 |
|  | Related | 311 | 10 | 32.3 | 16.7 | 51.4 | 30 | 6 | 20.0 | 7.7 | 38.6 | 81 | 9 | 11.1 | 5.2 | 20.0 | 80 | 8 | 10.0 | 4.4 | 18.8 |
|  | Grade 2 or 3 <br> Related | 316 | 6 | 19.4 | 7.5 | 37.5 | 30 | 2 | 6.7 | 0.8 | 22.1 | 81 | 5 | 6.2 | 2.0 | 13.8 | 80 | 6 | 7.5 | 2.8 | 15.6 |
|  | Grade 3 Related | 312 |  | 6.5 | 0.8 | 21.4 | 30 | 1 | 3.3 | 0.1 | 17.2 | 81 | 1 | 1.2 | 0.0 | 6.7 | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  | Medical advice | 310 | 0 | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 1 | 1.2 | 0.0 | 6.7 | 80 | 1 | 1.3 | 0.0 | 6.8 |
| Gastrointestinal symptoms | All | 311 | 18 | 58.1 | 39.1 | 75.5 | 30 | 16 | 53.3 | 34.3 | 71.7 | 81 | 33 | 40.7 | 29.9 | 52.2 | 80 | 33 | 41.3 | 30.4 | 52.8 |
|  | Grade 2 or 3 | 311 | 11 | 35.5 | 19.2 | 54.6 | 30 | 8 | 26.7 | 12.3 | 45.9 | 81 | 15 | 18.5 | 10.8 | 28.7 | 80 | 13 | 16.3 | 8.9 | 26.2 |
|  | Grade 3 | 313 | 3 | 9.7 | 2.0 | 25.8 | 30 | 3 | 10.0 | 2.1 | 26.5 | 81 | 3 | 3.7 | 0.8 | 10.4 | 80 | 4 | 5.0 | 1.4 | 12.3 |
|  | Related | 314 | 4 | 12.9 | 3.6 | 29.8 | 30 | 1 | 3.3 | 0.1 | 17.2 | 81 | 7 | 8.6 | 3.5 | 17.0 | 80 | 2 | 2.5 | 0.3 | 8.7 |
|  | Grade 2 or 3 <br> Related | 311 |  | 3.2 | 0.1 | 16.7 | 30 | 1 | 3.3 | 0.1 | 17.2 | 81 | 2 | 2.5 | 0.3 | 8.6 | 80 | 2 | 2.5 | 0.3 | 8.7 |
|  | Grade 3 Related | 311 |  | 3.2 | 0.1 | 16.7 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 0 | 0.0 | 0.0 | 4.5 | 80 | 1 | 1.3 | 0.0 | 6.8 |
|  | Medical advice | 310 | 0 | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 1 | 1.2 | 0.0 | 6.7 | 80 | 2 | 2.5 | 0.3 | 8.7 |
| Headache | All | 311 |  | 48.4 | 30.2 | 66.9 | 30 | 15 | 50.0 | 31.3 | 68.7 | 81 | 28 | 34.6 | 24.3 | 46.0 | 80 | 25 | 31.3 | 21.3 | 42.6 |
|  | Grade 2 or 3 | 318 | 8 | 25.8 | 11.9 | 44.6 | 30 | 6 | 20.0 | 7.7 | 38.6 | 81 | 14 | 17.3 | 9.8 | 27.3 | 80 | 8 | 10.0 | 4.4 | 18.8 |



18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:

## CONFIDENTIAL

[^11]Table 8.183 Number and percentage of subjects who reported temperature by half degree measured via oral route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  | Placebo |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |
|  |  | 95 \% Cl |  |  |  | 95 \% Cl |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |
| Symptom | Type | N | n \% | \% LL | LL UL | N | n \% |  | L UL | N | n \% | \% | LL | UL | N | n \% | LL | LL UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All |  |  | 6.50. | 0.821 .4 | 3010 | 00.0 |  | . 011.6 | 81 |  | 2.5 | 0.3 | 8.6 | 80 | 11.3 | 30.0 | 0.06 .8 |
|  | $\geq 35.5$ |  |  | 6.50. | 0.821 .4 | 30 | 00.0 | 00.0 | . 011.6 | 81 | 22 | 2.5 | 0.3 | 38.6 | 80 | 11.3 | 30.0 | 0.06 .8 |
|  | $>36.0$ | 31 | 126 | 6.50. | 0.821 .4 | 30 | 00.0 | 00.0 | . 011.6 | 81 | 22 | 2.5 | 0.3 | 38.6 | 80 | 11.3 | 30.0 | 0.06 .8 |
|  | $>36.5$ |  | 126 | 6.50. | 0.821 .4 | 30 | 00.0 | 00.0 | . 011.6 | 81 | 22 | 2.5 | 0.3 | 38.6 | 80 | 11.3 | 30.0 | 0.06 .8 |
|  | $>37.0$ | 31 | 126 | 6.50. | 0.821 .4 | 30 | 00.0 | 00.0 | . 011.6 | 81 | 22 | 2.5 | 0.3 | 38.6 | 80 | 11.3 | 30.0 | 0.06 .8 |
|  | $>37.5$ | 31 | 113 | 3.20. | 0.116 .7 | 30 | 00.0 |  | . 011.6 | 81 |  | 0.0 | 0.0 | . 4.5 | 80 | 11.3 | 30.0 | 0.06 .8 |
|  | $>38.0$ |  | 100. | 0.00. | 0.011 .2 | 300 | 00.0 | 00.0 | . 011.6 | 81 |  | 0.0 | 0.0 | 0.04.5 | 80 | 00.0 | 00.0 | 0.04 .5 |
|  | >38.5 | 31 | 100. | 0.00. | 0.011 .2 | 30 | 00.0 | 00.0 | . 011.6 | 81 |  | 0.0 | 0.0 | . 4.5 | 80 | 00.0 | 00.0 | 0.04 .5 |
|  | >39.0 | 31 | 100. | 0.00. | 0.011 .2 | 30 | 00.0 | 00.0 | . 011.6 | 81 |  | 0.0 | 0.0 | 0.0.5 | 80 | 00.0 | 00.0 | 0.04 .5 |
|  | >39.5 | 31 | 100. | 0.00. | 0.011 .2 | 30 | 00.0 | 00.0 | 0.011 .6 | 81 |  | 0.0 | 0.0 | . 4.5 | 80 | 00.0 | 00.0 | 0.04 .5 |
|  | >40.0 | 31 | 100 | 0.00. | 0.011 .2 | 30 | 00.0 |  | . 011.6 | 81 |  | 0.0 | 0.0 | 0, 4.5 | 80 | 00.0 | 00.0 | 0.04 .5 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 29 |  | 6.90. | 0.822 .8 | 291 | 00.0 | 00.0 | . 011.9 | 68 | 11 | 1.5 | 0.0 | O 7.9 | 75 | 00.0 | 00.0 | 0.04 .8 |
|  | $\geq 35.5$ | 29 | 26 | 6.90. | 0.822 .8 | 290 | 00.0 | 00.0 | . 011.9 | 68 | 11 | 1.5 | 0.0 | 0.0.9 | 75 | 00.0 | 00.0 | 0.04 .8 |
|  | >36.0 | 29 | 92 | 6.90. | 0.822 .8 | 290 | 00.0 | 00.0 | 0.011 .9 | 68 | 11 | 1.5 | 0.0 | 0.0.9 | 75 | 00.0 | 00.0 | 0.04 .8 |
|  | >36.5 | 29 |  | 6.90. | 0.822 .8 | 290 | 00.0 | 00.0 | . 011.9 | 68 | 11 | 1.5 | 0.0 | O 7.9 | 75 | 00.0 | 00.0 | 0.04 .8 |
|  | >37.0 | 29 | 926 | 6.90. | 0.822 .8 | 290 | 00.0 | 00.0 | 0.011 .9 | 68 | 11 | 1.5 | 0.0 | 0.0.9 | 75 | 00.0 | 00.0 | 0.04 .8 |
|  | >37.5 | 29 | 92 | 6.90. | 0.822 .8 | 290 | 00.0 | 00.0 | . 011.9 | 68 | 11 | 1.5 | 0.0 | 0.0 7.9 | 75 | 00.0 | 00.0 | 0.04 .8 |
|  | $>38.0$ | 29 |  | 3.40. | 0.117 .8 | 290 | 00.0 | 00.0 | 0.011 .9 | 68 | 00 | 0.0 | 0.0 | 5.3 | 75 | 00.0 | 00.0 | 0.04 .8 |
|  | $>38.5$ | 29 |  | 0.00. | 0.011 .9 | 290 | 00.0 | 00.0 | 0.011 .9 | 68 | 00 | 0.0 | 0.0 | 5.3 | 75 | 00.0 | 00.0 | 0.04 .8 |
|  | >39.0 | 29 |  | 0.00. | 0.011 .9 | 290 | 00.0 | 00.0 | . 011.9 | 68 | 00 | 0.0 | 0.0 | 5.3 | 75 | 00.0 |  | 0.04 .8 |
|  | >39.5 | 29 | 900 | 0.00. | 0.011 .9 | 290 | 00.0 | 00.0 | . 011.9 | 68 | 00 | 0.0 | 0.0 | 5.3 | 75 | 00.0 | 00.0 | 0.04 .8 |
|  | >40.0 | 29 |  | 0.00. | 0.011 .9 | 290 | 00.0 | 00.0 | . 011.9 | 68 |  | 0.0 | 0.0 | 5.3 | 75 | 00.0 | 00.0 | 0.04 .8 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 60 | 046 | 6.71. | 1.816 .2 | 591 | 00.0 | 00.0 | 0 0.1 | 149 |  | 2.0 | 0.4 | 45.8 | 155 | 10.6 | 60.0 | 0.03 .5 |
|  | $\geq 35.5$ | 60 |  | 6.71. | 1.816 .2 | 590 | 00.0 | 00.0 | .06.1 | 149 |  | 2.0 | 0.4 | . 5.8 | 155 | 10.6 | 60.0 | 0.03 .5 |
|  | >36.0 | 60 | 046 | 6.71. | 1.816 .2 | 590 | 00.0 | 00.0 | .06.1 | 149 |  | 2.0 | 0.4 | . 5.8 | 155 | 10.6 | 60.0 | 0.03 .5 |
|  | >36.5 | 60 | 046 | 6.71. | 1.816 .2 | 590 | 00.0 | 00.0 | 0.06.1 | 149 |  | 2.0 | 0.4 | . 5.8 | 155 | 10.6 | 60.0 | 0.03 .5 |
|  | >37.0 | 60 |  | 6.71. | 1.816 .2 | 590 | 00.0 | 00.0 | 0.06.1 | 149 |  | 2.0 | 0.4 | . 5.8 | 155 | 10.6 | 60.0 | 0.03 .5 |
|  | >37.5 | 60 |  | 5.01. | 1.013 .9 | 590 | 00.0 | 00.0 | .06.1 | 149 |  | 0.7 | 0.0 | 3.7 | 155 | 10.6 | 60.0 | 0.03 .5 |
|  | >38.0 | 60 |  | 1.70. | 0.08 .9 | 59 | 00.0 | 00.0 | .06.1 | 149 |  | 0.0 | 0.0 | 0. 2.4 | 155 | 00.0 | 00.0 | 0.02 .4 |
|  | >38.5 | 60 |  | 0.00. | 0.06 .0 | 59 | 00.0 | 00.0 | .06.1 | 149 |  | 0.0 | 0.0 | 2.4 | 155 | 00.0 | 00.0 | 0.02 .4 |
|  | >39.0 | 60 | 000 | 0.00. | 0.06 .0 | 590 | 00.0 | 00.0 | .06.1 | 149 | 00 | 0.0 | 0.0 | 2.4 | 155 | 00.0 | 00.0 | 0.02 .4 |
|  | >39.5 | 60 | 000 | 0.00. | 0.06 .0 | 590 | 00.0 | 00.0 | .06.1 | 149 |  | 0.0 | 0.0 | 2.4 | 155 | 00.0 | 00.0 | 0.02 .4 |
|  | >40.0 | 60 | 000 | 0.00 | 0.06 .0 | 590 | 00.0 | 00.0 | 0. 6.1 | 149 |  | 0.0 | 0.0 | 2.4 | 155 | 00.0 |  | 0.02 .4 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 31 | 139.7 | 9.72. | 2.025 .8 | 30 | 00.0 | 00.0 | . 011.6 | 81 |  | 3.7 | 0.8 | 10.4 | 80 | 11.3 | 30.0 | 0.06 .8 |
|  | $\geq 35.5$ | 31 | 139. | 9.72. | 2.025 .8 | 30 | 00.0 | 00.0 | . 011.6 | 81 | 33 | 3.7 | 0.8 | . 10.4 | 80 | 11.3 | 30.0 | 0.06 .8 |
|  | >36.0 | 31 | 139.7 | 9.72. | 2.025 .8 | 30 | 00.0 | 00.0 | . 011.6 | 81 | 33 | 3.7 | 0.8 | . 10.4 | 80 | 11.3 | 30.0 | 0.06 .8 |
|  | >36.5 | 31 | 139. | 9.72. | 2.025 .8 | 30 | 00.0 | 00.0 | . 011.6 | 81 | 33 | 3.7 | 0.8 | . 10.4 | 80 | 11.3 | 30.0 | 0.06 .8 |
|  | >37.0 | 31 | 139. | 9.72. | 2.025 .8 | 30 | 00.0 | 00.0 | . 011.6 | 81 | 33 | 3.7 | 0.8 | . 10.4 | 80 | 11.3 | 30.0 | 0.06 .8 |
|  | $>37.5$ | 31 | 126 | 6.50. | 0.821 .4 | 30 | 00.0 | 00.0 | . 011.6 | 81 | 11 | 1.2 | 0.0 | 6.7 | 80 | 11.3 | 30.0 | 0.06 .8 |
|  | $>38.0$ | 31 | 113 | 3.20. | 0.116 .7 | 30 | 00.0 | 00.0 | . 011.6 | 81 | 00 | 0.0 | 0.0 | 4.5 | 80 | 00.0 | 00.0 | 0.04 .5 |
|  | >38.5 | 31 | 100 | 0.00. | 0.011 .2 | 30 | 00.0 | 00.0 | .0 11.6 | 81 | 00 | 0.0 | 0.0 | . 4.5 | 80 | 00.0 | 00.0 | 0.04 .5 |
|  | $>39.0$ | 31 | 100 | 0.00. | 0.011 .2 | 30 | 00.0 | 00.0 | . 011.6 | 81 | 00 | 0.0 | 0.0 | . 4.5 | 80 | 00.0 | 00.0 | 0.04 .5 |
|  | $>39.5$ |  |  | 0.00. | 0.011 .2 |  | 00.0 | 00.0 | . 011.6 | 81 | 00 | 0.0 |  | 0. 4.5 | 80 | 00.0 |  | 0.04 .5 |


|  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  | Placebo |  | HZ/su |  |  |  | Placebo |  |  |  |
|  |  |  | $95 \% \mathrm{Cl}$ |  | $95 \% \mathrm{Cl}$ |  |  |  | 5 \% CI |  |  |  | \% Cl |
| Symptom | Type | N n \% | LL UL | N n \% | LL UL | N | n\% | LL | L UL | N | n\% | LL |  |
|  | >40.0 | 3100.0 | 00.011 .2 | 3000.0 | 0.011 .6 | 81 | 00.0 | 00.0 | 0.04.5 | 80 | 00.0 | 0. | 4.5 |

$18-49 y s=$ Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$N=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
n/\% = number/percentage of doses followed by at least one type of symptom
$95 \%$ CI = Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for oral route

Table 8.184 Number and percentage of subjects who reported temperature by half degree measured via axillary route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% Cl |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type N |  | n ${ }^{\text {\% }}$ | LL | UL N |  | n \% | \% | LL | UL | N |  | \% | LL | UL | N |  | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 312 | 26.5 | 0.8 | 21.4 | 3010 | 00. | 0.0 | 0.0 | 11.6 | 81 |  | 8.6 | 3.5 | 17.0 | 80 |  | 3.8 | 0.8 | 10.6 |
|  | $\geq 35.531$ | 312 | 26.5 | 0.8 | 21.4 | 300 | 00. | 0.0 | 0.0 | 11.6 | 81 | 7 | 8.6 | 3.5 | 17.0 | 80 | 3 | 3.8 | 0.8 | 10.6 |
|  | >36.0 31 | 312 | 26.5 | 0.8 | 21.4 | 300 | 00. | 0.0 | 0.0 | 11.6 | 81 | 7 | 8.6 | 3.5 | 17.0 | 80 | 3 | 3.8 | 0.8 | 10.6 |
|  | >36.5 | 31 | 26.5 | 0.8 | 21.4 | 300 | 00. | 0.0 | 0.0 | 11.6 | 81 | 7 | 8.6 | 3.5 | 17.0 | 80 | 3 | 3.8 | 0.8 | 10.6 |
|  | >37.0 | 31 | 26.5 | 0.8 | 21.4 | 300 | 00. | 0.0 | 0.0 | 11.6 | 81 | 7 | 8.6 | 3.5 | 17.0 | 80 | 3 | 3.8 | 0.8 | 10.6 |
|  | $>37.531$ | 312 | 26.5 | 0.8 | 21.4 | 300 | 00. | 0.0 | 0.0 | 11.6 | 81 |  | 6.2 | 2.0 | 13.8 | 80 | 3 | 3.8 | 0.8 | 10.6 |
|  | >38.0 31 | 310 | 00.0 | 0.0 | 11.2 | 300 | 00. | 0.0 | 0.0 | 11.6 | 81 |  | 2.5 | 0.3 | 8.6 | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  | $>38.531$ | 310 | 00.0 | 0.0 | 11.2 | 300 | 00. | 0.0 | 0.0 | 11.6 | 81 |  | 1.2 | 0.0 | 6.7 | 80 | 0 | 0.0 | 0.0 | 4.5 |
|  | >39.0 | 310 | 00.0 | 0.0 | 11.2 | 300 | 00. | 0.0 | 0.0 | 11.6 | 81 |  | 0.0 | 0.0 | 4.5 | 80 |  | 0.0 | 0.0 | 4.5 |
|  | >39.5 | 310 | 00.0 | 0.0 | 11.2 | 300 | 00. | 0.0 | 0.0 | 11.6 | 81 |  | 0.0 | 0.0 | 4.5 | 80 |  | 0.0 | 0.0 | 4.5 |
|  | >40.0 |  | 00.0 | 0.0 | 11.2 | 300 |  | 0.0 | 0.0 |  | 81 |  | 0.0 | 0.0 | 4.5 | 80 |  |  | 0.0 | 4.5 |

## Dose 2

 $\geq 35.52926 .9$ 0.8 22.82913 .40 .117 .868 2 2.9 0.4 10.275 0 0.00 .04 .8 $\rightarrow 36.02926 .9$ 0.8 22.82913 .40 .117 .868 2 2.9 0.4 10.275 0 0.00 .04 .8 | $>36.5$ | 29 | 2 | 6.9 | 0.8 | 22.8 | 29 | 1 | 3.4 | 0.1 | 17.8 | 68 | 2 | 2.9 | 0.4 | 10.2 | 75 | 0 | 0.0 | 0.0 | 4.8 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |

 $>37.52900 .0$ 0.0 11.929113 .40 .117 .868111 .5 \begin{tabular}{lllllllllllllllllllllll}
$>38.0$ \& 29 \& 0 \& 0.0 \& 0.0 \& 11.9 \& 29 \& 1 \& 3.4 \& 0.1 \& 17.8 \& 68 \& 0 \& 0.0 \& 0.0 \& 5.3 \& 75 \& 0 \& 0.0 \& 0.0 \& 4.8 <br>
\hline

 $>38.52900 .0 ~ 0.011 .929010 .00 .011 .968$ 0 0.0 $>39.02900 .0$ 0.0 11.929010 .00 .011 .968 0 0.0 

$>39.5$ \& 29 \& 0.0 \& 0.0 \& 11.9 \& 29 \& 0 \& 0.0 \& 0.0 \& 11.9 \& 68 \& 0 \& 0.0 \& 0.0 \& 5.3 \& 75 \& 0 \& 0.0 \& 0.0 \& 4.8 <br>
\hline
\end{tabular}



## Overall/dose

| Temperature/(Axillary) $\left({ }^{\circ} \mathrm{C}\right)$ | All | 60 | 4 | 6.7 | 1.8 | 16.2 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 9 | 6.0 | 2.8 | 11.2 | 155 | 3 | 1.9 | 0.4 | 5.6 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| $\geq 35.5$ | 60 | 4 | 6.7 | 1.8 | 16.2 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 9 | 6.0 | 2.8 | 11.2 | 155 | 3 | 1.9 | 0.4 | 5.6 |  |
| $>36.0$ | 60 | 4 | 6.7 | 1.8 | 16.2 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 9 | 6.0 | 2.8 | 11.2 | 155 | 3 | 1.9 | 0.4 | 5.6 |  |
| $>36.5$ | 60 | 4 | 6.7 | 1.8 | 16.2 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 9 | 6.0 | 2.8 | 11.2 | 155 | 3 | 1.9 | 0.4 | 5.6 |  |
| $>37.0$ | 60 | 4 | 6.7 | 1.8 | 16.2 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 9 | 6.0 | 2.8 | 11.2 | 155 | 3 | 1.9 | 0.4 | 5.6 |  |
| $>37.5$ | 60 | 2 | 3.3 | 0.4 | 11.5 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 6 | 4.0 | 1.5 | 8.6 | 155 | 3 | 1.9 | 0.4 | 5.6 |  |
| $>38.0$ | 60 | 0 | 0.0 | 0.0 | 6.0 | 59 | 1 | 1.7 | 0.0 | 9.1 | 149 | 2 | 1.3 | 0.2 | 4.8 | 155 | 0 | 0.0 | 0.0 | 2.4 |  |
| $>38.5$ | 60 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 1 | 0.7 | 0.0 | 3.7 | 155 | 0 | 0.0 | 0.0 | 2.4 |  |
| $>39.0$ | 60 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 0 | 0.0 | 0.0 | 2.4 | 155 | 0 | 0.0 | 0.0 | 2.4 |  |
|  | $>39.5$ | 60 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 0 | 0.0 | 0.0 | 2.4 | 155 | 0 | 0.0 | 0.0 | 2.4 |
|  | $>40.0$ | 60 | 0 | 0.0 | 0.0 | 6.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 149 | 0 | 0.0 | 0.0 | 2.4 | 155 | 0 | 0.0 | 0.0 | 2.4 |

Overall/subject

| Temperature/(Axillary) $\left({ }^{\circ} \mathrm{C}\right)$ | All | 31 | 4 | 12.9 | 3.6 | 29.8 | 30 | 1 | 3.3 | 0.1 | 17.2 | 81 | 9 | 11.1 | 5.2 | 20.0 | 80 | 3 | 3.8 | 0.8 | 10.6 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | $\geq 35.5314$ 12.9 3.629 .830113 .30 .117 .281 9 11.1 5.220 .080 >36.0 31412.93 .629 .830113 .30 .117 .281 9 11.15 .220 .080 $>36.531412 .93 .629 .830113 .30 .117 .2819911 .15 .220 .080$ >37.0 314 |  | 12.9 | 3.6 | 29.8 | 30 | 1 | 3.3 | 0.1 | 17.2 | 81 | 9 | 11.1 | 5.2 | 20.0 | 80 | 3 | 3.8 | 0.8 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | | $>37.5$ | 31 | 2 | 6.5 | 0.8 | 21.4 | 30 | 1 | 3.3 | 0.1 | 17.2 | 81 | 6 | 7.4 | 2.8 | 15.4 | 80 | 3 | 3.8 | 0.8 | 10.6 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | | $>38.0$ | 31 | 0 | 0.0 | 0.0 | 11.2 | 30 | 1 | 3.3 | 0.1 | 17.2 | 81 | 2 | 2.5 | 0.3 | 8.6 | 80 | 0 | 0.0 | 0.0 | 4.5 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | $>38.5310$|  | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 81 | 1 | 1.2 | 0.0 | 6.7 | 80 | 0 | 0.0 | 0.0 | 4.5 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | $>39.03100 .0 ~ 0.011 .230010 .00 .011 .681 \quad 0 \quad 0.0$



|  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  | Placebo |  | HZ/su |  |  | Placebo |  |  |
|  |  |  | $95 \% \mathrm{Cl}$ |  | $95 \% \mathrm{Cl}$ |  |  | $95 \% \mathrm{Cl}$ |  |  | $95 \% \mathrm{Cl}$ |
| Symptom | Type | N n\% | LL UL | N n \% | LL UL | N | n\% | LL UL | N | n\% | LL UL |
|  | >40.0 | 3100.0 | 0.011 .2 | 3000.0 | 0.011 .6 | 81 | 00.0 | 0.04 .5 | 80 | 00.0 | 0.04.5 |

$18-49 y s=$ Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%$ = number/percentage of doses followed by at least one type of symptom
$95 \%$ CI = Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for axillary route

Table 8.185 Number and percentage of subjects who reported temperature by half degree measured via tympanic route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |
|  |  | 95 \% Cl |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |
| Symptom | Type |  | n \% | \% LL | LL UL | N | n \% | \% L | LL U | UL | N | n \% | \% L | LL | UL | N | n \% | \% LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 31 | 00.0 | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 |  | 0.010 | 0.0 | 4.5 | 80 |  | 0.00 .0 | ) 4.5 |
|  | $\geq 35.5$ |  |  | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 00. | 0.00 | 0.0 | 4.5 | 80 | 00.0 | 0 0.0 | 4.5 |
|  | >36.0 | 31 | 00.0 | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 00. | 0.00 | 0.0 | 4.5 | 80 | 00.0 | 0.00 .0 | 4.5 |
|  | >36.5 | 31 | 00.0 | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 00. | 0.00 | 0.0 | 4.5 | 80 | 00.0 | 0.0 0.0 | 4.5 |
|  | >37.0 | 31 | 00.0 | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 00. | 0.00 | 0.0 | 4.5 | 80 | 00.0 | 0.0 0.0 | 4.5 |
|  | >37.5 | 31 | 00.0 | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 00. | 0.00 | 0.0 | 4.5 | 80 | 00.0 | 0.0 0.0 | 4.5 |
|  | >38.0 | 31 |  | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 00. | 0.00 | 0.0 | 4.5 | 80 | 00.0 | 0.00 .0 | ) 4.5 |
|  | >38.5 | 31 |  | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 00. | 0.00 | 0.0 | 4.5 | 80 | 00.0 | 0.0 0.0 | 4.5 |
|  | >39.0 | 31 |  | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 00. | 0.00 | 0.0 | 4.5 | 80 | 00.0 | 0.0 0.0 | 4.5 |
|  | >39.5 |  | 00.0 | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 00. | 0.00 | 0.0 | 4.5 | 80 | 00.0 | 0.00 .0 | 4.5 |
|  | >40.0 | 31 | 00.0 | 0.00 .0 | 0.011 .2 | 300 | 00 | 0.00 | 0.01 | 11.6 | 81 |  | 0.00 | 0.0 | 4.5 | 80 |  | 0.00 .0 | 4.5 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 29 |  | 0.00 .0 | 0.011 .9 | 291 | 90 | 0.010 | 0.01 | 11.9 | 68 | 11.5 | 1.50 | 0.0 | 7.9 | 75 | 00.0 | . 00.0 | \| 4.8 |
|  | $\geq 35.5$ | 29 |  | 0.00 .0 | 0.011 .9 | 290 | 00 | 0.00 | 0.01 | 11.9 | 68 | 11. | 1.50 | 0.0 | 7.9 | 75 | 00.0 | 0.0 0.0 | 4.8 |
|  | >36.0 | 29 |  | 0.00 .0 | 0.011 .9 | 290 | 00 | 0.00 | 0.01 | 11.9 | 68 | 11.5 | 1.50 | 0.0 | 7.9 | 75 | 00.0 | 0.0 0.0 | 4.8 |
|  | >36.5 | 29 |  | 0.00 .0 | 0.011 .9 | 290 | 00 | 0.00 | 0.01 | 11.9 | 68 |  | 1.50 | 0.0 | 7.9 | 75 | 00.0 | 0.00 .0 | ) 4.8 |
|  | >37.0 | 29 |  | 0.00 .0 | 0.011 .9 | 290 | 00 | 0.00 | 0.01 | 11.9 | 68 |  | 1.50 | 0.0 | 7.9 | 75 | 00.0 | 0.00 .0 | ) 4.8 |
|  | >37.5 | 29 |  | 0.00 .0 | 0.011 .9 | 290 | 00 | 0.00 | 0.01 | 11.9 | 68 | 00. | 0.00 | 0.0 | 5.3 | 75 | 00.0 | 0.00 .0 | 4.8 |
|  | $>38.0$ | 29 |  | 0.00 .0 | 0.011 .9 | 290 | 00 | 0.00 | 0.01 | 11.9 | 68 | 00. | 0.00 | 0.0 | 5.3 | 75 | 00.0 | 0.0 0.0 | 4.8 |
|  | $>38.5$ | 29 |  | 0.00 .0 | 0.011 .9 | 29 | 00 | 0.00 | 0.01 | 11.9 | 68 | 00. | 0.00 | 0.0 | 5.3 | 75 | 00.0 | 0.0 0.0 | 4.8 |
|  | >39.0 | 29 |  | 0.00 .0 | 0.011 .9 | 290 | 00 | 0.00 | 0.01 | 11.9 | 68 | 00. | 0.00 | 0.0 | 5.3 | 75 | 00.0 | 0.00 .0 | ) 4.8 |
|  | >39.5 | 29 |  | 0.00 .0 | 0.011 .9 | 290 | 00 | 0.00 | 0.01 | 11.9 | 68 | 00. | 0.00 | 0.0 | 5.3 | 75 | 00.0 | 0.0 0.0 | 4.8 |
|  | >40.0 | 29 | 00.0 | 0.00 .0 | 0.011 .9 | 290 | 00 | 0.010 | 0.01 | 11.9 | 68 |  | 0.00 | 0.0 | 5.3 | 75 | 00.0 | . 00.0 | - 4.8 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 60 | 00.0 | 0.00 .0 | 0.06 .0 | 591 | 00 | 0.010 | 0.06 | 6.1 | 149 |  | 0.70 | 0.0 | 3.7 | 155 | 00.0 | . 00.0 | 2.4 |
|  | $\geq 35.5$ | 60 |  | 0.00 .0 | 0.06 .0 | 59 | 00 | 0.00 | 0.06 | 6.1 | 149 |  | 0.70 | 0.0 | 3.7 | 1550 | 00.0 | 0.00 .0 | 2.4 |
|  | >36.0 | 60 |  | 0.00 .0 | 0.06 .0 | 59 | 00 | 0.00 | 0.06 | 6.1 | 149 |  | 0.70 | 0.0 | 3.7 | 1550 | 00.0 | 0.00 .0 | 2.4 |
|  | >36.5 | 60 |  | 0.00 .0 | 0.06 .0 | 590 | 00 | 0.00 | 0.06 | 6.1 | 149 |  | 0.70 | 0.0 | 3.7 | 155 | 00.0 | 0.00 .0 | 2.4 |
|  | >37.0 | 60 |  | 0.00 .0 | 0.06 .0 | 59 | 00 | 0.00 | 0.06 | 6.1 | 149 |  | 0.70 | 0.0 | 3.7 | 1550 | 00.0 | 0.00 .0 | 2.4 |
|  | >37.5 | 60 |  | 0.00 | 0.06 .0 | 59 | 00 | 0.00 | 0.06 | 6.1 | 149 |  | 0.00 | 0.0 | 2.4 | 155 | 00.0 | 0.0 0.0 | 2.4 |
|  | >38.0 | 60 |  | 0.00 .0 | 0.06 .0 | 59 | 00 | 0.00 | 0.06 | 6.1 | 149 | 00. | 0.00 | 0.0 | 2.4 | 1550 | 00.0 | 0.00 .0 | 2.4 |
|  | >38.5 | 60 |  | 0.00 .0 | 0.06 .0 | 59 | 00 | 0.00 | 0.06 | 6.1 | 149 | 00. | 0.00 | 0.0 | 2.4 | 1550 | 00.0 | 0.0 0.0 | 2.4 |
|  | >39.0 | 60 |  | 0.00 .0 | 0.06 .0 | 59 | 00 | 0.00 | 0.06 | 6.1 | 149 | 00. | 0.00 | 0.0 | 2.4 | 155 | 00.0 | 0.00.0 | 2.4 |
|  | >39.5 | 60 |  | 0.00 .0 | 0.06 .0 | 59 | 00 | 0.00 | 0.06 | 6.1 | 149 | 00. | 0.00 | 0.0 | 2.4 | 1550 | 00.0 | 0.00.0 | 2.4 |
|  | >40.0 | 60 |  | 0.00 .0 | 0.06 .0 | 59 | 00 | 0.00 | 0.06 | 6.1 | 149 |  | 0.00 | 0.0 | 2.4 | 1550 | 00.0 | 0.0.0 | 2.4 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 31 | 00.0 | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 11.2 | 1.20 | 0.0 | 6.7 | 80 | 00.0 | . 00.0 | ) 4.5 |
|  | $\geq 35.5$ | 31 |  | 0.00 .0 | 0.011 .2 | 300 | 00 | 0.00 | 0.01 | 11.6 | 81 | 11.2 | 1.20 | 0.0 | 6.7 | 80 | 00.0 | 0.00 .0 | 4.5 |
|  | $>36.0$ | 31 |  | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 11.2 | 1.20 | 0.0 | 6.7 | 80 | 00.0 | 0.0 0.0 | 4.5 |
|  | >36.5 | 31 |  | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 11.2 | 1.20 | 0.0 | 6.7 | 80 | 00.0 | 0.0 0.0 | 4.5 |
|  | >37.0 | 31 | 00.0 | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 11.2 | 1.20 | 0.0 | 6.7 | 80 | 00.0 | 0.00 .0 | ) 4.5 |
|  | >37.5 | 31 | 00.0 | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 00. | 0.00 | 0.0 | 4.5 | 80 | 00.0 | 0.0 0.0 | ) 4.5 |
|  | >38.0 | 31 | 00.0 | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 00. | 0.00 | 0.0 | 4.5 | 80 | 00.0 | 0.00 .0 | 4.5 |
|  | >38.5 | 31 | 00.0 | 0.00 .0 | 0.011 .2 | 30 | 00 | 0.00 | 0.01 | 11.6 | 81 | 00. | 0.00 | 0.0 | 4.5 | 80 | 00.0 | 0.00 .0 | 4.5 |
|  | >39.0 | 31 | 00.0 | 0.00 .0 | 0.011 .2 | 300 | 00 | 0.00 | 0.01 | 11.6 | 81 | 00. | 0.00 | 0.0 | 4.5 | 80 | 00.0 | 0.00 .0 | 4.5 |
|  | >39.5 |  | 00.0 | 0.00 .0 | 0.011 .2 | 30 |  | 0.00 | 0.01 | 11.6 | 81 |  | 0.00 |  |  | 80 | 00.0 | 0.0.0 | 4.5 |


|  |  | 18-49ys |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |
|  |  | $95 \%$ Cl |  | $95 \%$ Cl |  |  |  |  | $95 \% \mathrm{Cl}$ |  |  |  |  | $95 \% \mathrm{Cl}$ |  |  |
| Symptom | Type | N n $\%$ | \% LL UL | N | n\% |  | UL | N | N | n\% | LL | UL | N | n\% |  | LL UL |
|  | >40.0 | 3100 | 0.00 .011 .2 | 30 | 00.0 | 00.0 | 011. | 1.68 | 81 | 00.0 | 0.0 | 0.5 | 80 | 00.0 |  | 0.04 .5 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for tympanic route
Table 8.186 Number and percentage of subjects who reported temperature by half degree measured via rectal route during the 7-day (Days 0-6) post-vaccination period following each dose (no conversion) by age strata (Total Vaccinated Cohort)

No records exist in this table

Table 8.187 Number of days with grade 3 local symptoms during the solicited post-vaccination period by age strata (Total Vaccinated Cohort)

| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Pain | Dose 1 | 18-49ys | HZ/su | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 4 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Dose 2 | 18-49ys | HZ/su | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | $\geq 50 y s$ | HZ/su | 3 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
|  | Overall/dose | 18-49ys | HZ/su | 5 | 1.2 | 1.0 | 1.0 | 1.0 | 1.0 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 7 | 1.9 | 1.0 | 1.0 | 1.0 | 3.0 | 3.0 |
| Redness | Dose 1 | $\geq 50 y s$ | HZ/su | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | $\geq 50 y s$ | HZ/su | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=$ 25th percentile
Q3 $=75$ th percentile

Table 8.188 Number of days with grade 3 general symptoms during the solicited post-vaccination period by age strata (Total Vaccinated Cohort)

| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Fatigue | Dose 1 | 18-49ys | HZ/su | 5 | 2.0 | 1.0 | 1.0 | 2.0 | 2.0 | 4.0 |
|  |  |  | Placebo | 2 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 5 | 2.2 | 1.0 | 1.0 | 2.0 | 3.0 | 4.0 |
|  |  |  | Placebo | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  | Dose 2 | 18-49ys | HZ/su | 4 | 2.0 | 1.0 | 1.5 | 2.0 | 2.5 | 3.0 |
|  |  |  | Placebo | 3 | 2.7 | 1.0 | 1.0 | 3.0 | 4.0 | 4.0 |
|  |  | $\geq 50 y s$ | HZ/su | 5 | 4.2 | 1.0 | 2.0 | 4.0 | 7.0 | 7.0 |
|  |  |  | Placebo | 3 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | 18-49ys | HZ/su | 9 | 2.0 | 1.0 | 1.0 | 2.0 | 2.0 | 4.0 |
|  |  |  | Placebo | 5 | 2.4 | 1.0 | 2.0 | 2.0 | 3.0 | 4.0 |
|  |  | $\geq 50 y s$ | HZ/su | 10 | 3.2 | 1.0 | 1.0 | 2.5 | 4.0 | 7.0 |
|  |  |  | Placebo | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
| Gastrointestinal symptoms | Dose 1 | 18-49ys | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
|  |  | $\geq 50 y s$ | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  | Dose 2 | 18-49ys | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 2.5 | 1.0 | 1.0 | 2.5 | 4.0 | 4.0 |
|  |  | $\geq 50 y s$ | HZ/su | 3 | 2.7 | 2.0 | 2.0 | 2.0 | 4.0 | 4.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | 18-49ys | HZ/su | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 4 | 2.8 | 1.0 | 2.0 | 3.0 | 3.5 | 4.0 |
|  |  | $\geq 50 y s$ | HZ/su | 4 | 2.5 | 2.0 | 2.0 | 2.0 | 3.0 | 4.0 |
|  |  |  | Placebo | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
| Headache | Dose 1 | 18-49ys | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Dose 2 | 18-49ys | HZ/su | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  |  | Placebo | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  | Overall/dose | 18-49ys | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 4 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Myalgia | Dose 1 | 18-49ys | HZ/su | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
|  |  |  | Placebo | 2 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
|  |  | $\geq 50 y s$ | HZ/su | 4 | 2.5 | 1.0 | 1.0 | 1.5 | 4.0 | 6.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Dose 2 | 18-49ys | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 1 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 |
|  |  | $\geq 50 \mathrm{ys}$ | HZ/su | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  | Overall/dose | 18-49ys | HZ/su | 5 | 1.4 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 3 | 3.7 | 3.0 | 3.0 | 3.0 | 5.0 | 5.0 |
|  |  | $\geq 50 y s$ | HZ/su | 7 | 2.1 | 1.0 | 1.0 | 2.0 | 2.0 | 6.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Shivering | Dose 1 | 18-49ys | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  | Dose 2 | 18-49ys | HZ/su | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | $\geq 50 y s$ | HZ/su | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | 18-49ys | HZ/su | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |


| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  |  | $\geq 50 y s$ | HZ/su | 5 | 1.4 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.189 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=30 \end{aligned}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=85 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 25 | 80.6 | 62.5 | 92.5 | 27 | 90.0 | 73.5 | 97.9 | 75 | 87.2 | 78.3 | 93.4 | 76 | 89.4 | 80.8 | 95.0 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 1 | 3.2 | 0.1 | 16.7 | 3 | 10.0 | 2.1 | 26.5 | 4 | 4.7 | 1.3 | 11.5 | 3 | 3.5 | 0.7 | 10.0 |
|  | Febrile neutropenia (10016288) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 4 | 4.7 | 1.3 | 11.5 | 2 | 2.4 | 0.3 | 8.2 |
|  | Iron deficiency anaemia (10022972) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Leukocytosis (10024378) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Leukopenia (10024384) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Lymphopenia (10025327) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Neutropenia (10029354) | 2 | 6.5 | 0.8 | 21.4 | 3 | 10.0 | 2.1 | 26.5 | 9 | 10.5 | 4.9 | 18.9 | 12 | 14.1 | 7.5 | 23.4 |
|  | Thrombocytopenia (10043554) | 1 | 3.2 | 0.1 | 16.7 | 1 | 3.3 | 0.1 | 17.2 | 4 | 4.7 | 1.3 | 11.5 | 2 | 2.4 | 0.3 | 8.2 |
| Cardiac disorders (10007541) | Palpitations (10033557) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Tachycardia (10043071) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Tinnitus (10043882) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 3 | 3.5 | 0.7 | 10.0 |
| Eye disorders (10015919) | Eye discharge (10015915) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Eye irritation (10015946) | 0 | 0.0 | 0.0 | 11.2 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Eye swelling (10015967) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Lacrimation increased (10023644) | 2 | 6.5 | 0.8 | 21.4 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
|  | Myopia (10028651) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Visual acuity reduced (10047531) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 2 | 6.5 | 0.8 | 21.4 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Abdominal pain (10000081) | 2 | 6.5 | 0.8 | 21.4 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
|  | Abdominal pain upper (10000087) | 1 | 3.2 | 0.1 | 16.7 | 1 | 3.3 | 0.1 | 17.2 | 3 | 3.5 | 0.7 | 9.9 | 2 | 2.4 | 0.3 | 8.2 |
|  | Aerophagia (10052813) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Aphthous ulcer (10002959) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Constipation (10010774) | 3 | 9.7 | 2.0 | 25.8 | 4 | 13.3 | 3.8 | 30.7 | 13 | 15.1 | 8.3 | 24.5 | 8 | 9.4 | 4.2 | 17.7 |
|  | Diarrhoea (10012735) | 3 | 9.7 | 2.0 | 25.8 | 0 | 0.0 | 0.0 | 11.6 | 6 | 7.0 | 2.6 | 14.6 | 10 | 11.8 | 5.8 | 20.6 |

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|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 \mathrm{ys}$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  |  |  | Placebo$N=30$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | $\begin{aligned} & \hline \text { Placebo } \\ & \mathrm{N}=85 \end{aligned}$ |  |  |  |
|  |  | 95\% Cl |  |  |  |  |  | 95\% CI |  | 95\% Cl |  |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Dry mouth (10013781) | 0 | 0.0 | 0.0 | 11.2 |  | 3.3 | 0.1 | 17.2 | 2 | 2.3 | 0.3 | 8.1 | 2 | 2.4 | 0.3 | 8.2 |
|  | Dyspepsia (10013946) | 0 | 0.0 | 0.0 | 11.2 | 2 | 6.7 | 0.8 | 22.1 | 6 | 7.0 | 2.6 | 14.6 | 11 | 12.9 | 6.6 | 22.0 |
|  | Dysphagia (10013950) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
|  | Epigastric discomfort (10053155) | 0 | 0.0 | 0.0 | 11.2 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Flatulence (10016766) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
|  | Gastrointestinal disorder (10017944) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 3 | 3.5 | 0.7 | 10.0 |
|  | Gastrointestinal pain (10017999) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Gastrooesophageal reflux disease (10017885) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 2 | 2.3 | 0.3 | 8.1 | 0 | 0.0 | 0.0 | 4.2 |
|  | Gingival pain (10018286) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Glossitis (10018386) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Haemorrhoidal haemorrhage (10054787) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.0 | 11.2 | 2 | 6.7 | 0.8 | 22.1 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Hiatus hernia (10020028) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 11.2 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Nausea (10028813) | 12 | 38.7 | 21.8 | 57.8 | 9 | 30.0 | 14.7 | 49.4 | 19 | 22.1 | 13.9 | 32.3 | 19 | 22.4 | 14.0 | 32.7 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 3 | 3.5 | 0.7 | 10.0 |
|  | Oesophagitis (10030216) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Oral pain (10031009) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Proctalgia (10036772) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.4 | 0.3 | 8.2 |
|  | Rectal tenesmus (10057071) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Stomatitis (10042128) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 4 | 4.7 | 1.3 | 11.5 | 2 | 2.4 | 0.3 | 8.2 |
|  | Swollen tongue (10042727) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Vomiting (10047700) |  | 3.2 | 0.1 | 16.7 | 6 | 20.0 | 7.7 | 38.6 | 9 | 10.5 | 4.9 | 18.9 | 8 | 9.4 | 4.2 | 17.7 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 13 | 41.9 | 24.5 | 60.9 | 4 | 13.3 | 3.8 | 30.7 | 17 | 19.8 | 12.0 | 29.8 | 24 | 28.2 | 19.0 | 39.0 |
|  | Axillary pain (10048750) | 0 | 0.0 | 0.0 | 11.2 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Catheter site pain (10052268) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Chest pain (10008479) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Chills (10008531) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Fatigue (10016256) | 1 | 3.2 | 0.1 | 16.7 | 3 | 10.0 | 2.1 | 26.5 | 3 | 3.5 | 0.7 | 9.9 | 3 | 3.5 | 0.7 | 10.0 |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.0 | 11.2 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |

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|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  |  |  | Placebo$N=30$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | $\begin{array}{\|l} \hline \text { Placebo } \\ \mathrm{N}=85 \end{array}$ |  |  |  |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Dizziness postural (10013578) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Dysaesthesia (10013886) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Dysgeusia (10013911) | 0 | 0.0 | 0.0 | 11.2 | 1 | 3.3 | 0.1 | 17.2 | 1 | 1.2 | 0.0 | 6.3 | 5 | 5.9 | 1.9 | 13.2 |
|  | Headache (10019211) | 1 | 3.2 | 0.1 | 16.7 | 2 | 6.7 | 0.8 | 22.1 | 2 | 2.3 | 0.3 | 8.1 | 1 | 1.2 | 0.0 | 6.4 |
|  | Hepatic encephalopathy (10019660) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Hypoaesthesia (10020937) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Lethargy (10024264) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | O | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Motor dysfunction (10061296) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Muscle contractions involuntary (10028293) | - | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Neuropathy peripheral (10029331) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 4 | 4.7 | 1.3 | 11.5 | 4 | 4.7 | 1.3 | 11.6 |
|  | Neurotoxicity (10029350) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 2 | 2.4 | 0.3 | 8.2 |
|  | Paraesthesia (10033775) | 2 | 6.5 | 0.8 | 21.4 | 1 | 3.3 | 0.1 | 17.2 | 3 | 3.5 | 0.7 | 9.9 | 3 | 3.5 | 0.7 | 10.0 |
|  | Paresis (10033985) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Peripheral sensory neuropathy (10034620) | 3 | 9.7 | 2.0 | 25.8 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.4 | 0.3 | 8.2 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 11.2 |  | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
|  | Syncope (10042772) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 |  | 0.0 | 0.0 | 4.2 |
|  | Tremor (10044565) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 2 | 2.4 | 0.3 | 8.2 |
| Psychiatric disorders (10037175) | Aggression (10001488) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Anxiety (10002855) | 2 | 6.5 | 0.8 | 21.4 | O | 0.0 | 0.0 | 11.6 | 2 | 2.3 | 0.3 | 8.1 | 2 | 2.4 | 0.3 | 8.2 |
|  | Depression (10012378) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Insomnia (10022437) | 1 | 3.2 | 0.1 | 16.7 | 1 | 3.3 | 0.1 | 17.2 | 3 | 3.5 | 0.7 | 9.9 | 1 | 1.2 | 0.0 | 6.4 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) |  | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 |  | 0.0 | 0.0 | 4.2 | 2 | 2.4 | 0.3 | 8.2 |
|  | Bladder spasm (10048994) | 0 | 0.0 | 0.0 | 11.2 |  | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Chronic kidney disease (10064848) | 0 | 0.0 | 0.0 | 11.2 | - | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Dysuria (10013990) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
|  | Hydronephrosis (10020524) |  | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Renal impairment (10062237) | 0 | 0.0 | 0.0 | 11.2 |  | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Urinary retention (10046555) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 |  | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
| Reproductive system and breast disorders (10038604) | Oedema genital (10030104) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 |  | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Asthma (10003553) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | - | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Catarrh (10007774) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |

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|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=30 \end{aligned}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=85 \end{aligned}$ |  |  |  |
|  |  |  |  | 95\% CI |  |  |  | 95\% Cl |  |  |  | 95\% CI |  |  |  | 95\% Cl |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Cough (10011224) | 2 | 6.5 | 0.8 | 21.4 | 0 | 0.0 | 0.0 | 11.6 | 2 | 2.3 | 0.3 | 8.1 | 0 | 0.0 | 0.0 | 4.2 |
|  | Dysaesthesia pharynx (10062665) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Dysphonia (10013952) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
|  | Dyspnoea (10013968) | 2 | 6.5 | 0.8 | 21.4 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.4 | 0.3 | 8.2 |
|  | Epistaxis (10015090) | 1 | 3.2 | 0.1 | 16.7 | 1 | 3.3 | 0.1 | 17.2 | 2 | 2.3 | 0.3 | 8.1 | 3 | 3.5 | 0.7 | 10.0 |
|  | Haemoptysis (10018964) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Hiccups (10020039) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 2 | 2.4 | 0.3 | 8.2 |
|  | Nasal congestion (10028735) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Oropharyngeal discomfort (10068318) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Oropharyngeal pain (10068319) | 0 | 0.0 | 0.0 | 11.2 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Pulmonary embolism (10037377) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 7 | 22.6 | 9.6 | 41.1 | 13 | 43.3 | 25.5 | 62.6 | 14 | 16.3 | 9.2 | 25.8 | 10 | 11.8 | 5.8 | 20.6 |
|  | Dermatitis (10012431) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Dry skin (10013786) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Erythema (10015150) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 3 | 3.5 | 0.7 | 9.9 | 1 | 1.2 | 0.0 | 6.4 |
|  | Nail dystrophy (10028698) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Onychalgia (10064251) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Palmar-plantar erythrodysaesthesia syndrome (10033553) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Pruritus (10037087) | 0 | 0.0 | 0.0 | 11.2 | 2 | 6.7 | 0.8 | 22.1 | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.4 | 0.3 | 8.2 |
|  | Pruritus generalised (10052576) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Rash (10037844) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 4 | 4.7 | 1.3 | 11.6 |
|  | Rash macular (10037867) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 11.2 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 11.2 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Scar pain (10049002) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Skin disorder (10040831) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 11.2 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Swelling face (10042682) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Urticaria (10046735) | 2 | 6.5 | 0.8 | 21.4 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |

CONFIDENTIAL
116427 (ZOSTER-028)
Report Final

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=30 \end{aligned}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=85$ |  |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| Social circumstances (10041244) | Menopause (10027308) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.0 | 11.2 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Haematoma (10018852) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
|  | Hot flush (10060800) | 0 | 0.0 | 0.0 | 11.2 | 2 | 6.7 | 0.8 | 22.1 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Hypotension (10021097) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
|  | Lymphocele (10048642) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Phlebitis (10034879) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Thrombosis (10043607) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 |  | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Vascular pain (10047095) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
n/\% = number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{CI}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.190 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=60 \end{aligned}$ |  |  |  | Placebo$N=60$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=157 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=165 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  | - $95 \% \mathrm{Cl}$ |  |  |  | 95\% CI |  |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | $n$ | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 40 | 66.7 | 53.3 | 78.3 | 46 | 76.7 | 64.0 | 86.6 | 113 | 72.0 | 64.3 | 78.8 | 120 | 72.7 | 65.3 | 79.4 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 1 | 1.7 | 0.0 | 8.9 | 3 | 5.0 | 1.0 | 13.9 | 4 | 2.5 | 0.7 | 6.4 | 3 | 1.8 | 0.4 | 5.2 |
|  | Febrile neutropenia (10016288) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 4 | 2.5 | 0.7 | 6.4 | 3 | 1.8 | 0.4 | 5.2 |
|  | Iron deficiency anaemia (10022972) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Leukocytosis (10024378) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Leukopenia (10024384) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Lymphopenia (10025327) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Neutropenia (10029354) | 2 | 3.3 | 0.4 | 11.5 | 4 | 6.7 | 1.8 | 16.2 | 10 | 6.4 | 3.1 | 11.4 | 13 | 7.9 | 4.3 | 13.1 |
|  | Thrombocytopenia (10043554) | 1 | 1.7 | 0.0 | 8.9 | 2 | 3.3 | 0.4 | 11.5 | 5 | 3.2 | 1.0 | 7.3 | 2 | 1.2 | 0.1 | 4.3 |
| Cardiac disorders (10007541) | Palpitations (10033557) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Tachycardia (10043071) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Tinnitus (10043882) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 3 | 1.8 | 0.4 | 5.2 |
| Eye disorders (10015919) | Eye discharge (10015915) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Eye irritation (10015946) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Eye swelling (10015967) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Lacrimation increased (10023644) | 2 | 3.3 | 0.4 | 11.5 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Myopia (10028651) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Visual acuity reduced (10047531) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 |  | 0.6 | 0.0 | 3.3 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 2 | 3.3 | 0.4 | 11.5 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Abdominal pain (10000081) | 2 | 3.3 | 0.4 | 11.5 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Abdominal pain upper (10000087) | 1 | 1.7 | 0.0 | 8.9 | 1 | 1.7 | 0.0 | 8.9 | 4 | 2.5 | 0.7 | 6.4 | 2 | 1.2 | 0.1 | 4.3 |
|  | Aerophagia (10052813) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Aphthous ulcer (10002959) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Constipation (10010774) | 3 | 5.0 | 1.0 | 13.9 | 4 | 6.7 | 1.8 | 16.2 | 15 | 9.6 | 5.4 | 15.3 | 8 | 4.8 | 2.1 | 9.3 |
|  | Diarrhoea (10012735) | 4 | 6.7 | 1.8 | 16.2 | 0 | 0.0 | 0.0 | 6.0 | 7 | 4.5 | 1.8 | 9.0 | 10 | 6.1 | 2.9 | 10.9 |
|  | Dry mouth (10013781) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 2 | 1.3 | 0.2 | 4.5 | 2 | 1.2 | 0.1 | 4.3 |



|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=60 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=60 \end{gathered}$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=157 \end{aligned}$ |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=165 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Generalised oedema (10018092) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Inflammation (10061218) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Influenza like illness (10022004) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.3 |
|  | Injection site pruritus (10022093) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Malaise (10025482) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 3 | 1.9 | 0.4 | 5.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Mucosal dryness (10028111) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Mucosal inflammation (10028116) | 3 | 5.0 | 1.0 | 13.9 | 0 | 0.0 | 0.0 | 6.0 | 8 | 5.1 | 2.2 | 9.8 | 8 | 4.8 | 2.1 | 9.3 |
|  | Oedema peripheral (10030124) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 3 | 1.9 | 0.4 | 5.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Pain (10033371) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Peripheral swelling (10048959) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.5 | 5 | 3.0 | 1.0 | 6.9 |
|  | Temperature intolerance (10057040) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Hepatic steatosis (10019708) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | - | 0.0 | 0.0 | 2.2 |
|  | Hepatomegaly (10019842) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Hyperbilirubinaemia (10020578) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 |  | 0.6 | 0.0 | 3.3 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Hypersensitivity (10020751) | 1 | 1.7 | 0.0 | 8.9 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Seasonal allergy (10048908) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.3 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Bacterial infection (10060945) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Bronchitis (10006451) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Cystitis (10011781) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Erysipelas (10015145) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Folliculitis (10016936) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |


|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=60 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=60 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=157 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=165 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% CI |  | 95\% CI |  |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Gastroenteritis (10017888) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Gingivitis (10018292) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Herpes zoster (10019974) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Infection (10021789) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Influenza (10022000) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Nasopharyngitis (10028810) | 3 | 5.0 | 1.0 | 13.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Neutropenic sepsis (10049151) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.3 |
|  | Oral fungal infection (10061324) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Oral herpes (10067152) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Oral infection (10048685) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Pneumonia (10035664) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 3 | 1.9 | 0.4 | 5.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Post procedural infection (10067268) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Respiratory tract infection (10062352) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Sepsis (10040047) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Sinusitis (10040753) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 |  | 0.0 | 0.0 | 2.2 |
|  | Upper respiratory tract infection (10046306) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 3 | 1.9 | 0.4 | 5.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Urinary tract infection (10046571) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | , | 1.8 | 0.4 | 5.2 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Injury, poisoning and procedural complications (10022117) | Arthropod bite (10003399) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Gastrostomy failure (10050056) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | - | 0.0 | 0.0 | 2.2 |
|  | Ligament sprain (10024453) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Post procedural complication (10058046) | 0 | 0.0 | 0.0 | 6.0 | 3 | 5.0 | 1.0 | 13.9 | 2 | 1.3 | 0.2 | 4.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Post procedural diarrhoea (10057585) | 2 | 3.3 | 0.4 | 11.5 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Radiation skin injury (10063562) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 2 | 1.2 | 0.1 | 4.3 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |


|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=60 \end{aligned}$ |  |  |  | Placebo$N=60$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=157 \end{aligned}$ |  |  | Placebo$N=165$ |  |  |  |
|  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| Investigations (10022891) | Blood iron decreased (10005619) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Body temperature fluctuation (10063488) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Haemoglobin decreased (10018884) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Platelet count decreased (10035528) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Weight decreased (10047895) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Weight increased (10047899) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) | 4 | 6.7 | 1.8 | 16.2 | 0 | 0.0 | 0.0 | 6.0 | 7 | 4.5 | 1.8 | 9.0 | 5 | 3.0 | 1.0 | 6.9 |
|  | Hypercholesterolaemia (10020603) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Hyperglycaemia (10020635) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Hypocalcaemia (10020947) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Iron deficiency (10022970) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 1 | 1.7 | 0.0 | 8.9 | 1 | 1.7 | 0.0 | 8.9 | 2 | 1.3 | 0.2 | 4.5 | 2 | 1.2 | 0.1 | 4.3 |
|  | Back pain (10003988) | 2 | 3.3 | 0.4 | 11.5 | - | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 2 | 1.2 | 0.1 | 4.3 |
|  | Bone pain (10006002) | 3 | 5.0 | 1.0 | 13.9 | 1 | 1.7 | 0.0 | 8.9 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Groin pain (10018735) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Muscle contracture (10062575) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Muscle spasms (10028334) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Musculoskeletal discomfort (10053156) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Musculoskeletal pain (10028391) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 3 | 1.8 | 0.4 | 5.2 |
|  | Musculoskeletal stiffness (10052904) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Myalgia (10028411) | 2 | 3.3 | 0.4 | 11.5 | 2 | 3.3 | 0.4 | 11.5 | 4 | 2.5 | 0.7 | 6.4 | 3 | 1.8 | 0.4 | 5.2 |
|  | Neck pain (10028836) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 3 | 1.9 | 0.4 | 5.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Osteoarthritis (10031161) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Pain in extremity (10033425) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.5 | 2 | 1.2 | 0.1 | 4.3 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Prostate cancer (10060862) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 3 | 1.9 | 0.4 | 5.5 | 3 | 1.8 | 0.4 | 5.2 |


|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
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|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=60 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=60 \end{gathered}$ |  |  |  |  | $\begin{aligned} & \text { HZ/su } \\ & \mathrm{N}=157 \end{aligned}$ |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=165 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Dizziness postural (10013578) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Dysaesthesia (10013886) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Dysgeusia (10013911) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 1 | 0.6 | 0.0 | 3.5 | 5 | 3.0 | 1.0 | 6.9 |
|  | Headache (10019211) | 1 | 1.7 | 0.0 | 8.9 | 2 | 3.3 | 0.4 | 11.5 | 3 | 1.9 | 0.4 | 5.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Hepatic encephalopathy (10019660) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Hypoaesthesia (10020937) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Lethargy (10024264) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.3 |
|  | Motor dysfunction (10061296) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Muscle contractions involuntary (10028293) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Neuropathy peripheral (10029331) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 4 | 2.5 | 0.7 | 6.4 | 5 | 3.0 | 1.0 | 6.9 |
|  | Neurotoxicity (10029350) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 2 | 1.2 | 0.1 | 4.3 |
|  | Paraesthesia (10033775) | 3 | 5.0 | 1.0 | 13.9 | 1 | 1.7 | 0.0 | 8.9 | 4 | 2.5 | 0.7 | 6.4 | 4 | 2.4 | 0.7 | 6.1 |
|  | Paresis (10033985) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Peripheral sensory neuropathy (10034620) | 3 | 5.0 | 1.0 | 13.9 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.3 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Syncope (10042772) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Tremor (10044565) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 3 | 1.8 | 0.4 | 5.2 |
| Psychiatric disorders (10037175) | Aggression (10001488) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Anxiety (10002855) | 3 | 5.0 | 1.0 | 13.9 | 0 | 0.0 | 0.0 | 6.0 | 3 | 1.9 | 0.4 | 5.5 | 2 | 1.2 | 0.1 | 4.3 |
|  | Depression (10012378) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Insomnia (10022437) | 1 | 1.7 | 0.0 | 8.9 | 1 | 1.7 | 0.0 | 8.9 | 3 | 1.9 | 0.4 | 5.5 | 1 | 0.6 | 0.0 | 3.3 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.3 |
|  | Bladder spasm (10048994) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Chronic kidney disease (10064848) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Dysuria (10013990) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Renal impairment (10062237) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Urinary retention (10046555) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Reproductive system and breast disorders (10038604) | Oedema genital (10030104) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Asthma (10003553) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |


|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
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|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=60 \end{aligned}$ |  |  |  | Placebo$N=60$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=157 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=165 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  | - $95 \% \mathrm{Cl}$ |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Catarrh (10007774) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Cough (10011224) | 2 | 3.3 | 0.4 | 11.5 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Dysaesthesia pharynx (10062665) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Dysphonia (10013952) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Dyspnoea (10013968) | 2 | 3.3 | 0.4 | 11.5 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.3 |
|  | Epistaxis (10015090) | 1 | 1.7 | 0.0 | 8.9 | 1 | 1.7 | 0.0 | 8.9 | 2 | 1.3 | 0.2 | 4.5 | 3 | 1.8 | 0.4 | 5.2 |
|  | Haemoptysis (10018964) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Hiccups (10020039) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 3 | 1.8 | 0.4 | 5.2 |
|  | Nasal congestion (10028735) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Oropharyngeal discomfort (10068318) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Oropharyngeal pain (10068319) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Pulmonary embolism (10037377) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 7 | 11.7 | 4.8 | 22.6 | 13 | 21.7 | 12.1 | 34.2 | 14 | 8.9 | 5.0 | 14.5 | 10 | 6.1 | 2.9 | 10.9 |
|  | Dermatitis (10012431) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Dry skin (10013786) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Erythema (10015150) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 4 | 2.5 | 0.7 | 6.4 | 1 | 0.6 | 0.0 | 3.3 |
|  | Nail dystrophy (10028698) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Onychalgia (10064251) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Palmar-plantar erythrodysaesthesia syndrome (10033553) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Pruritus (10037087) | 0 | 0.0 | 0.0 | 6.0 | 2 | 3.3 | 0.4 | 11.5 | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.3 |
|  | Pruritus generalised (10052576) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Rash (10037844) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 4 | 2.4 | 0.7 | 6.1 |
|  | Rash macular (10037867) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Scar pain (10049002) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | - | 0.0 | 0.0 | 2.2 |
|  | Skin disorder (10040831) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Swelling face (10042682) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |

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|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=60 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=60 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=157 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=165 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% CI |  | 95\% CI |  |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Urticaria (10046735) | 2 | 3.3 | 0.4 | 11.5 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
| Social circumstances (10041244) | Menopause (10027308) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Haematoma (10018852) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Hot flush (10060800) | 0 | 0.0 | 0.0 | 6.0 | 2 | 3.3 | 0.4 | 11.5 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Hypotension (10021097) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Lymphocele (10048642) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Phlebitis (10034879) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Thrombosis (10043607) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Vascular pain (10047095) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.191 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period by age strata (Total Vaccinated Cohort)


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|  |  | 18-49ys |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  |  | Placebo$N=30$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=85$ |  |  |  |
|  |  | 95\% CI |  |  | 95\% Cl |  |  |  | 95\% CI |  |  |  | 95\% Cl |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL | UL | n ${ }^{\text {\% }}$ | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Renal impairment (10062237) | 00.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Pleural effusion (10035598) | 00.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Pulmonary embolism (10037377) | 00.0 | 0.0 | . 11.2 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 00.0 | 0.0 | 0 11.2 | 1 | 3.3 | 0.1 | 17.2 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Skin haemorrhage (10064265) | 00.0 | 0.0 | . 11.2 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
| Vascular disorders (10047065) | Lymphocele (10048642) | 00.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{CI}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.192 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the $\mathbf{3 0 - d a y}$ (Days $\mathbf{0 - 2 9}$ ) post-vaccination period by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=60 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=60 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { HZ/su } \\ & \mathrm{N}=157 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=165 \end{aligned}$ |  |  |  |
|  |  |  |  |  | \% Cl |  |  |  | \% CI |  |  | 95\% | Cl |  |  |  | \% CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) |  | \% | LL | UL |  | \% |  | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 4 | 6.7 | 1.8 | 16.2 | 4 | 6.7 | 1.8 | 816.2 | 18 | 11.5 | 6.9 | 17.5 | 11 | 6.7 | 3.4 | 11.6 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 0 | 0.0 | 0.0 | 0.0 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Febrile neutropenia (10016288) | 0 | 0.0 | 0.0 | .0.0 | 0 | 0.0 | 0.0 | 06.0 | 4 | 2.5 | 0.7 | 6.4 | 2 | 1.2 | 0.1 | 4.3 |
|  | Neutropenia (10029354) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 08.9 | 4 | 2.5 | 0.7 | 6.4 | 2 | 1.2 | 0.1 | 4.3 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Gastrointestinal disorders (10017947) | Abdominal pain (10000081) | 0 | 0.0 | 0.0 | 6.0 |  | 0.0 | 0.0 | 06.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Constipation (10010774) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 |  | 06.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.0 | 0.0 | 1 | 1.7 | 0.0 | 08.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 0 | 0.0 | 0.0 | 0.0 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Malaise (10025482) |  | 0.0 | 0.0 | 6.0 |  | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 0.0 | 0 | 0.0 |  | 06.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 0.0 | 0 | 0.0 | 0.0 | 06.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Nasopharyngitis (10028810) |  | 1.7 | 0.0 | 88.9 |  | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Sepsis (10040047) | 0 | 0.0 | 0.0 | . 6.0 | 0 | 0.0 | 0.0 | 06.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
| Injury, poisoning and procedural complications (10022117) | Post procedural diarrhoea (10057585) | 2 | 3.3 | 0.4 | 411.5 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
| Investigations (10022891) | Platelet count decreased (10035528) | 0 | 0.0 | 0.0 | . 6.0 | 0 | 0.0 |  | 06.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Weight increased (10047899) | 0 | 0.0 | 0.0 | 0.0 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 06.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Prostate cancer (10060862) | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.02 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Nervous system disorders (10029205) | Hepatic encephalopathy (10019660) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 06.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 06.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
| Psychiatric disorders (10037175) | Insomnia (10022437) | 0 | 0.0 | 0.0 | . 6.0 | 1 | 1.7 | 0.0 | 08.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.0 | 0.0 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.3 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Renal impairment (10062237) |  | 0.0 | 0.0 | 6.0 | 0 | 0.0 |  | 06.0 | 2 | 1.3 | 0.2 | 4.5 | 0 | 0.0 | 0.0 | 2.2 |

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18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of administered doses
n/\% = number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.193 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) postvaccination period by age strata (Total Vaccinated Cohort)

|  |  |  | 18-49ys |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  |  | Placebo$N=30$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  | Placebo$N=85$ |  |  |
|  |  |  | 95\% Cl |  |  | 95\% CI |  |  |  | 95\% CI |  |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) |  | \% | LL | UL | n \% | \% LL | LL | UL | n \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 4 | 12.9 | 3.6 | 29.8 | 26.7 | 6.70. | 0.8 | 22.1 | 67.0 | 2.6 | 14.6 | 78.2 | 3.4 | 16.2 |
| Blood and lymphatic system disorders (10005329) | Neutropenia (10029354) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.00. | 0.0 | 11.6 | 00. | 0.0 | 4.2 | 11.2 | 0.0 | 6.4 |
| Cardiac disorders (10007541) | Tachycardia (10043071) |  | 3.2 | 0.1 | 16.7 | 00.0 | 0.00. | 0.0 | 11.6 | 00. | 0.0 | 4.2 | 11.2 | 0.0 | 6.4 |
| Gastrointestinal disorders (10017947) | Swollen tongue (10042727) |  | 3.2 | 0.1 | 16.7 | 00.0 | 0.00. | 0.0 | 11.6 | 00. | 0.0 | 4.2 | 00.0 | 0.0 | 4.2 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) |  | 6.5 | 0.8 | 21.4 | 00.0 | 0.00. | 0.0 | 11.6 | 00. | 0.0 | 4.2 | 11.2 | 0.0 | 6.4 |
|  | Axillary pain (10048750) | 0 | 0.0 | 0.0 | 11.2 |  | 3.30. | 0.1 | 17.2 | 00. | 0.0 | 4.2 | 00.0 | 0.0 | 4.2 |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.00. | 0.0 | 11.6 | 00. | 0.0 | 4.2 | 11.2 | 0.0 | 6.4 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 11.2 | 13.3 | 3.30. | 0.1 | 17.2 | 00.0 | 0.0 | 4.2 | 00.0 | 0.0 | 4.2 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.0 | 11.2 | 13.3 | 3.30. | 0.1 | 17.2 | 00. | 0.0 | 4.2 | 00.0 | 0.0 | 4.2 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.00. | 0.0 | 11.6 | 00.0 | 0.0 | 4.2 | 11.2 | 0.0 | 6.4 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.00. | 0.0 | 11.6 | 00. | 0.0 | 4.2 | 22.4 | 0.3 | 8.2 |
|  | Injection site pruritus (10022093) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.00 | 0.0 | 11.6 | 22.3 | 0.3 | 8.1 | 00.0 | 0.0 | 4.2 |
|  | Malaise (10025482) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.00. | 0.0 | 11.6 | 11.2 | 0.0 | 6.3 | 00.0 | 0.0 | 4.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.00. | 0.0 | 11.6 | 00. | 0.0 | 4.2 | 11.2 | 0.0 | 6.4 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) |  | 3.2 | 0.1 | 16.7 | 00.0 | 0.00. | 0.0 | 11.6 | 00. | 0.0 | 4.2 | 00.0 | 0.0 | 4.2 |
|  | Oral herpes (10067152) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.00. | 0.0 | 11.6 | 11.2 | 0.0 | 6.3 | 00.0 | 0.0 | 4.2 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.00. | 0.0 | 11.6 | 00. | 0.0 | 4.2 | 11.2 | 0.0 | 6.4 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) |  | 3.2 | 0.1 | 16.7 | 00.0 | 0.00. | 0.0 | 11.6 | 00. | 0.0 | 4.2 | 11.2 | 0.0 | 6.4 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.00. | 0.0 | 11.6 | 00.0 | 0.0 | 4.2 | 11.2 | 0.0 | 6.4 |
|  | Muscle contractions involuntary (10028293) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.00. | 0.0 | 11.6 | 11.2 | 0.0 | 6.3 | 00.0 | 0.0 | 4.2 |
| Skin and subcutaneous tissue disorders (10040785) | Erythema (10015150) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.00. | 0.0 | 11.6 | 11.2 | 0.0 | 6.3 | 00.0 | 0.0 | 4.2 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.00. | 0.0 | 11.6 | 00. | 0.0 | 4.2 | 11.2 | 0.0 | 6.4 |
|  | Urticaria (10046735) | 0 | 0.0 | 0.0 | 11.2 |  | 3.30. |  | 17.20 | 00. | 0.0 | 4.2 | 00.0 | 0.0 | 4.2 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group

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At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.194 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by age strata (Total Vaccinated Cohort)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group

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At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of administered doses
n/\% = number/percentage of doses with the symptom
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.195 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  |  |  | Placebo$N=30$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$\mathrm{N}=85$ |  |  |  |
|  |  |  | 95\% CI |  |  |  | 95\% CI |  |  | $\begin{aligned} & 95 \% \\ & \mathrm{Cl} \\ & \hline \end{aligned}$ |  |  |  |  | $\begin{aligned} & 95 \% \\ & \mathrm{Cl} \\ & \hline \end{aligned}$ |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 1 | 3.2 | 0.1 | 16.7 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit
Table 8.196 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=60 \end{aligned}$ |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=60 \end{gathered}$ |  |  | $\begin{aligned} & \begin{array}{l} \mathrm{HZ} / \mathrm{su} \\ \mathrm{~N}=157 \end{array} \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=165 \\ & \hline \end{aligned}$ |  |  |
|  |  |  | $\begin{aligned} & 95^{\circ} \\ & \mathrm{Cl} \end{aligned}$ | $5 \%$ |  | $\begin{aligned} & 95^{\circ} \\ & \mathrm{CI} \end{aligned}$ |  |  |  | ${ }_{9}^{95}$ |  |  | CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n\% | LL | UL | n \% |  | UL | n | \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 11.7 | 70.0 | 08.9 | 00.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 00.0 | 0. | 2.2 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 11.7 | 70.0 | 08.9 | 00.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.3 | 00 | 0. | 2.2 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.197 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 30-day (Days 0-29) post-vaccination period by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ N=30 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  | Placebo$N=85$ |  |  |  |
|  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) |  | \% | LL | UL | n \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 9 | 29.0 | 14.2 | 48.0 | 826.7 | 12.3 | 45.9 | 22 | 25.6 | 16.8 | 36.1 | 25 | 29.4 | 20.0 | 40.3 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) |  | 0.0 | 0.0 | 11.2 | 13.3 | 0.1 | 17.2 | 2 | 2.3 | 0.3 | 8.1 | 2 | 2.4 | 0.3 | 8.2 |
|  | Febrile neutropenia (10016288) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 4 | 4.7 | 1.3 | 11.5 | 2 | 2.4 | 0.3 | 8.2 |
|  | Neutropenia (10029354) |  | 0.0 | 0.0 | 11.2 | 13.3 | 0.1 | 17.2 | 2 | 2.3 | 0.3 | 8.1 | 2 | 2.4 | 0.3 | 8.2 |
|  | Thrombocytopenia (10043554) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
| Cardiac disorders (10007541) | Tachycardia (10043071) |  | 3.2 | 0.1 | 16.7 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) |  | 3.2 | 0.1 | 16.7 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Abdominal pain (10000081) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Abdominal pain upper (10000087) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
|  | Constipation (10010774) |  | 0.0 | 0.0 | 11.2 | 13.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.4 | 0.3 | 8.2 |
|  | Diarrhoea (10012735) |  | 3.2 | 0.1 | 16.7 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Dyspepsia (10013946) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Dysphagia (10013950) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Gastrooesophageal reflux disease (10017885) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Haemorrhoids (10019022) |  | 0.0 | 0.0 | 11.2 | 13.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Mouth ulceration (10028034) |  | 0.0 | 0.0 | 11.2 | 13.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Nausea (10028813) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 3 | 3.5 | 0.7 | 9.9 | 0 | 0.0 | 0.0 | 4.2 |
|  | Odynophagia (10030094) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Stomatitis (10042128) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Swollen tongue (10042727) |  | 3.2 | 0.1 | 16.7 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | - | 0.0 | 0.0 | 4.2 |
|  | Vomiting (10047700) |  | 0.0 | 0.0 | 11.2 | 310.0 | 2.1 | 26.5 |  | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 3 | 3.5 | 0.7 | 9.9 | 0 | 0.0 | 0.0 | 4.2 |
|  | Injection site mass (10022081) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |

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18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \%$ CI $=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.198 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 30-day (Days 0-29) post-vaccination period by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=60 \end{aligned}$ |  |  |  | Placebo$N=60$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=157 \end{aligned}$ |  |  |  | Placebo$N=165$ |  |  |  |
|  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 10 | 16.7 | 8.3 | 28.5 | 11 | 18.3 | 9.5 | 30.4 | 26 | 16.6 | 11.1 | 23.3 | 32 | 19.4 | 13.7 | 26.3 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 2 | 1.3 | 0.2 | 4.5 | 2 | 1.2 | 0.1 | 4.3 |
|  | Febrile neutropenia (10016288) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 4 | 2.5 | 0.7 | 6.4 | 3 | 1.8 | 0.4 | 5.2 |
|  | Neutropenia (10029354) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | - | 1.9 | 0.4 | 5.5 | 2 | 1.2 | 0.1 | 4.3 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | - | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Abdominal pain (10000081) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Abdominal pain upper (10000087) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Constipation (10010774) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.3 |
|  | Diarrhoea (10012735) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Dyspepsia (10013946) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Dysphagia (10013950) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | - | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Gastrooesophageal reflux disease (10017885) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Nausea (10028813) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | - | 1.9 | 0.4 | 5.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Stomatitis (10042128) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 |  | 0.6 | 0.0 | 3.5 |  | 0.0 | 0.0 | 2.2 |
|  | Swollen tongue (10042727) | 0 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Vomiting (10047700) | 0 | 0.0 | 0.0 | 6.0 | 3 | 5.0 | 1.0 | 13.9 |  | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 3 | 1.9 | 0.4 | 5.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |

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|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=60 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=60 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=157 \end{aligned}$ |  |  |  | Placebo$N=165$ |  |  |  |
|  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  | 95\% Cl |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Mucosal inflammation (10028116) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Hepatomegaly (10019842) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Cystitis (10011781) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Gastroenteritis (10017888) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Nasopharyngitis (10028810) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Neutropenic sepsis (10049151) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.3 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Post procedural infection (10067268) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Respiratory tract infection (10062352) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Sepsis (10040047) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Upper respiratory tract infection (10046306) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Platelet count decreased (10035528) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 |  | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |

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|  |  |  |  |  |  |  |  |  |  |  |  |  |  | 0y |  |  |  |
|  |  |  |  | $\begin{aligned} & \mathrm{Z} / \mathrm{su} \\ & =60 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { cebo } \\ & =60 \end{aligned}$ |  |  |  |  |  |  |  | $\begin{aligned} & \text { aceb } \\ & =1 \end{aligned}$ |  |
|  |  |  |  |  | \% CI |  |  |  | \% C |  |  |  | \% CI |  |  |  | Cl |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| Musculoskeletal and connective tissue disorders (10028395) | Back pain (10003988) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Muscle spasms (10028334) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Neck pain (10028836) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Pain in extremity (10033425) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.5 | 0 | 0.0 | 0.0 | 2.2 |
| Neoplasms benign, malignant and unspecified (incl cysts and | Adenocarcinoma of colon (10001167) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
| polyps) (10029104) | Prostate cancer (10060862) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Headache (10019211) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Hepatic encephalopathy (10019660) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Motor dysfunction (10061296) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Neuropathy peripheral (10029331) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Paraesthesia (10033775) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 1 | 0.6 | 0.0 | 3.3 |
|  | Syncope (10042772) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
| Psychiatric disorders (10037175) | Anxiety (10002855) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 2 | 1.2 | 0.1 | 4.3 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Cough (10011224) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
|  | Epistaxis (10015090) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Hiccups (10020039) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Pulmonary embolism (10037377) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.6 | 0.0 | 3.5 | 0 | 0.0 | 0.0 | 2.2 |
| Skin and subcutaneous tissue disorders (10040785) | Erythema (10015150) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Rash (10037844) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 1 | 0.6 | 0.0 | 3.3 |
|  | Scar pain (10049002) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
|  | Urticaria (10046735) | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.0 | 6.0 | 1 | 1.7 |  | 8.9 | 0 | 0.0 | 0.0 | 2.3 | 0 | 0.0 | 0.0 | 2.2 |

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18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.199 Global Summary of unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period by age strata (Total Vaccinated Cohort)

|  | Group |  |  |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :---: | :---: | :---: | :---: | :---: | :---: |
|  | 18-49ys |  |  |  |  |  |  |  |  | $\geq$ 50ys |  | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |  |  |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 25 | 27 | 75 | 76 | 100 | 103 |  |  |  |  |  |  |
| Number of doses followed by at least one unsolicited symptom | 40 | 46 | 113 | 120 | 153 | 166 |  |  |  |  |  |  |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 130 | 100 | 285 | 298 | 415 | 398 |  |  |  |  |  |  |
| Number of unsolicited symptoms reported** | 136 | 103 | 294 | 307 | 430 | 410 |  |  |  |  |  |  |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.200 Global Summary of grade 3 unsolicited signs and symptoms reported within the 30-day (Days $0-29$ ) post-vaccination period by age strata (Total Vaccinated Cohort)

|  | Group |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  | 18-49ys |  | $\geq$ 50ys |  | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su |
|  | Placebo |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 3 | 4 | 15 | 11 | 18 |
| Number of doses followed by at least one unsolicited symptom | 4 | 4 | 18 | 11 | 22 |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 4 | 5 | 19 | 17 | 23 |
| Number of unsolicited symptoms reported** | 4 | 5 | 19 | 17 | 22 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once ** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.201 Global Summary of unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by age strata (Total Vaccinated Cohort)

|  | Group |  |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :---: | :---: | :---: | :---: | :---: |
|  | 18-49ys |  |  |  |  |  |  |  | $\geq$ 50ys |  | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |  |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 4 | 2 | 6 | 7 | 10 | 9 |  |  |  |  |  |
| Number of doses followed by at least one unsolicited symptom | 4 | 3 | 7 | 8 | 11 | 11 |  |  |  |  |  |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 6 | 5 | 7 | 12 | 13 | 17 |  |  |  |  |  |
| Number of unsolicited symptoms reported** | 6 | 5 | 7 | 12 | 13 | 17 |  |  |  |  |  |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.202 Global Summary of grade 3 unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days $0-29$ ) post-vaccination period by age strata (Total Vaccinated Cohort)

|  | Group |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | 18-49ys |  | $\geq$ 50ys |  | All |  |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |
| Number of subjects with at least one unsolicited symptom reported | 1 | 0 | 0 | 0 | 1 | 0 |
| Number of doses followed by at least one unsolicited symptom | 1 | 0 | 0 | 0 | 1 | 0 |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 1 | 0 | 0 | 0 | 1 | 0 |
| Number of unsolicited symptoms reported** | 1 | 0 | 0 | 0 | 1 | 0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once ** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.203 Global Summary of unsolicited signs and symptoms reported with medically attended visit, within the 30 -day (Days $0-29$ ) postvaccination period by age strata (Total Vaccinated Cohort)

|  | Group |  |  |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :---: | :---: | :---: | :---: | :---: | :---: |
|  | 18-49ys |  |  |  |  |  |  |  |  | $\geq$ 50ys |  | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |  |  |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 9 | 8 | 22 | 25 | 31 | 33 |  |  |  |  |  |  |
| Number of doses followed by at least one unsolicited symptom | 10 | 11 | 26 | 32 | 36 | 43 |  |  |  |  |  |  |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 12 | 17 | 48 | 45 | 60 | 62 |  |  |  |  |  |  |
| Number of unsolicited symptoms reported** | 12 | 17 | 48 | 45 | 60 | 62 |  |  |  |  |  |  |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.204 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to 30 days post last vaccination by age strata (Total Vaccinated Cohort)

No records exist in this table

Table 8.205 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from 30 days post last vaccination up to the study end by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  |  | Placebo$N=30$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ N=85 \end{gathered}$ |  |  |
|  |  | 95\% CI |  |  | 95\% CI |  |  |  |  | $\begin{gathered} 95 \% \\ \text { CI } \end{gathered}$ |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% |  | UL n | n \% | LL | LU |  | n \% |  | L UL | n | \% |  | L UL |
| At least one symptom |  | 00.0 | 0.0 | 11.20 | 00.0 | 00.0 | . 011 | 11.6 | 00 | 0 | 0.0 | 21 | 1.2 | 0.0 | . 06.4 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 00.0 | 0.0 | 11.20 |  | 00.0 | . 011 | 11.6 | 00. |  | 0. 4. | . 21 | 1.2 |  | . 06.4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.206 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to the study end by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  |  | Placebo$N=30$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=85$ |  |  |
|  |  | 95\% CI |  |  | 95\% CI |  |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \\ \hline \end{gathered}$ |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL | UL |  | \% | LL | UL | n | \% | LL | UL | n \% | LL | UL |
| At least one symptom |  | 00.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 11.2 | 0.0 | 6.4 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 00.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 11.2 | 0.0 | 6.4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.207 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from the first vaccination up to 30 days post last vaccination by age strata (Total Vaccinated Cohort)


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18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.208 Global Summary of serious adverse events reported from the first vaccination up to 30 days post last vaccination by age strata (Total Vaccinated Cohort)


Table 8.209 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relation to vaccination from first vaccination up to 30 days post last vaccination by age strata (Total Vaccinated Cohort)

No records exist in this table

Table 8.210 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from 30 days post last vaccination up to the study end by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  |  |  | Placebo$N=30$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  | Placebo$N=85$ |  |  |  |
|  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n ${ }^{\text {\% }}$ | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 4 | 12.9 | 3.6 | 29.8 | 7 | 23.3 | 9.9 | 92.3 | 26 | 30.2 | 20.8 | 41.1 | 24 | 28.2 | 19.0 | 39.0 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 0.0.6 | 2 | 2.3 | 0.3 | 8.1 | 1 | 1.2 | 0.0 | 6.4 |
|  | Febrile neutropenia (10016288) | 0 | 0.0 | 0.0 | 11.2 | 00 | 0.0 | 0.0 | 0 11.6 | 3 | 3.5 | 0.7 | 9.9 | 0 | 0.0 | 0.0 | 4.2 |
|  | Neutropenia (10029354) | 1 | 3.2 | 0.1 | 116.7 | 13 | 3.3 | 0.1 | . 117.2 | 1 | 1.2 | 0.0 | 6.3 | 2 | 2.4 | 0.3 | 8.2 |
|  | Pancytopenia (10033661) | 1 | 3.2 | 0.1 | 116.7 | 00 | 0.0 | 0.0 | 0. 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | . 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
| Cardiac disorders (10007541) | Cardiac arrest (10007515) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | . 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Cardiac failure (10007554) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 0.0.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Cardiac failure congestive (10007559) | 0 | 0.0 | 0.0 | 0 11.2 | 13 | 3.3 | 0.1 | . 117.2 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Myocardial infarction (10028596) | 0 | 0.0 | 0.0 | 0 11.2 | 0 | 0.0 | 0.0 | 211.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | . 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
| Gastrointestinal disorders (10017947) | Constipation (10010774) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | , 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Diarrhoea (10012735) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | . 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Dysphagia (10013950) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 0.0 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Enteritis (10014866) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | , 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 0. 11.2 | 0 | 0.0 | 0.0 | 0.0 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Nausea (10028813) | 0 | 0.0 | 0.0 | 11.2 | 00 | 0.0 | 0.0 | . 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | 0.0 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Oesophagitis (10030216) | 0 | 0.0 | 0.0 | 0 11.2 | 00 | 0.0 | 0.0 | 2 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
| General disorders and administration site conditions (10018065) | Death (10011906) | 0 | 0.0 | 0.0 | 11.2 | 00 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Mucosal inflammation (10028116) | 0 | 0.0 | 0.0 | 11.2 | 00 | 0.0 | 0.0 | . 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 0 11.2 | 00 | 0.0 | 0.0 | 0.011.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
| Hepatobiliary disorders (10019805) | Cholangitis acute (10008605) | 0 | 0.0 | 0.0 | 0 11.2 | 00 | 0.0 | 0.0 | . 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
| Infections and infestations (10021881) | Anal abscess (10048946) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | . 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Bacteraemia (10003997) | 0 | 0.0 | 0.0 | 11.2 | 0 | 0.0 | 0.0 | . 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 11.2 | 00 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |

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18-49ys = Subjects aged between 18 and 49 years
$\geq 50$ ys $=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%$ = number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.211 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, from 30 days post last vaccination up to the study end by age strata (Total Vaccinated Cohort)

No records exist in this table

Table 8.212 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to the study end by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  |  |  | Placebo$N=30$ |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  |  |  | Placebo$N=85$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) |  | \% | LL | UL | n \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 5 | 16.1 | 5.5 | 33.7 | 930.0 | 14.7 | 49.4 | 31 | 36.0 | 26.0 | 47.1 | 33 | 38.8 | 28.4 | 50.0 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 2 | 2.3 | 0.3 | 8.1 | 3 | 3.5 | 0.7 | 10.0 |
|  | Febrile neutropenia (10016288) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 6 | 7.0 | 2.6 | 14.6 | 2 | 2.4 | 0.3 | 8.2 |
|  | Neutropenia (10029354) |  | 3.2 | 0.1 | 16.7 | 13.3 | 0.1 | 17.2 | 1 | 1.2 | 0.0 | 6.3 | 3 | 3.5 | 0.7 | 10.0 |
|  | Pancytopenia (10033661) |  | 3.2 | 0.1 | 16.7 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.4 | 0.3 | 8.2 |
| Cardiac disorders (10007541) | Cardiac arrest (10007515) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Cardiac failure (10007554) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Cardiac failure congestive (10007559) | 0 | 0.0 | 0.0 | 11.2 | 13.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
|  | Myocardial infarction (10028596) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
| Gastrointestinal disorders (10017947) | Constipation (10010774) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 2 | 2.4 | 0.3 | 8.2 |
|  | Diarrhoea (10012735) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Dysphagia (10013950) |  | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Enteritis (10014866) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Nausea (10028813) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Oesophagitis (10030216) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
| General disorders and administration site conditions (10018065) | Death (10011906) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
|  | Mucosal inflammation (10028116) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 2 | 2.3 | 0.3 | 8.1 | 0 | 0.0 | 0.0 | 4.2 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 1 | 1.2 | 0.0 | 6.4 |
| Hepatobiliary disorders (10019805) | Cholangitis acute (10008605) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 11.2 | 13.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.2 | 0 | 0.0 | 0.0 | 4.2 |
| Infections and infestations (10021881) | Anal abscess (10048946) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.2 | 1 | 1.2 | 0.0 | 6.4 |
|  | Bacteraemia (10003997) | 0 | 0.0 | 0.0 | 11.2 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.3 | 0 | 0.0 | 0.0 | 4.2 |

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18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \%$ CI $=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.213 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, from first vaccination up to the study end by age strata (Total Vaccinated Cohort)

No records exist in this table

Table 8.214 Global Summary of potential immune mediated diseases reported from the first vaccination up to 30 days post last vaccination by age strata (Total Vaccinated Cohort)

No records exist in this table

Table 8.215 Number and percentage of subjects with fatal outcome reported up to the study end by age strata (Total Vaccinated Cohort)

|  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=31 \end{aligned}$ |  | Placebo $N=30$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=86 \end{aligned}$ |  | Placebo $N=85$ |
| Characteristics | n | \% | n | \% | n | \% | n | \% |
| Fatalities | 1 | 3.2 | 2 | 6.7 | 11 | 12.8 | 9 | 10.6 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once

Table 8.216 Percentage of subjects with concomitant medication during the 30day (Day 0-29) post vaccination period by age strata (Total Vaccinated Cohort)

|  | 18-49ys |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  |
|  | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 31 | 27 | 87.1 | 70.2 | 96.4 | 30 | 29 | 96.7 | 82.8 | 99.9 | 86 | 82 | 95.3 | 88.5 | 98.7 | 85 | 80 | 94.1 | 86.8 | 98.1 |
| Steroids to prevent chemotherapy nausea and vomiting | 31 | 25 | 80.6 | 62.5 | 92.5 | 30 | 26 | 86.7 | 69.3 | 96.2 | 86 | 74 | 86.0 | 76.9 | 92.6 | 85 | 72 | 84.7 | 75.3 | 91.6 |
| Any in anticipation of study vaccine reaction | 31 | 0 | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 86 | 0 | 0.0 | 0.0 | 4.2 | 85 | 0 | 0.0 | 0.0 | 4.2 |
| Any chronic use | 31 | 0 | 0.0 | 0.0 | 11.2 | 30 | 1 | 3.3 | 0.1 | 17.2 | 86 | 4 | 4.7 | 1.3 | 11.5 | 85 | 7 | 8.2 | 3.4 | 16.2 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 29 | 24 | 82.8 | 64.2 | 94.2 | 30 | 27 | 90.0 | 73.5 | 97.9 | 71 | 66 | 93.0 | 84.3 | 97.7 | 80 | 67 | 83.8 | 73.8 | 91.1 |
| Steroids to prevent chemotherapy nausea and vomiting | 29 | 23 | 79.3 | 60.3 | 92.0 | 30 | 23 | 76.7 | 57.7 | 90.1 | 71 | 59 | 83.1 | 72.3 | 91.0 | 80 | 59 | 73.8 | 62.7 | 83.0 |
| Any in anticipation of study vaccine reaction | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 71 | 0 | 0.0 | 0.0 | 5.1 | 80 | 0 | 0.0 | 0.0 | 4.5 |
| Any chronic use | 29 |  | 3.4 | 0.1 | 17.8 | 30 | 1 | 3.3 | 0.1 | 17.2 | 71 | 1 | 1.4 | 0.0 | 7.6 | 80 | 6 | 7.5 | 2.8 | 15.6 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 60 | 51 | 85.0 | 73.4 | 92.9 | 60 | 56 | 93.3 | 83.8 | 98.2 | 157 | 148 | 94.3 | 89.4 | 97.3 | 165 | 147 | 89.1 | 83.3 | 93.4 |
| Steroids to prevent chemotherapy nausea and vomiting | 60 | 48 | 80.0 | 67.7 | 89.2 | 60 | 49 | 81.7 | 69.6 | 90.5 | 157 | 133 | 84.7 | 78.1 | 90.0 | 165 | 131 | 79.4 | 72.4 | 85.3 |
| Any in anticipation of study vaccine reaction | 60 | 0 | 0.0 | 0.0 | 6.0 | 60 | 0 | 0.0 | 0.0 | 6.0 | 157 | 0 | 0.0 | 0.0 | 2.3 | 165 | 0 | 0.0 | 0.0 | 2.2 |
| Any chronic use | 60 |  | 1.7 | 0.0 | 8.9 | 60 | 2 | 3.3 | 0.4 | 11.5 | 157 | 5 | 3.2 | 1.0 | 7.3 | 165 | 13 | 7.9 | 4.3 | 13.1 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 31 | 30 | 96.8 | 83.3 | 99.9 | 30 | 30 | 100 | 88.4 | 100 | 86 | 83 | 96.5 | 90.1 | 99.3 | 85 | 83 | 97.6 | 91.8 | 99.7 |
| Steroids to prevent chemotherapy nausea and vomiting | 31 | 29 | 93.5 | 78.6 | 99.2 | 30 | 28 | 93.3 | 77.9 | 99.2 | 86 | 75 | 87.2 | 78.3 | 93.4 | 85 | 73 | 85.9 | 76.6 | 92.5 |
| Any in anticipation of study vaccine reaction | 31 | 0 | 0.0 | 0.0 | 11.2 | 30 | 0 | 0.0 | 0.0 | 11.6 | 86 | 0 | 0.0 | 0.0 | 4.2 | 85 | 0 | 0.0 | 0.0 | 4.2 |
| Any chronic use | 31 | 1 | 3.2 | 0.1 | 16.7 | 30 | 2 | 6.7 | 0.8 | 22.1 | 86 | 5 | 5.8 | 1.9 | 13.0 | 85 | 11 | 12.9 | 6.6 | 22.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one administered dose
$n / \%=$ number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.217 Number and percentage of subjects who received vaccine dose(s) by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  | Total |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=29 \end{aligned}$ |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=30 \end{aligned}$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=84 \end{aligned}$ |  | Placebo$N=82$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=113 \end{aligned}$ |  | Placebo$N=112$ |  |
| Total number of doses received |  | \% | n | \% | n | \% | n | \% | n | \% | n | \% |
| 1 | 2 | 6.9 | 0 | 0.0 | 15 | 517.9 | , | 6.1 | 17 | 15.0 | 5 | 4.5 |
| 2 | 27 | 93.1 | 30 | 100 | 69 | 982.1 | 77 | 93.9 | 96 | 85.0 | 107 | 95.5 |
| Any | 29 | 100 | 30 | 100 | 84 | 4100 | 82 | 100 | 113 | 100 | 112 | 100 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of subjects in each group or in total included in the considered cohort
$\mathrm{n} / \%=$ number/percentage of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least one dose
Table 8.218 Compliance in returning symptom sheets by age strata (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

| Dose | Sub-group | Group | Number of doses | Doses NOT according to protocol | Number of general SS | Compliance \% general SS | Number of local SS | ```Compliance % local SS``` |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 1 | 18-49ys | HZ/su | 29 | 0 | 29 | 100 | 29 | 100 |
|  |  | Placebo | 30 | 3 | 30 | 100 | 30 | 100 |
|  | $\geq 50 y s$ | HZ/su | 84 | 3 | 79 | 94.0 | 79 | 94.0 |
|  |  | Placebo | 82 | 3 | 77 | 93.9 | 77 | 93.9 |
| 2 | 18-49ys | HZ/su | 27 | 1 | 27 | 100 | 27 | 100 |
|  |  | Placebo | 30 | 4 | 29 | 96.7 | 29 | 96.7 |
|  | $\geq 50 y s$ | HZ/su | 69 | 3 | 66 | 95.7 | 67 | 97.1 |
|  |  | Placebo | 77 | 3 | 74 | 96.1 | 74 | 96.1 |
| Total | 18-49ys | HZ/su | 56 | 1 | 56 | 100 | 56 | 100 |
|  |  | Placebo | 60 | 7 | 59 | 98.3 | 59 | 98.3 |
|  | $\geq 50 y s$ | HZ/su | 153 | 6 | 145 | 94.8 | 146 | 95.4 |
|  |  | Placebo | 159 | 6 | 151 | 95.0 | 151 | 95.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
SS = Symptom screens/sheets used for the collection of local and general solicited AEs
Compliance \% = (number of doses with symptom screen/sheet return / number of administered doses) X 100

Table 8.219 Incidence and nature of symptoms (solicited and unsolicited) reported during the 7 -day (Days 0-6) post-vaccination period following each dose and overall by age strata (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | 18-49ys | HZ/su | 29 | 28 | 96.6 | 82.2 | 99.9 | 29 | 23 | 79.3 | 60.3 | 92.0 | 29 | 25 | 86.2 | 68.3 | 96.1 |
|  |  | Placebo | 30 | 17 | 56.7 | 37.4 | 74.5 | 30 | 16 | 53.3 | 34.3 | 71.7 | 30 | 4 | 13.3 | 3.8 | 30.7 |
|  | $\geq 50 y s$ | HZ/su | 84 | 74 | 88.1 | 79.2 | 94.1 | 84 | 58 | 69.0 | 58.0 | 78.7 | 84 | 59 | 70.2 | 59.3 | 79.7 |
|  |  | Placebo | 82 | 39 | 47.6 | 36.4 | 58.9 | 82 | 39 | 47.6 | 36.4 | 58.9 | 82 | 0 | 0.0 | 0.0 | 4.4 |
| Dose 2 | 18-49ys | HZ/su | 27 | 23 | 85.2 | 66.3 | 95.8 | 27 | 21 | 77.8 | 57.7 | 91.4 | 27 | 20 | 74.1 | 53.7 | 88.9 |
|  |  | Placebo | 30 | 24 | 80.0 | 61.4 | 92.3 | 30 | 24 | 80.0 | 61.4 | 92.3 | 30 | 4 | 13.3 | 3.8 | 30.7 |
|  | $\geq 50 y s$ | HZ/su | 69 | 55 | 79.7 | 68.3 | 88.4 | 69 | 51 | 73.9 | 61.9 | 83.7 | 69 | 33 | 47.8 | 35.6 | 60.2 |
|  |  | Placebo | 77 | 58 | 75.3 | 64.2 | 84.4 | 77 | 58 | 75.3 | 64.2 | 84.4 | 77 | 2 | 2.6 | 0.3 | 9.1 |
| Overall/dose | 18-49ys | HZ/su | 56 | 51 | 91.1 | 80.4 | 97.0 | 56 | 44 | 78.6 | 65.6 | 88.4 | 56 | 45 | 80.4 | 67.6 | 89.8 |
|  |  | Placebo | 60 | 41 | 68.3 | 55.0 | 79.7 | 60 | 40 | 66.7 | 53.3 | 78.3 | 60 | 8 | 13.3 | 5.9 | 24.6 |
|  | $\geq 50 y s$ | HZ/su | 153 | 129 | 84.3 | 77.6 | 89.7 | 153 | 109 | 71.2 | 63.4 | 78.3 | 153 | 92 | 60.1 | 51.9 | 67.9 |
|  |  | Placebo | 159 | 97 | 61.0 | 53.0 | 68.6 | 159 | 97 | 61.0 | 53.0 | 68.6 | 159 | 2 | 1.3 | 0.2 | 4.5 |
| Overall/subject | 18-49ys | HZ/su | 29 | 29 | 100 | 88.1 | 100 | 29 | 26 | 89.7 | 72.6 | 97.8 | 29 | 27 | 93.1 | 77.2 | 99.2 |
|  |  | Placebo | 30 | 25 | 83.3 | 65.3 | 94.4 | 30 | 25 | 83.3 | 65.3 | 94.4 | 30 | 7 | 23.3 | 9.9 | 42.3 |
|  | $\geq 50 y s$ | HZ/su | 84 | 76 | 90.5 | 82.1 | 95.8 | 84 | 69 | 82.1 | 72.3 | 89.6 | 84 | 63 | 75.0 | 64.4 | 83.8 |
|  |  | Placebo | 82 | 65 | 79.3 | 68.9 | 87.4 | 82 | 65 | 79.3 | 68.9 | 87.4 | 82 | 2 | 2.4 | 0.3 | 8.5 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.220 Incidence and nature of grade 3 symptoms (solicited and unsolicited) reported during the 7 -day (Days 0-6) post-vaccination period following each dose and overall by age strata (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 95\% Cl |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N |  | \% | LL | U |
| Dose 1 | 18-49ys | HZ/su | 29 | 6 | 20.7 | 8.0 | 39.7 | 29 | 6 | 20.7 | 8.0 | 39.7 | 29 | 3 | 10.3 | 2.2 | 27.4 |
|  |  | Placebo | 30 | 4 | 13.3 | 3.8 | 30.7 | 30 | 4 | 13.3 | 3.8 | 30.7 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 84 | 15 | 17.9 | 10.4 | 27.7 | 84 | 11 | 13.1 | 6.7 | 22.2 | 84 | 6 | 7.1 | 2.7 | 14.9 |
|  |  | Placebo | 82 | 9 | 11.0 | 5.1 | 19.8 | 82 | 9 | 11.0 | 5.1 | 19.8 | 82 | 0 | 0.0 | 0.0 | 4.4 |
| Dose 2 | 18-49ys | HZ/su | 27 | 6 | 22.2 | 8.6 | 42.3 | 27 | 5 | 18.5 | 6.3 | 38.1 | 27 |  | 3.7 | 0.1 | 19.0 |
|  |  | Placebo | 30 | 7 | 23.3 | 9.9 | 42.3 | 30 | 7 | 23.3 | 9.9 | 42.3 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 69 | 12 | 17.4 | 9.3 | 28.4 | 69 | 12 | 17.4 | 9.3 | 28.4 | 69 | 3 | 4.3 | 0.9 | 12.2 |
|  |  | Placebo | 77 | 5 | 6.5 | 2.1 | 14.5 | 77 | 5 | 6.5 | 2.1 | 14.5 | 77 | 0 | 0.0 | 0.0 | 4.7 |
| Overall/dose | 18-49ys | HZ/su | 56 | 12 | 21.4 | 11.6 | 34.4 | 56 | 11 | 19.6 | 10.2 | 32.4 | 56 | 4 | 7.1 | 2.0 | 17.3 |
|  |  | Placebo | 60 | 11 | 18.3 | 9.5 | 30.4 | 60 | 11 | 18.3 | 9.5 | 30.4 | 60 | 0 | 0.0 | 0.0 | 6.0 |
|  | $\geq 50 y s$ | HZ/su | 153 | 27 | 17.6 | 12.0 | 24.6 | 153 | 23 | 15.0 | 9.8 | 21.7 | 153 | 9 | 5.9 | 2.7 | 10.9 |
|  |  | Placebo | 159 | 14 | 8.8 | 4.9 | 14.3 | 159 | 14 | 8.8 | 4.9 | 14.3 | 159 | 0 | 0.0 | 0.0 | 2.3 |
| Overall/subject | 18-49ys | HZ/su | 29 | 9 | 31.0 | 15.3 | 50.8 | 29 | 9 | 31.0 | 15.3 | 50.8 | 29 | 3 | 10.3 | 2.2 | 27.4 |
|  |  | Placebo | 30 | 8 | 26.7 | 12.3 | 45.9 | 30 | 8 | 26.7 | 12.3 | 45.9 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 84 | 20 | 23.8 | 15.2 | 34.3 | 84 | 18 | 21.4 | 13.2 | 31.7 | 84 | 9 | 10.7 | 5.0 | 19.4 |
|  |  | Placebo | 82 | 13 | 15.9 | 8.7 | 25.6 | 82 | 13 | 15.9 | 8.7 | 25.6 | 82 | 0 | 0.0 | 0.0 | 4.4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered 95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.221 Incidence and nature of symptoms (solicited only) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | 18-49ys | HZ/su | 29 | 28 | 96.6 | 82.2 | 99.9 | 29 | 22 | 75.9 | 56.5 | 89.7 | 29 | 25 | 86.2 | 68.3 | 96. |
|  |  | Placebo | 30 | 16 | 53.3 | 34.3 | 71.7 | 30 | 15 | 50.0 | 31.3 | 68.7 | 30 | 3 | 10.0 | 2.1 | 26.5 |
|  | $\geq 50 y s$ | HZ/su | 79 | 72 | 91.1 | 82.6 | 96.4 | 79 | 55 | 69.6 | 58.2 | 79.5 | 79 | 59 | 74.7 | 63.6 | 83.8 |
|  |  | Placebo | 77 | 35 | 45.5 | 34.1 | 57.2 | 77 | 35 | 545.5 | 34.1 | 57.2 | 77 | 0 | 0.0 | 0.0 | 4.7 |
| Dose 2 | 18-49ys | HZ/su | 27 | 23 | 85.2 | 66.3 | 95.8 | 27 | 20 | 74.1 | 53.7 | 88.9 | 27 | 20 | 74.1 | 53.7 | 88. |
|  |  | Placebo | 29 | 20 | 69.0 | 49.2 | 84.7 | 29 | 20 | 69.0 | 49.2 | 84.7 | 29 | 4 | 13.8 | 3.9 | 31. |
|  | $\geq 50 y s$ | HZ/su | 67 | 48 | 71.6 | 59.3 | 82.0 | 66 | 43 | 65.2 | 52.4 | 76.5 | 67 | 33 | 49.3 | 36.8 | 61. |
|  |  | Placebo | 74 | 39 | 52.7 | 40.7 | 64.4 | 74 | 39 | 52.7 | 40.7 | 64.4 | 74 | 1 | 1.4 | 0.0 | 7.3 |
| Overall/dose | 18-49ys | HZ/su | 56 | 51 | 91.1 | 80.4 | 97.0 | 56 | 42 | 75.0 | 61.6 | 85.6 | 56 | 45 | 80.4 | 67.6 | 89.8 |
|  |  | Placebo | 59 | 36 | 61.0 | 47.4 | 73.5 | 59 | 35 | 59.3 | 45.7 | 71.9 | 59 | 7 | 11.9 | 4.9 | 22.9 |
|  | $\geq 50 y s$ | HZ/su | 146 | 120 | 82.2 | 75.0 | 88.0 | 145 | 98 | 67.6 | 59.3 | 75.1 | 146 | 92 | 63.0 | 54.6 | 70.8 |
|  |  | Placebo | 151 | 74 | 49.0 | 40.8 | 57.3 | 151 | 74 | 44.0 | 40.8 | 57.3 | 151 | 1 | 0.7 | 0.0 | 3.6 |
| Overall/subject | 18-49ys | HZ/su | 29 | 29 | 100 | 88.1 | 100 | 29 | 25 | 86.2 | 68.3 | 96.1 | 29 | 27 | 93.1 | 77.2 | 99.2 |
|  |  | Placebo | 30 | 22 | 73.3 | 54.1 | 87.7 | 30 | 22 | 73.3 | 54.1 | 87.7 | 30 | 6 | 20.0 | 7.7 | 38.6 |
|  | $\geq 50 y s$ | HZ/su | 79 | 74 | 93.7 | 85.8 | 97.9 | 79 |  | 278.5 | 67.8 | 86.9 | 79 | 63 | 79.7 | 69.2 | 88.0 |
|  |  | Placebo | 77 | 49 | 63.6 | 51.9 | 74.3 | 77 | 49 | 63.6 | 51.9 | 74.3 | 77 | 1 | 1.3 | 0.0 | 7.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.222 Incidence and nature of grade 3 symptoms (solicited only) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N |  | \% | LL | UL |
| Dose 1 | 18-49ys | HZ/su | 29 | 6 | 20.7 | 8.0 | 39.7 | 29 | 6 | 20.7 | 8.0 | 39.7 | 29 | 3 | 10.3 | 2.2 | 27.4 |
|  |  | Placebo | 30 | 4 | 13.3 | 3.8 | 30.7 | 30 | 4 | 13.3 | 3.8 | 30.7 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 79 | 13 | 16.5 | 9.1 | 26.5 | 79 | 9 | 11.4 | 5.3 | 20.5 | 79 | 6 | 7.6 | 2.8 | 15.8 |
|  |  | Placebo | 77 | 7 | 9.1 | 3.7 | 17.8 | 77 | 7 | 9.1 | 3.7 | 17.8 | 77 | 0 | 0.0 | 0.0 | 4.7 |
| Dose 2 | 18-49ys | HZ/su | 27 | 6 | 22.2 | 8.6 | 42.3 | 27 | 5 | 18.5 | 6.3 | 38.1 | 27 | 1 | 3.7 | 0.1 | 19.0 |
|  |  | Placebo | 29 | 6 | 20.7 | 8.0 | 39.7 | 29 | 6 | 20.7 | 8.0 | 39.7 | 29 | 0 | 0.0 | 0.0 | 11.9 |
|  | $\geq 50 y s$ | HZ/su | 67 | 10 | 14.9 | 7.4 | 25.7 | 66 | 10 | 015.2 | 7.5 | 26.1 | 67 | 3 | 4.5 | 0.9 | 12.5 |
|  |  | Placebo | 74 | 4 | 5.4 | 1.5 | 13.3 | 74 | 4 | 5.4 | 1.5 | 13.3 | 74 | 0 | 0.0 | 0.0 | 4.9 |
| Overall/dose | 18-49ys | HZ/su | 56 | 12 | 21.4 | 11.6 | 34.4 | 56 | 11 | 119.6 | 10.2 | 32.4 | 56 |  | 7.1 | 2.0 | 17.3 |
|  |  | Placebo | 59 | 10 | 16.9 | 8.4 | 29.0 | 59 | 10 | 16.9 | 8.4 | 29.0 | 59 | 0 | 0.0 | 0.0 | 6.1 |
|  | $\geq 50 y s$ | HZ/su | 146 | 23 | 15.8 | 10.3 | 22.7 | 145 | 19 | 913.1 | 8.1 | 19.7 | 146 | 9 | 6.2 | 2.9 | 11.4 |
|  |  | Placebo | 151 | 11 | 7.3 | 3.7 | 12.7 | 151 | 11 | 17.3 | 3.7 | 12.7 | 151 |  | 0.0 | 0.0 | 2.4 |
| Overall/subject | 18-49ys | HZ/su | 29 | 9 | 31.0 | 15.3 | 50.8 | 29 | 9 | 31.0 | 15.3 | 50.8 | 29 | 3 | 10.3 | 2.2 | 27.4 |
|  |  | Placebo | 30 | 7 | 23.3 | 9.9 | 42.3 | 30 | 7 | 23.3 | 9.9 | 42.3 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 79 | 17 | 21.5 | 13.1 | 32.2 | 79 | 15 | 519.0 | 11.0 | 29.4 | 79 | 9 | 11.4 | 5.3 | 20.5 |
|  |  | Placebo | 77 | 10 | 13.0 | 6.4 | 22.6 | 77 | 10 | 013.0 | 6.4 | 22.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered 95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.223 Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

|  |  | 18-49ys |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |
|  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |
| Symptom | Type | N | n | \% | LL | UL |  | n \% |  | UL | N | n | \% | LL | UL | N | n \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 29 | 24 | 82.8 | 64.2 | 94.2 | 30 | 26.7 | 0.8 | 822 | 79 | 55 | 69.6 | 58.2 | 79.5 | 77 | 00.0 | 0.0 | . 7 |
|  | Grade 2 or 3 | 29 | 10 | 34.5 | 17.9 | 54.3 | 30 | 00.0 | 0.0 | 011.6 | 79 | 15 | 19.0 | 11.0 | 29.4 | 77 | 00.0 | 0.0 | 4.7 |
|  | Grade 3 | 29 | 3 | 10.3 | 2.2 | 27.4 | 30 | 00.0 | 0.0 | 011.6 | 79 | 4 | 5.1 | 1.4 | 12.5 | 77 | 00.0 | 0.0 | 4.7 |
|  | Medical advice | 290 | 0 | 0.0 | 0.0 | 11.9 | 30 | 00.0 | 0.0 | 011.6 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 | 00.0 | 0.0 | 4.7 |
| Redness (mm) | All | 29 | 10 | 34.5 | 17.9 | 54.3 | 30 | 00.0 | 0.0 | 011.6 | 79 | 20 | 25.3 | 16.2 | 36.4 | 77 | 00.0 | 0.0 | 4.7 |
|  | $>50$ | 29 | 7 | 24.1 | 10.3 | 43.5 | 30 | 00.0 | 0.0 | 011.6 | 79 | 10 | 12.7 | 6.2 | 22.0 | 77 | 00.0 | 0.0 | 4.7 |
|  | >100 | 290 | 0 | 0.0 | 0.0 | 11.9 | 30 | 00.0 | 0.0 | 011.6 | 79 | 2 | 2.5 | 0.3 | 8.8 | 77 | 00.0 | 0.0 | 4.7 |
|  | Medical advice | 290 | 0 | 0.0 | 0.0 | 11.9 | 30 | 00.0 | 0.0 | 011.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 00.0 | 0.0 | 4.7 |
| Swelling (mm) | All | 29 | 6 | 20.7 | 8.0 | 39.7 | 30 | 13.3 | 0.1 | 117.2 | 79 | 8 | 10.1 | 4.5 | 19.0 | 77 | 00.0 | 0.0 | 4.7 |
|  | $>50$ | 29 | 3 | 10.3 | 2.2 | 27.4 | 30 | 00.0 | 0.0 | 011.6 | 79 | 5 | 6.3 | 2.1 | 14.2 | 77 | 00.0 | 0.0 | 4.7 |
|  | >100 | 290 | 0 | 0.0 | 0.0 | 11.9 | 30 | 00.0 | 0.0 | 011.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 00.0 | 0.0 | 4.7 |
|  | Medical advice | 290 | 0 | 0.0 | 0.0 | 11.9 | 30 | 00.0 | 0.0 | 011.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 00.0 | 0.0 | 4.7 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 27 | 18 | 66.7 | 46.0 | 83.5 | 29 | 4 13.8 | 3.9 | 931.7 | 67 | 31 | 46.3 | 34.0 | 58.9 | 74 | 11.4 | 0.0 | 7.3 |
|  | Grade 2 or 3 | 27 | 5 | 18.5 | 6.3 | 38.1 | 29 | 00.0 | 0.0 | 011.9 | 67 | 13 | 19.4 | 10.8 | 30.9 | 74 | 11.4 | 10.0 | 7.3 |
|  | Grade 3 | 27 | 1 | 3.7 | 0.1 | 19.0 | 29 | 00.0 | 0.0 | 011.9 | 67 | 3 | 4.5 | 0.9 | 12.5 | 74 | 00.0 | 0.0 | 4.9 |
|  | Medical advice | 270 | 0 | 0.0 | 0.0 | 12.8 | 29 | 90.0 | 0.0 | 011.9 | 67 | 0 | 0.0 | 0.0 | 5.4 | 74 | 00.0 | 0.0 | 4.9 |
| Redness (mm) | All | 27 | 8 | 29.6 | 13.8 | 50.2 | 29 | 90.0 | 0.0 | 011.9 | 67 | 10 | 14.9 | 7.4 | 25.7 | 74 | 00.0 | 0.0 | 4.9 |
|  | $>50$ | 27 | 3 | 11.1 | 2.4 | 29.2 | 29 | 00.0 | 0.0 | 011.9 | 67 | 4 | 6.0 | 1.7 | 14.6 | 74 | 00.0 | 0.0 | 4.9 |
|  | >100 | 270 | 0 | 0.0 | 0.0 | 12.8 | 29 | 00.0 | 0.0 | 011.9 | 67 | 0 | 0.0 | 0.0 | 5.4 | 74 | 00.0 | 0.0 | 4.9 |
|  | Medical advice | 270 | 0 | 0.0 | 0.0 | 12.8 | 29 | 90.0 | 0.0 | 011.9 | 67 | 0 | 0.0 | 0.0 | 5.4 | 74 | 00.0 | 0.0 | 4.9 |
| Swelling (mm) | All | 27 | 4 | 14.8 | 4.2 | 33.7 | 29 | 900.0 | 0.0 | 011.9 | 67 | 4 | 6.0 | 1.7 | 14.6 | 74 | 00.0 | 0.0 | 4.9 |
|  | >50 | 27 | 1 | 3.7 | 0.1 | 19.0 | 29 | 900.0 | 0.0 | 011.9 | 67 | 3 | 4.5 | 0.9 | 12.5 | 74 | 00.0 | 0.0 | 4.9 |
|  | >100 | 270 | 0 | 0.0 | 0.0 | 12.8 | 29 | 00.0 | 0.0 | 011.9 | 67 | 0 | 0.0 | 0.0 | 5.4 | 74 | 00.0 | 0.0 | 4.9 |
|  | Medical advice | 270 | 0 | 0.0 | 0.0 | 12.8 | 29 | 00.0 | 0.0 | 011.9 | 67 | 0 | 0.0 | 0.0 | 5.4 | 74 | 00.0 | 0.0 | 4.9 |

## Overall/dose

| Pain | All | 564 | 42 | 75.0 | 61.6 | 85.6 | 59 | 6 | 10.2 | 3.8 | 20.8 | 146 | 86 | 58.9 | 50.5 | 67.0 | 151 | 1 | 0.7 | 0.0 | 3.6 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Grade 2 or 3 | 561 | 15 | 26.8 | 15.8 | 40.3 | 59 | 0 | 0.0 | 0.0 | 6.1 | 146 | 28 | 19.2 | 13.1 | 26.5 | 151 | 1 | 0.7 | 0.0 | 3.6 |
|  | Grade 3 | 564 |  | 7.1 | 2.0 | 17.3 | 59 | 0 | 0.0 | 0.0 | 6.1 | 146 | 7 | 4.8 | 1.9 | 9.6 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | Medical advice | 560 |  | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 146 | 1 | 0.7 | 0.0 | 3.8 | 151 | 0 | 0.0 | 0.0 | 2.4 |
| Redness (mm) | All | 561 | 18 | 32.1 | 20.3 | 46.0 | 59 | 0 | 0.0 | 0.0 | 6.1 | 146 | 30 | 20.5 | 14.3 | 28.0 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | $>50$ | 561 | 10 | 17.9 | 8.9 | 30.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 146 | 14 | 9.6 | 5.3 | 15.6 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | >100 | 560 |  | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 146 | 2 | 1.4 | 0.2 | 4.9 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | Medical advice | 560 |  | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 146 | 0 | 0.0 | 0.0 | 2.5 | 151 | 0 | 0.0 | 0.0 | 2.4 |
| Swelling (mm) | All | 56 | 10 | 17.9 | 8.9 | 30.4 | 59 | 1 | 1.7 | 0.0 | 9.1 | 146 | 12 | 8.2 | 4.3 | 13.9 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | $>50$ | 564 |  | 7.1 | 2.0 | 17.3 | 59 | 0 | 0.0 | 0.0 | 6.1 | 146 | 8 | 5.5 | 2.4 | 10.5 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | >100 | 560 |  | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 146 | 0 | 0.0 | 0.0 | 2.5 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | Medical advice | 560 | 0 | 0.0 | 0.0 | 6.4 | 59 |  | 0.0 | 0.0 | 6.1 | 146 | 0 | 0.0 | 0.0 | 2.5 | 151 | O | 0.0 | 0.0 | 2.4 |
|  |  |  |  |  |  |  |  |  | sub |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | All | 29 | 26 | 89.7 | 72.6 | 97.8 | 30 | 6 | 20.0 | 7.7 | 38.6 | 79 | 60 | 75.9 | 65.0 | 84.9 | 77 | 1 | 1.3 | 0.0 | 7.0 |
|  | Grade 2 or 3 | 291 | 11 | 37.9 | 20.7 | 57.7 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 21 | 26.6 | 17.3 | 37.7 | 77 | 1 | 1.3 | 0.0 | 7.0 |
|  | Grade 3 | 293 |  | 10.3 | 2.2 | 27.4 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 7 | 8.9 | 3.6 | 17.4 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | Medical advice | 290 |  | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 | 0 | 0.0 | 0.0 | 4.7 |
| Redness (mm) | All | 291 | 13 | 44.8 | 26.4 | 64.3 | 30 |  | 0.0 | 0.0 | 11.6 | 79 | 24 | 30.4 | 20.5 | 41.8 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | $>50$ | 297 |  | 24.1 | 10.3 | 43.5 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 11 | 13.9 | 7.2 | 23.5 | 77 |  | 0.0 | 0.0 | 4.7 |
|  | >100 | 290 | 0 | 0.0 | 0.0 | 11.9 | 30 |  | 0.0 | 0.0 | 11.6 | 79 | 2 | 2.5 | 0.3 | 8.8 | 77 | 0 | 0.0 | 0.0 | 4.7 |


|  |  | 18-49ys |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  | Placebo |  |  |  |
|  |  | $95 \% \mathrm{Cl}$ |  |  |  |  | $95 \%$ Cl |  |  |  |  | $95 \%$ CI |  |  |  |  | 95\% Cl |  |  |
| Symptom | Type | N | n | \% | LL | UL N | N | n\% | LL U |  | N | n | \% | LL | UL | N | n\% | LL | UL |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.930 | 300 | 00.0 | 0.01 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 00.0 | 0.0 | 4.7 |
| Swelling (mm) | All | 29 |  | 24.1 | 10.3 | 43.530 | 301 | 13.3 | 0.11 | 17.2 | 79 | 10 | 12.7 | 6.2 | 22.0 | 77 | 00.0 | 0.0 | 4.7 |
|  | >50 | 29 |  | 13.8 | 3.9 | 31.730 | 30 | 00.0 | 0.01 | 11.6 | 79 | 6 | 7.6 | 2.8 | 15.8 | 77 | 00.0 | 0.0 | 4.7 |
|  | $>100$ | 29 |  | 0.0 | 0.0 | 11.930 | 30 | 00.0 | 0.01 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 00.0 | 0.0 | 4.7 |
|  | Medical advice | 29 |  | 0.0 | 0.0 | 11.930 | 30 | 00.0 | 0.01 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 00.0 | 0.0 | 4.7 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit
Table 8.224 Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  | 18-49ys |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 29 | 16 | 55.2 | 35.7 | 73.6 | 30 | 14 | 46.7 | 28.3 | 65.7 | 79 | 37 | 46.8 | 35.5 | 58.4 | 77 | 28 | 36.4 | 25.7 | 48.1 |
|  | Grade 2 or 3 | 29 | 9 | 31.0 | 15.3 | 50.8 | 305 | 5 | 16.7 | 5.6 | 34.7 | 79 | 20 | 25.3 | 16.2 | 36.4 | 77 | 10 | 13.0 | 6.4 | 22.6 |
|  | Grade 3 | 29 | 5 | 17.2 | 5.8 | 35.8 | 30 | 2 | 6.7 | 0.8 | 22.1 | 79 | 5 | 6.3 | 2.1 | 14.2 | 77 | 1 | 1.3 | 0.0 | 7.0 |
|  | Related | 29 | 7 | 24.1 | 10.3 | 43.5 | 305 | 5 | 16.7 | 5.6 | 34.7 | 79 | 6 | 7.6 | 2.8 | 15.8 | 77 | 5 | 6.5 | 2.1 | 14.5 |
|  | $\begin{aligned} & \text { Grade } 2 \\ & \text { or 3 } \\ & \text { Related } \\ & \hline \end{aligned}$ | 29 | 4 | 13.8 | 3.9 | 31.7 | 30 | 1 | 3.3 | 0.1 | 17.2 | 79 | 4 | 5.1 | 1.4 | 12.5 | 77 | 3 | 3.9 | 0.8 | 11.0 |
|  | Grade 3 <br> Related | 29 | 2 | 6.9 | 0.8 | 22.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
| Gastrointestinal symptoms | All | 29 | 8 | 27.6 | 12.7 | 47.2 | 30 | 6 | 20.0 | 7.7 | 38.6 | 79 | 24 | 30.4 | 20.5 | 41.8 | 77 | 15 | 19.5 | 11.3 | 30.1 |
|  | Grade 2 or 3 | 29 | 5 | 17.2 | 5.8 | 35.8 | 30 | 4 | 13.3 | 3.8 | 30.7 | 79 | 9 | 11.4 | 5.3 | 20.5 | 77 | 7 | 9.1 | 3.7 | 17.8 |
|  | Grade 3 | 29 | 1 | 3.4 | 0.1 | 17.8 | 30 | 2 | 6.7 | 0.8 | 22.1 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 | 3 | 3.9 | 0.8 | 11.0 |
|  | Related | 29 | 2 | 6.9 | 0.8 | 22.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 7 | 8.9 | 3.6 | 17.4 | 77 | 2 | 2.6 | 0.3 | 9.1 |
|  | Grade 2 or 3 <br> Related | 29 | 1 | 3.4 | 0.1 | 17.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 | 1 | 1.3 | 0.0 | 7.0 |
|  | Grade 3 <br> Related | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 1 | 1.3 | 0.0 | 7.0 |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 2 | 2.6 | 0.3 | 9.1 |

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|  |  | 18-49ys |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  | Placebo |  |  |  |  |
|  |  | $95 \%$ CI |  |  |  | $95 \%$ Cl |  |  |  |  | 95 \% CI |  |  |  | $95 \% \mathrm{Cl}$ |  |  |  |  |
| Symptom Headache | Type | N n | \% | LL | UL | N n | n \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | All | 299 | 31.0 | 15.3 | 50.8 | 309 | 930.0 | 14.7 | 49.4 | 79 | 17 | 21.5 | 13.1 | 32.2 | 77 | 14 | 18.2 | 10.3 | 328.6 |
|  | Grade 2 or 3 | 294 | 13.8 | 3.9 | 31.7 | 303 | 310.0 | 2.1 | 26.5 | 79 | 9 | 11.4 | 5.3 | 20.5 | 77 | 4 | 5.2 | 1.4 | 12.8 |
|  | Grade 3 | 291 | 3.4 | 0.1 | 17.8 | 300 | 00.0 | 0.0 | 11.6 | 79 | 2 | 2.5 | 0.3 | 8.8 | 77 | 1 | 1.3 | 0.0 | 7.0 |
|  | Related | 293 | 10.3 | 2.2 | 27.4 | 302 | 26.7 | 0.8 | 22.1 | 79 | 6 | 7.6 | 2.8 | 15.8 | 77 | 2 | 2.6 | 0.3 | 9.1 |
|  | $\begin{aligned} & \text { Grade 2 } \\ & \text { or 3 } \\ & \text { Related } \end{aligned}$ | 291 | 3.4 | 0.1 | 17.83 | 300 | 00.0 | 0.0 | 11.6 | 79 | 4 | 5.1 | 1.4 | 12.5 | 77 | 1 | 1.3 | 0.0 | 7.0 |
|  | Grade 3 | 291 | 3.4 | 0.1 | 17.8 | 300 | 00.0 | 0.0 | 11.6 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | Related |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Medical advice | 290 | 0.0 | 0.0 | 11.93 | 300 | 00.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
| Myalgia | All | 2914 | 48.3 | 29.4 | 67.5 | 303 | 310.0 | 2.1 | 26.5 | 79 | 35 | 44.3 | 33.1 | 55.9 | 77 |  | 18.2 | 10.3 | 28.6 |
|  | Grade 2 or 3 | 297 | 24.1 | 10.3 | 43.5 | 302 | 26.7 | 0.8 | 22.1 | 79 | 13 | 16.5 | 9.1 | 26.5 | 77 | 7 | 9.1 | 3.7 | 17.8 |
|  | Grade 3 | 294 | 13.8 | 3.9 | 31.7 | 302 | 26.7 | 0.8 | 22.1 | 79 | 4 | 5.1 | 1.4 | 12.5 | 77 | 1 | 1.3 | 0.0 | 7.0 |
|  | Related | 2910 | 34.5 | 17.9 | 54.3 | 300 | 00.0 | 0.0 | 11.6 | 79 | 14 | 17.7 | 10.0 | 27.97 | 77 | 3 | 3.9 | 0.8 | 11.0 |
|  | $\begin{aligned} & \text { Grade 2 } \\ & \text { or } 3 \\ & \text { Related } \\ & \hline \end{aligned}$ | 295 | 17.2 | 5.8 | 35.83 | 300 | 00.0 | 0.0 | 11.6 | 79 | 8 | 10.1 | 4.5 | 19.0 | 77 | 2 | 2.6 | 0.3 | 9.1 |
|  | Grade 3 Related | 293 | 10.3 | 2.2 | 27.4 | 300 | 00.0 | 0.0 | 11.6 | 79 | 4 | 5.1 | 1.4 | 12.5 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | Medical advice | 290 | 0.0 | 0.0 | 11.93 | 300 | 00.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
| Shivering | All | 298 | 27.6 | 12.7 | 47.23 | 305 | 516.7 | 5.6 | 34.7 | 79 | 18 | 22.8 | 14.1 | 33.6 | 77 | 8 | 10.4 | 4.6 | 19.4 |
|  | Grade 2 <br> or 3 | 292 | 6.9 | 0.8 | 22.83 | 300 | 00.0 | 0.0 | 11.6 | 79 | 6 | 7.6 | 2.8 | 15.8 | 77 | 6 | 7.8 | 2.9 | 16.2 |
|  | Grade 3 | 292 | 6.9 | 0.8 | 22.8 | 300 | 00.0 | 0.0 | 11.6 | 79 | 3 | 3.8 | 0.8 | 10.7 | 77 | 2 | 2.6 | 0.3 | 9.1 |
|  | Related | 295 | 17.2 | 5.8 | 35.8 | 301 | 13.3 | 0.1 | 17.2 | 79 | 6 | 7.6 | 2.8 | 15.87 | 77 | 3 | 3.9 | 0.8 | 11.0 |
|  | $\begin{aligned} & \text { Grade 2 } \\ & \text { or 3 } \\ & \text { Related } \end{aligned}$ | 292 | 6.9 | 0.8 | 22.83 | 300 | 00.0 | 0.0 | 11.6 | 79 | 4 | 5.1 | 1.4 | 12.5 | 77 | 2 | 2.6 | 0.3 | 9.1 |
|  | Grade 3 Related | 292 | 6.9 | 0.8 | 22.83 |  | 00.0 | 0.0 | 11.6 | 79 | 2 | 2.5 | 0.3 | 8.8 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | Medical advice | 290 | 0.0 | 0.0 | 11.93 | 300 | 00.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
| Temperature/(*) <br> $\left({ }^{\circ} \mathrm{C}\right)$ | All | 294 | 13.8 | 3.9 | 31.73 | 300 | 00.0 | 0.0 | 11.6 | 79 | 9 | 11.4 | 5.3 | 20.57 | 77 | 4 | 5.2 | 1.4 | 12.8 |
|  | $\geq 37.5$ | 294 | 13.8 | 3.9 | 31.7 | 300 | 00.0 | 0.0 | 11.6 | 79 | 9 | 11.4 | 5.3 | 20.5 | 77 | 4 | 5.2 | 1.4 | 12.8 |
|  | $>38.0$ | 290 | 0.0 | 0.0 | 11.93 | 300 | 00.0 | 0.0 | 11.6 | 79 | 2 | 2.5 | 0.3 | 8.8 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | $>38.5$ | 290 | 0.0 | 0.0 | 11.93 | 300 | 00.0 | 0.0 | 11.6 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | $>39.0$ | 290 | 0.0 | 0.0 | 11.93 | 300 | 00.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | >39.5 | 290 | 0.0 | 0.0 | 11.93 | 300 | 00.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | $>40.0$ | 290 | 0.0 | 0.0 | 11.93 | 300 | 00.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | Related | 294 | 13.8 | B 3.9 | 31.73 | 300 | 00.0 | 0.0 | 11.6 | 79 | 7 | 8.9 | 3.6 | 17.4 | 77 | 1 | 1.3 | 0.0 | 7.0 |
|  | $>38.0$ Related | 290 | 0.0 | 0.0 | 11.93 | 300 | 00.0 | 0.0 | 11.6 | 79 | 2 | 2.5 | 0.3 | 8.8 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | $>39.0$ <br> Related | 290 | 0.0 | 0.0 | 11.93 |  | 00.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | Medical advice | 290 | 0.0 | 0.0 | 11.93 | 300 | 00.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 1 | 1.3 | 0.0 | 7.0 |

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|  |  | 18-49ys |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  | \% $95 \%$ Cl |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 3 | 270 | 0 | 0.0 | 0.0 | 12.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 66 | 2 | 3.0 | 0.4 | 10.5 | 74 | 1 | 1.4 | 0.0 | 7.3 |
|  | Related | 27 | 1 | 3.7 | 0.1 | 19.0 | 29 | 1 | 3.4 | 0.1 | 17.8 | 66 | 5 | 7.6 | 2.5 | 16.8 | 74 | 3 | 4.1 | 0.8 | 11.4 |
|  | Grade 2 or 3 <br> Related | 27 |  | 0.0 | 0.0 | 12.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 66 | 3 | 4.5 | 0.9 | 12.7 | 74 | 0 | 0.0 | 0.0 | 4.9 |
|  | Grade 3 Related | 27 | 0 | 0.0 | 0.0 | 12.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 66 | 1 | 1.5 | 0.0 | 8.2 | 74 | 0 | 0.0 | 0.0 | 4.9 |
|  | Medical advice | 27 | 0 | 0.0 | 0.0 | 12.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 66 | 0 | 0.0 | 0.0 | 5.4 | 74 | 0 | 0.0 | 0.0 | 4.9 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 27 |  | 14.8 | 4.2 | 33.7 | 29 | 1 | 3.4 | 0.1 | 17.8 | 66 | 4 | 6.1 | 1.7 | 14.8 | 74 | 0 | 0.0 | 0.0 | 4.9 |
|  | $\geq 37.5$ | 27 | 4 | 14.8 | 4.2 | 33.7 | 29 | 1 | 3.4 | 0.1 | 17.8 | 66 | 4 | 6.1 | 1.7 | 14.8 | 74 | 0 | 0.0 | 0.0 | 4.9 |
|  | >38.0 | 27 | 1 | 3.7 | 0.1 | 19.0 | 29 | 1 | 3.4 | 0.1 | 17.8 | 66 | O | 0.0 | 0.0 | 5.4 | 74 | 0 | 0.0 | 0.0 | 4.9 |
|  | $>38.5$ | 270 | 0 | 0.0 | 0.0 | 12.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 66 | 0 | 0.0 | 0.0 | 5.4 | 74 | 0 | 0.0 | 0.0 | 4.9 |
|  | $>39.0$ | 270 | 0 | 0.0 | 0.0 | 12.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 66 | 0 | 0.0 | 0.0 | 5.4 | 74 | 0 | 0.0 | 0.0 | 4.9 |
|  | >39.5 | 270 | 0 | 0.0 | 0.0 | 12.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 66 | 0 | 0.0 | 0.0 | 5.4 | 74 | 0 | 0.0 | 0.0 | 4.9 |
|  | >40.0 | 27 | 0 | 0.0 | 0.0 | 12.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 66 | 0 | 0.0 | 0.0 | 5.4 | 74 | 0 | 0.0 | 0.0 | 4.9 |
|  | Related | 27 |  | 7.4 | 0.9 | 24.3 | 29 | 0 | 0.0 | 0.0 | 11.9 | 66 | 2 | 3.0 | 0.4 | 10.5 | 74 | 0 | 0.0 | 0.0 | 4.9 |
|  | $\begin{array}{\|l\|} \hline>38.0 \\ \text { Related } \end{array}$ | 27 |  | 3.7 | 0.1 | 19.0 | 29 | 0 | 0.0 | 0.0 | 11.9 | 66 | 0 | 0.0 | 0.0 | 5.4 | 74 | 0 | 0.0 | 0.0 | 4.9 |
|  | $\begin{aligned} & >39.0 \\ & \text { Related } \end{aligned}$ | 27 | 0 | 0.0 | 0.0 | 12.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 66 | 0 | 0.0 | 0.0 | 5.4 | 74 | 0 | 0.0 | 0.0 | 4.9 |
|  | Medical advice | 27 |  | 0.0 | 0.0 | 12.8 | 29 | 0 | 0.0 | 0.0 | 11.9 | 66 | 0 | 0.0 | 0.0 | 5.4 | 74 | 0 | 0.0 | 0.0 | 4.9 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 56 | 32 | 57.1 | 43.2 | 70.3 | 59 | 32 | 54.2 | 40.8 | 67.3 | 145 | 75 | 51.7 | 43.3 | 60.1 | 151 | 66 | 43.7 | 35.7 | 52.0 |
|  | Grade 2 or 3 | 56 | 17 | 30.4 | 18.8 | 44.1 | 59 | 13 | 22.0 | 12.3 | 34.7 | 145 | 39 | 26.9 | 19.9 | 34.9 | 151 | 31 | 20.5 | 14.4 | 27.9 |
|  | Grade 3 | 56 | 9 | 16.1 | 7.6 | 28.3 | 59 | 5 | 8.5 | 2.8 | 18.7 | 145 | 10 | 6.9 | 3.4 | 12.3 | 151 | 4 | 2.6 | 0.7 | 6.6 |
|  | Related | 56 | 10 | 17.9 | 8.9 | 30.4 | 59 | 9 | 15.3 | 7.2 | 27.0 | 145 | 9 | 6.2 | 2.9 | 11.5 | 151 | 9 | 6.0 | 2.8 | 11.0 |
|  | Grade 2 or 3 <br> Related | 56 | 5 | 8.9 | 3.0 | 19.6 | 59 | 2 | 3.4 | 0.4 | 11.7 | 145 | 5 | 3.4 | 1.1 | 7.9 | 151 | 6 | 4.0 | 1.5 | 8.4 |
|  | Grade 3 <br> Related | 56 |  | 3.6 | 0.4 | 12.3 | 59 | 1 | 1.7 | 0.0 | 9.1 | 145 | 1 | 0.7 | 0.0 | 3.8 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | Medical advice | 56 | 0 | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 1 | 0.7 | 0.0 | 3.8 | 151 | 1 | 0.7 | 0.0 | 3.6 |
| Gastrointestinal symptoms | All | 56 | 22 | 39.3 | 26.5 | 53.2 | 59 | 19 | 32.2 | 20.6 | 45.6 | 145 | 48 | 33.1 | 25.5 | 41.4 | 151 | 40 | 26.5 | 19.6 | 34.3 |
|  | Grade 2 or 3 | 56 | 14 | 25.0 | 14.4 | 38.4 | 59 | 10 | 16.9 | 8.4 | 29.0 | 145 | 19 | 13.1 | 8.1 | 19.7 | 151 | 16 | 10.6 | 6.2 | 16.6 |
|  | Grade 3 | 56 | 3 | 5.4 | 1.1 | 14.9 | 59 | 4 | 6.8 | 1.9 | 16.5 | 145 | 4 | 2.8 | 0.8 | 6.9 | 151 | 4 | 2.6 | 0.7 | 6.6 |
|  | Related | 56 | 5 | 8.9 | 3.0 | 19.6 | 59 | 1 | 1.7 | 0.0 | 9.1 | 145 | 10 | 6.9 | 3.4 | 12.3 | 151 | 3 | 2.0 | 0.4 | 5.7 |
|  | Grade 2 or 3 <br> Related | 56 |  | 3.6 | 0.4 | 12.3 | 59 | 1 | 1.7 | 0.0 | 9.1 | 145 | 2 | 1.4 | 0.2 | 4.9 | 151 | 2 | 1.3 | 0.2 | 4.7 |
|  | Grade 3 Related | 56 |  | 1.8 | 0.0 | 9.6 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 1 | 0.7 | 0.0 | 3.6 |
|  | Medical advice | 56 | 0 | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 1 | 0.7 | 0.0 | 3.8 | 151 | 2 | 1.3 | 0.2 | 4.7 |
| Headache | All | 56 | 18 | 32.1 | 20.3 | 46.0 | 59 | 21 | 135.6 | 23.6 | 49.1 | 145 | 37 | 25.5 | 18.6 | 33.4 | 151 | 26 | 17.2 | 11.6 | 24.2 |
|  | Grade 2 or 3 | 56 |  | 14.3 | 6.4 | 26.2 | 59 | 6 | 10.2 | 3.8 | 20.8 | 145 | 19 | 13.1 | 8.1 | 19.7 | 151 | 8 | 5.3 | 2.3 | 10.2 |

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|  |  | 18-49ys |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 3 | 56 | 2 | 3.6 | 0.4 | 12.3 | 59 | 2 | 3.4 | 0.4 | 11.7 | 145 | 4 | 2.8 | 0.8 | 6.9 | 151 | 1 | 0.7 | 0.0 | 3.6 |
|  | Related | 56 |  | 7.1 | 2.0 | 17.3 | 59 | 2 | 3.4 | 0.4 | 11.7 | 145 | 12 | 8.3 | 4.3 | 14.0 | 151 | 4 | 2.6 | 0.7 | 6.6 |
|  | Grade 2 or 3 <br> Related | 56 | 2 | 3.6 | 0.4 | 12.3 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 7 | 4.8 | 2.0 | 9.7 | 151 | 2 | 1.3 | 0.2 | 4.7 |
|  | Grade 3 Related | 56 | 1 | 1.8 | 0.0 | 9.6 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 1 | 0.7 | 0.0 | 3.8 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | Medical advice | 56 | 1 | 1.8 | 0.0 | 9.6 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 0 | 0.0 | 0.0 | 2.4 |
| Myalgia | All | 56 | 23 | 41.1 | 28.1 | 55.0 | 59 | 9 | 15.3 | 7.2 | 27.0 | 145 | 56 | 38.6 | 30.7 | 47.1 | 151 | 30 | 19.9 | 13.8 | 27.1 |
|  | Grade 2 or 3 | 56 | 10 | 17.9 | 8.9 | 30.4 | 59 | 5 | 8.5 | 2.8 | 18.7 | 145 | 24 | 16.6 | 10.9 | 23.6 | 151 | 16 | 10.6 | 6.2 | 16.6 |
|  | Grade 3 | 56 | 4 | 7.1 | 2.0 | 17.3 | 59 | 3 | 5.1 | 1.1 | 14.1 | 145 | 7 | 4.8 | 2.0 | 9.7 | 151 | 1 | 0.7 | 0.0 | 3.6 |
|  | Related | 56 | 15 | 26.8 | 15.8 | 40.3 | 59 | 1 | 1.7 | 0.0 | 9.1 | 145 | 22 | 15.2 | 9.8 | 22.1 | 151 | 6 | 4.0 | 1.5 | 8.4 |
|  | Grade 2 or 3 <br> Related | 56 | 6 | 10.7 | 4.0 | 21.9 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 13 | 9.0 | 4.9 | 14.8 | 151 | 4 | 2.6 | 0.7 | 6.6 |
|  | Grade 3 Related | 56 |  | 5.4 | 1.1 | 14.9 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 4 | 2.8 | 0.8 | 6.9 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | Medical advice | 56 | 0 | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 0 | 0.0 | 0.0 | 2.4 |
| Shivering | All | 56 | 13 | 23.2 | 13.0 | 36.4 | 59 | 13 | 22.0 | 12.3 | 34.7 | 145 | 31 | 21.4 | 15.0 | 29.0 | 151 | 17 | 11.3 | 6.7 | 17.4 |
|  | Grade 2 or 3 | 56 | 4 | 7.1 | 2.0 | 17.3 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 13 | 9.0 | 4.9 | 14.8 | 151 | 7 | 4.6 | 1.9 | 9.3 |
|  | Grade 3 | 56 | 2 | 3.6 | 0.4 | 12.3 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 5 | 3.4 | 1.1 | 7.9 | 151 | 3 | 2.0 | 0.4 | 5.7 |
|  | Related | 56 |  | 10.7 | 4.0 | 21.9 | 59 | 2 | 3.4 | 0.4 | 11.7 | 145 | 11 | 7.6 | 3.8 | 13.2 | 151 | 6 | 4.0 | 1.5 | 8.4 |
|  | Grade 2 or 3 <br> Related | 56 | 2 | 3.6 | 0.4 | 12.3 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 7 | 4.8 | 2.0 | 9.7 | 151 | 2 | 1.3 | 0.2 | 4.7 |
|  | Grade 3 <br> Related | 56 | 2 | 3.6 | 0.4 | 12.3 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 3 | 2.1 | 0.4 | 5.9 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | Medical advice | 56 | 0 | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 0 | 0.0 | 0.0 | 2.4 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 56 | 8 | 14.3 | 6.4 | 26.2 | 59 | 1 | 1.7 | 0.0 | 9.1 | 145 | 13 | 9.0 | 4.9 | 14.8 | 151 | 4 | 2.6 | 0.7 | 6.6 |
|  | $\geq 37.5$ | 56 | 8 | 14.3 | 6.4 | 26.2 | 59 | 1 | 1.7 | 0.0 | 9.1 | 145 | 13 | 9.0 | 4.9 | 14.8 | 151 |  | 2.6 | 0.7 | 6.6 |
|  | >38.0 | 56 | 1 | 1.8 | 0.0 | 9.6 | 59 | 1 | 1.7 | 0.0 | 9.1 | 145 | 2 | 1.4 | 0.2 | 4.9 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | $>38.5$ | 56 | 0 | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 1 | 0.7 | 0.0 | 3.8 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | $>39.0$ | 56 | 0 | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | >39.5 | 56 | 0 | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | >40.0 | 56 | 0 | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | Related | 56 | 6 | 10.7 | 4.0 | 21.9 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 9 | 6.2 | 2.9 | 11.5 | 151 | 1 | 0.7 | 0.0 | 3.6 |
|  | $\begin{aligned} & \hline>38.0 \\ & \text { Related } \end{aligned}$ | 56 | 1 | 1.8 | 0.0 | 9.6 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 2 | 1.4 | 0.2 | 4.9 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | $>39.0$ <br> Related | 56 |  | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | Medical advice | 56 |  | 0.0 | 0.0 | 6.4 | 59 | 0 | 0.0 | 0.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 1 | 0.7 | 0.0 | 3.6 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | All | 29 | 22 | 75.9 | 56.5 | 89.7 | 30 | 20 | 66.7 | 47.2 | 82.7 | 79 | 52 | 65.8 | 54.3 | 76.1 | 77 | 46 | 59.7 | 47.9 | 70.8 |
|  | Grade 2 or 3 | 29 | 13 | 44.8 | 26.4 | 64.3 | 30 | 11 | 1136.7 | 19.9 | 56.1 | 79 | 30 | 38.0 | 27.3 | 49.6 | 77 | 25 | 32.5 | 22.2 | 44.1 |
|  | Grade 3 | 29 | 8 | 27.6 | 12.7 | 47.2 | 30 | 5 | 16.7 | 5.6 | 34.7 | 79 | 8 | 10.1 | 4.5 | 19.0 | 77 | 3 | 3.9 | 0.8 | 11.0 |

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|  |  | 18-49ys |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Related | 29 | 9 | 31.0 | 15.3 | 50.8 | 30 | 6 | 20.0 | 7.7 | 38.6 | 79 | 8 | 10.1 | 4.5 | 19.0 | 77 | 8 | 10.4 | 4.6 | 19.4 |
|  | Grade 2 or 3 <br> Related | 29 | 5 | 17.2 | 5.8 | 35.8 | 30 | 2 | 6.7 | 0.8 | 22.1 | 79 | 5 | 6.3 | 2.1 | 14.2 | 77 | 6 | 7.8 | 2.9 | 16.2 |
|  | Grade 3 <br> Related | 29 | 2 | 6.9 | 0.8 | 22.8 | 30 | 1 | 3.3 | 0.1 | 17.2 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 | 1 | 1.3 | 0.0 | 7.0 |
| Gastrointestinal symptoms | All | 29 | 16 | 55.2 | 35.7 | 73.6 | 30 | 16 | 53.3 | 34.3 | 71.7 | 79 | 32 | 40.5 | 29.6 | 52.1 | 77 | 32 | 41.6 | 30.4 | 53.4 |
|  | Grade 2 or 3 | 29 | 10 | 34.5 | 17.9 | 54.3 | 30 | 8 | 26.7 | 12.3 | 45.9 | 79 | 14 | 17.7 | 10.0 | 27.9 | 77 | 13 | 16.9 | 9.3 | 27.1 |
|  | Grade 3 | 29 | 3 | 10.3 | 2.2 | 27.4 | 30 | 3 | 10.0 | 2.1 | 26.5 | 79 | 3 | 3.8 | 0.8 | 10.7 | 77 | 4 | 5.2 | 1.4 | 12.8 |
|  | Related | 29 | 4 | 13.8 | 3.9 | 31.7 | 30 | 1 | 3.3 | 0.1 | 17.2 | 79 | 7 | 8.9 | 3.6 | 17.4 | 77 | 2 | 2.6 | 0.3 | 9.1 |
|  | Grade 2 or 3 <br> Related | 29 | 1 | 3.4 | 0.1 | 17.8 | 30 | 1 | 3.3 | 0.1 | 17.2 | 79 | 2 | 2.5 | 0.3 | 8.8 | 77 | 2 | 2.6 | 0.3 | 9.1 |
|  | Grade 3 <br> Related | 29 | 1 | 3.4 | 0.1 | 17.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 1 | 1.3 | 0.0 | 7.0 |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 | 2 | 2.6 | 0.3 | 9.1 |
| Headache | All | 29 | 14 | 48.3 | 29.4 | 67.5 | 30 | 15 | 50.0 | 31.3 | 68.7 | 79 | 27 | 34.2 | 23.9 | 45.7 | 77 | 23 | 29.9 | 20.0 | 41.4 |
|  | Grade 2 or 3 | 29 | 7 | 24.1 | 10.3 | 43.5 | 30 | 6 | 20.0 | 7.7 | 38.6 | 79 | 14 | 17.7 | 10.0 | 27.9 | 77 | 7 | 9.1 | 3.7 | 17.8 |
|  | Grade 3 | 29 | 2 | 6.9 | 0.8 | 22.8 | 30 | 2 | 6.7 | 0.8 | 22.1 | 79 | 4 | 5.1 | 1.4 | 12.5 | 77 | 1 | 1.3 | 0.0 | 7.0 |
|  | Related | 29 | 4 | 13.8 | 3.9 | 31.7 | 30 | 2 | 6.7 | 0.8 | 22.1 | 79 | 11 | 13.9 | 7.2 | 23.5 | 77 | 4 | 5.2 | 1.4 | 12.8 |
|  | Grade 2 or 3 <br> Related | 29 | 2 | 6.9 | 0.8 | 22.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 6 | 7.6 | 2.8 | 15.8 | 77 | 2 | 2.6 | 0.3 | 9.1 |
|  | Grade 3 Related | 29 | 1 | 3.4 | 0.1 | 17.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | Medical advice | 29 | 1 | 3.4 | 0.1 | 17.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
| Myalgia | All | 29 | 16 | 55.2 | 35.7 | 73.6 | 30 | 7 | 23.3 | 9.9 | 42.3 | 79 | 42 | 53.2 | 41.6 | 64.5 | 77 | 23 | 29.9 | 20.0 | 41.4 |
|  | Grade 2 or 3 | 29 | 10 | 34.5 | 17.9 | 54.3 | 30 | 4 | 13.3 | 3.8 | 30.7 | 79 | 19 | 24.1 | 15.1 | 35.0 | 77 | 14 | 18.2 | 10.3 | 28.6 |
|  | Grade 3 | 29 | 4 | 13.8 | 3.9 | 31.7 | 30 | 3 | 10.0 | 2.1 | 26.5 | 79 | 7 | 8.9 | 3.6 | 17.4 | 77 | 1 | 1.3 | 0.0 | 7.0 |
|  | Related | 29 | 12 | 41.4 | 23.5 | 61.1 | 30 | 1 | 3.3 | 0.1 | 17.2 | 79 | 17 | 21.5 | 13.1 | 32.2 | 77 | 4 | 5.2 | 1.4 | 12.8 |
|  | Grade 2 or 3 <br> Related | 29 | 6 | 20.7 | 8.0 | 39.7 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 10 | 12.7 | 6.2 | 22.0 | 77 | 4 | 5.2 | 1.4 | 12.8 |
|  | Grade 3 Related | 29 | 3 | 10.3 | 2.2 | 27.4 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 4 | 5.1 | 1.4 | 12.5 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
| Shivering | All | 29 | 12 | 41.4 | 23.5 | 61.1 | 30 | 10 | 033.3 | 17.3 | 52.8 | 79 | 25 | 31.6 | 21.6 | 43.1 | 77 | 15 | 19.5 | 11.3 | 30.1 |
|  | Grade 2 or 3 | 29 | 4 | 13.8 | 3.9 | 31.7 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 9 | 11.4 | 5.3 | 20.5 | 77 | 7 | 9.1 | 3.7 | 17.8 |
|  | Grade 3 | 29 | 2 | 6.9 | 0.8 | 22.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 3 | 3.8 | 0.8 | 10.7 | 77 | 3 | 3.9 | 0.8 | 11.0 |
|  | Related | 29 | 6 | 20.7 | 8.0 | 39.7 | 30 | 1 | 3.3 | 0.1 | 17.2 | 79 | 9 | 11.4 | 5.3 | 20.5 | 77 | 4 | 5.2 | 1.4 | 12.8 |
|  | Grade 2 or 3 <br> Related | 29 |  | 6.9 | 0.8 | 22.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 5 | 6.3 | 2.1 | 14.2 | 77 | 2 | 2.6 | 0.3 | 9.1 |

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Report Final

|  |  | 18-49ys |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  | 95 \% CI |  |  |  |  |  |  |  | 95 \% CI |  |
| Symptom | Type | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
|  | Grade 3 Related | 29 | 2 | 6.9 | 0.8 | 22.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 2 | 2.5 | 0.3 | 8.8 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
| $\begin{aligned} & \text { Temperature/(*) } \\ & \left({ }^{\circ} \mathrm{C}\right) \end{aligned}$ | All | 29 | 7 | 24.1 | 10.3 | 43.5 | 30 | 1 | 3.3 | 0.1 | 17.2 | 79 | 13 | 16.5 | 9.1 | 26.5 | 77 | 4 | 5.2 | 1.4 | 12.8 |
|  | $\geq 37.5$ | 29 | 7 | 24.1 | 10.3 | 43.5 | 30 | 1 | 3.3 | 0.1 | 17.2 | 79 | 13 | 16.5 | 9.1 | 26.5 | 77 | 4 | 5.2 | 1.4 | 12.8 |
|  | >38.0 | 29 | 1 | 3.4 | 0.1 | 17.8 | 30 | 1 | 3.3 | 0.1 | 17.2 | 79 | 2 | 2.5 | 0.3 | 8.8 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | >38.5 | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | >39.0 | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | >39.5 | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | >40.0 | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | Related | 29 | 5 | 17.2 | 5.8 | 35.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 9 | 11.4 | 5.3 | 20.5 | 77 | 1 | 1.3 | 0.0 | 7.0 |
|  | $\begin{array}{\|l\|} \hline>38.0 \\ \text { Related } \end{array}$ | 29 | 1 | 3.4 | 0.1 | 17.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 2 | 2.5 | 0.3 | 8.8 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | $\begin{aligned} & \hline>39.0 \\ & \text { Related } \\ & \hline \end{aligned}$ | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 0 | 0.0 | 0.0 | 4.7 |
|  | Medical advice | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 1 | 1.3 | 0.0 | 7.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit
$\left(^{*}\right)=$ Temperature is measured by oral, axillary or tympanic routes
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for oral, axillary or tympanic route

Table 8.225 Number and percentage of subjects who reported temperature by half degree measured via oral route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  | 18-49ys |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |
|  |  | 95 \% Cl |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |
| Symptom | Type | N | n \% | \% | LL UL |  | n $\%$ | \% L | LL | UL | N |  | \% | LL | UL | N | n \% |  | LL UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 29 |  | 6.9 | 0.822 .8 | 30 | O10. | 0.00 | 0.01 | 11.6 | 79 | 2 | 2.5 | 0.3 | 8.8 | 77 | 11.3 | . 30.0 | 0.07 .0 |
|  | $\geq 35.5$ | 29 | 26. | 6.9 | 0.822 .8 | 30 | 00 | 0.00 | 0.0 | 11.6 | 79 | 2 | 2.5 | 0.3 | 8.8 | 77 | 11.3 | . 30.0 | 0.07 .0 |
|  | >36.0 | 29 | 26. | 6.9 | 0.822 .8 | 30 | 00 | 0.00 | 0.0 | 11.6 | 679 | 2 | 2.5 | 0.3 | 8.8 | 77 | 11.3 | . 30.0 | 0.07 .0 |
|  | >36.5 | 29 | 26. | 6.9 | 0.822 .8 | 30 | 00 | 0.00 | 0.0 | 11.6 | 679 | 2 | 2.5 | 0.3 | 8.8 | 77 | 11.3 | . 30.0 | 0.07 .0 |
|  | >37.0 | 29 |  | 6.9 | 0.822 .8 | 30 | 00 | 0.00 | 0.0 | 11.6 | 679 | 2 | 2.5 | 0.3 | 8.8 | 77 | 11.3 | . 30.0 | 0.07 .0 |
|  | >37.5 | 29 |  | 3.4 | 0.117 .8 | 30 | 00 | 0.00 | 0.0 | 11.6 | 679 | 0 | 0.0 | 0.0 | 4.6 | 77 | 11.3 | . 30.0 | 0.07 .0 |
|  | >38.0 | 29 |  | 0.0 | 0.011 .9 | 30 | 000 | 0.00 | 0.0 | 11.6 | 679 | 0 | 0.0 | 0.0 | 4.6 | 77 | 00.0 | . 00.0 | 0.04 .7 |
|  | >38.5 | 29 |  | 0.0 | 0.011 .9 | 30 | 00 | 0.00 | 0.0 | 11.6 | 679 | 0 | 0.0 | 0.0 | 4.6 | 77 | 00.0 |  | 0.04 .7 |
|  | >39.0 | 29 | 00. | 0.0 | 0.011 .9 | 30 | 00 | 0.00 | 0.0 | 11.6 | 79 |  | 0.0 | 0.0 | 4.6 | 77 | 00.0 |  | 0.04 .7 |
|  | >39.5 | 29 | 00. | 0.0 | 0.011 .9 | 30 | 00 | 0.00 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 00.0 | . 0.0 | 0.04 .7 |
|  | >40.0 | 29 |  | 0.0 | 0.011 .9 | 30 | 000 | 0.00 | 0.01 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 00.0 | .0 0.0 | 0.04 .7 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All |  | 27. | 7.4 | 0.924 .3 | 29 | 900 | 0.00 | 0.0 | 11.9 | 66 | 1 | 1.5 | 0.0 | 8.2 | 74 | 00.0 |  | 0.04 .9 |
|  | $\geq 35.5$ |  |  | 7.4 | 0.924 .3 | 29 | 90 | 0.00 | 0.0 | 11.9 | 66 | 1 | 1.5 | 0.0 | 8.2 | 74 | 00.0 | . 0.0 | 0.04 .9 |
|  | >36.0 |  |  | 7.4 | 0.924 .3 | 29 | 90 | 0.00 | 0.0 | 11.9 | 66 | 1 | 1.5 | 0.0 | 8.2 | 74 | 00.0 | . 0.0 | 0.04 .9 |
|  | >36.5 |  |  | 7.4 | 0.924 .3 | 29 | 00 | 0.00 | 0.0 | 11.9 | 66 | 1 | 1.5 | 0.0 | 8.2 | 74 | 00.0 |  | 0.04 .9 |
|  | >37.0 |  |  | 7.4 | 0.924 .3 | 29 | 90 | 0.00 | 0.0 | 11.9 | 66 |  | 1.5 | 0.0 | 8.2 | 74 | 00.0 |  | 0.04 .9 |
|  | >37.5 |  |  | 7.4 | 0.924 .3 | 29 | 90 | 0.00 | 0.0 | 11.9 | 66 |  | 1.5 | 0.0 | 8.2 | 74 | 00.0 |  | 0.04 .9 |
|  | >38.0 | 27 |  | 3.7 | 0.119 .0 | 29 | 90 | 0.00 | 0.0 | 11.9 | 66 | 0 | 0.0 | 0.0 | 5.4 | 74 | 00.0 |  | 0.04 .9 |
|  | >38.5 | 27 | 00. | 0.0 | 0.012 .8 | 29 | 00 | 0.00 | 0.0 | 11.9 | 66 | 0 | 0.0 | 0.0 | 5.4 | 74 | 00.0 |  | 0.04 .9 |
|  | >39.0 | 27 | 00. | 0.0 | 0.012 .8 | 29 | 90 | 0.00 | 0.0 | 11.9 | 66 | 0 | 0.0 | 0.0 | 5.4 | 74 | 00.0 | . 0.0 | 0.04 .9 |
|  | >39.5 | 27 | 00. | 0.0 | 0.012 .8 | 29 | 90 | 0.00 | 0.0 | 11.9 | 66 | 0 | 0.0 | 0.0 | 5.4 | 74 | 00.0 | . 0.0 | 0.04 .9 |
|  | >40.0 | 27 |  | 0.0 | 0.012 .8 | 290 | 90 | 0.00 | 0.011 | 11.9 | 66 | 0 | 0.0 | 0.0 | 5.4 | 74 | 00.0 |  | 0.04 .9 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 56 |  | 7.1 | 2.017 .3 | 59 | 90 | 0.00 | 0.0 | 6.1 | 145 | 3 | 2.1 | 0.4 | 45.9 | 151 | 10.7 | . 0.0 | 0.03 .6 |
|  | $\geq 35.5$ | 56 |  | 7.1 | 2.017 .3 | 59 | 00 | 0.00 | 0.0 | 6.1 | 145 | 3 | 2.1 | 0.4 | 5.9 | 151 | 10.7 | . 70.0 | 0.03 .6 |
|  | >36.0 | 56 |  | 7.1 | 2.017 .3 | 59 | 90 | 0.00 | 0.0 | 6.1 | 145 | 3 | 2.1 | 0.4 | . 5.9 | 151 | 10.7 | . 70.0 | 0.03 .6 |
|  | >36.5 | 56 |  | 7.1 | 2.017 .3 | 59 | 90 | 0.00 | 0.0 | 6.1 | 145 | 3 | 2.1 | 0.4 | . 5.9 | 151 | 10.7 | . 70.0 | 0.03 .6 |
|  | >37.0 | 56 |  | 7.1 | 2.017 .3 | 59 | 90 | 0.00 | 0.0 | 6.1 | 145 | 3 | 2.1 | 0.4 | 5.9 | 151 | 10.7 | . 70.0 | 0.03 .6 |
|  | >37.5 | 56 |  | 5.4 | 1.114 .9 | 59 | 00 | 0.00 | 0.0 | 6.1 | 145 |  | 0.7 | 0.0 | 3.8 | 151 | 10.7 |  | 0.03 .6 |
|  | >38.0 | 56 |  | 1.8 | 0.09 .6 | 59 | 000 | 0.00 | 0.06 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 00.0 | . 0.0 | 0.02 .4 |
|  | >38.5 | 56 | 00. | 0.0 | 0.06 .4 | 59 | 90 | 0.00 | 0.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 00.0 | . 0.0 | 0.02 .4 |
|  | >39.0 | 56 | 00. | 0.0 | 0.06 .4 | 59 | 90 | 0.00 | 0.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 00.0 | . 0.0 | 0.02 .4 |
|  | >39.5 | 56 |  | 0.0 | 0.06 .4 | 59 | 900 | 0.00 | 0.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 00.0 | . 0.0 | 0.02 .4 |
|  | >40.0 | 56 |  | 0.0 | 0.06 .4 | 59 | 00 | 0.00 | 0.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 | 00.0 | . 0.0 | 0.02 .4 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Oral) ( ${ }^{\circ} \mathrm{C}$ ) | All | 29 | 310 | 10.3 | 2.227 .4 | 30 | 000 | 0.00 | 0.0 | 11.6 | 79 | 3 | 3.8 | 0.8 | 10.7 | 77 | 11.3 | . 0.0 | 0.07 .0 |
|  | $\geq 35.5$ | 29 | 310 | 10.3 | 2.227 .4 | 30 | 000 | 0.00 | 0.0 | 11.6 | 79 | 3 | 3.8 | 0.8 | 10.7 | 77 | 11.3 | . 30.0 | 0.07 .0 |
|  | >36.0 | 29 | 310 | 10.3 | 2.227 .4 | 30 | 00 | 0.00 | 0.0 | 11.6 | 79 | 3 | 3.8 | 0.8 | 10.7 | 77 | 11.3 | . 30.0 | 0.07 .0 |
|  | >36.5 | 29 | 310 | 10.3 | 2.227 .4 | 30 | 00 | 0.00 | 0.0 | 11.6 | 79 | 3 | 3.8 | 0.8 | 10.7 | 77 | 11.3 | . 30.0 | 0.07 .0 |
|  | >37.0 | 29 | 310 | 10.3 | 2.227 .4 | 30 | 00 | 0.00 | 0.0 | 11.6 | 79 | 3 | 3.8 | 0.8 | 10.7 | 77 | 11.3 | . 30.0 | 0.07 .0 |
|  | >37.5 | 29 | 26. | 6.9 | 0.822 .8 | 30 | 00 | 0.00 | 0.0 | 11.6 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 | 11.3 | . 30.0 | 0.07 .0 |
|  | >38.0 | 29 |  | 3.4 | 0.117 .8 | 30 | 00 | 0.00 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 00.0 | . 00.0 | 0.04 .7 |
|  | >38.5 | 29 | 00. | 0.0 | 0.011 .9 | 30 | 00 | 0.00 | 0.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 | 00.0 | . 0.0 | 0.04 .7 |
|  | >39.0 | 29 |  | 0.0 | 0.011 .9 | 30 | 00 | 0.00 | 0.0 | 11.6 | 679 | 0 | 0.0 | 0.0 | 4.6 | 77 | 00.0 | . 0.0 | 0.04 .7 |
|  | >39.5 | 29 |  | 0.0 | 0.011 .9 | 30 | 00 | 0.00 | 0.0 | 11.6 | 79 |  | 0.0 | 0.0 | 4.6 | 77 | 00.0 | . 0.0 | 0.04 .7 |


|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  | Placebo |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% Cl |  |  |  | $95 \% \mathrm{Cl}$ |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type | N | n \% | LL | UL | N | n \% | LL | UL | N | n | \% | LL | UL | N |  | \% | LL | UL |
|  | >40.0 | 29 | 00.0 | 0.0 | 11.9 | 30 | 00.0 | 0.0 | 11.6 | 79 | 0 | 0.0 | 00.0 | 4.6 | 77 |  | 0.0 | 0.0 | 4.7 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for oral route
Table 8.226 Number and percentage of subjects who reported temperature by half degree measured via axillary route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  | 18-49ys |  |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  |  |  | 95 \% Cl |  |  |  |  | 95 \% Cl |  |  |  |  |
| Symptom | Type | N | n \% |  |  | UL | N | n | n \% |  | UL |  | N |  | \% |  | UL | N |  | \% |  | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All |  | 26. | 6.9 | 0.8 | 822.8 |  | 0 | 00.0 | 0.0 |  | 1.6 | 79 |  | 8.9 | 3.6 | 617.4 | 7.47 |  | 3.9 | 0.8 | 811.0 |
|  | $\geq 35.5$ |  | 26.9 | 6.9 | 0.8 | 822.8 |  | 0 | 00.0 | 0.0 |  | 11.6 | 79 |  | 8.9 | 3.6 | 617.4 | 7.477 |  | 33.9 | 0.8 | 811.0 |
|  | >36.0 |  | 26.9 | 6.9 | 0.8 | 822.8 | 30 | 0 | 00.0 | 0.0 |  | 11.6 | 79 |  | 8.9 | 3.6 | 617.4 | 7.477 |  | 33.9 | 0.8 | 811.0 |
|  | >36.5 | 292 | 26.9 | 6.9 | 0.8 | 822.8 | 30 | 0 | 00.0 | 0.0 |  | 11.6 | 79 |  | 8.9 | 3.6 | . 17.4 | 7.477 |  | 33.9 | 0.8 | 811.0 |
|  | >37.0 |  | 26.9 | 6.9 | 0.8 | 822.8 | 30 | 0 | 0.0 | 0.0 |  | 11.6 | 79 |  | 8.9 | 3.6 | 617.4 | 7.47 |  | 33.9 | 0.8 | 811.0 |
|  | >37.5 | 292 | 26. | 6.9 | 0.8 | 822.8 | 30 | 0 | 0.0 | 0.0 |  | 11.6 | 79 |  | 6.3 | 2.1 | 114.2 | 77 |  | 33.9 | 0.8 | 811.0 |
|  | $>38.0$ | 290 | 00.0 | 0.0 | 0.0 | 011.9 | 30 | 0 | 0.0 | 0.0 |  | 11.6 | 79 |  | 2.5 | 0.3 | 38.8 | 77 |  | 0.0 | 0.0 | 04.7 |
|  | $>38.5$ | 290 | 00. | 0.0 | 0.0 | 011.9 | 30 | 0 | 0.0 | 0.0 |  | 1.6 | 79 |  | 1.3 | 0.0 | 06.9 | 77 |  | 0.0 | 0.0 | 04.7 |
|  | >39.0 | 290 | 00.0 | 0.0 | 0.0 | 011.9 | 30 | 0 | 0.0 | 0.0 |  | 1.6 | 79 | 0 | 0.0 | 0.0 | 04.6 | 77 | 0 | 0.0 | 0.0 | 04.7 |
|  | >39.5 | 290 | 00.0 | 0.0 | 0.0 | 011.9 | 30 | 0 | 0.0 | 0.0 |  | 11.6 | 79 | 0 | 0.0 | 0.0 | 04.6 | 77 |  | 0.0 | 0.0 | . 4.7 |
|  | >40.0 |  | 00. | 0.0 | 0.0 | 011.9 |  | 0 | 0.0 | 0.0 |  | 1.6 | 79 |  | 0.0 | 0.0 | 04.6 | 77 |  | 0.0 |  | 04.7 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All |  | 27. | 7.4 | 0.9 | 924.3 | 291 | 11 | 13.4 | 0.1 |  | 17.8 | 66 |  | 3.0 | 0.4 | 410.5 | 574 |  | 0.0 | 0.0 | 04.9 |
|  | $\geq 35.5$ |  | 27.4 | 7.4 | 0.9 | 924.3 | 29 | 1 | 13.4 | 0.1 |  | 17.8 | 66 |  | 3.0 | 0.4 | 410.5 | . 74 |  | 0.0 | 0.0 | . 4.9 |
|  | >36.0 |  | 27.4 | 7.4 | 0.9 | 924.3 | 291 | 1 | 13.4 | 0.1 |  | 17.8 | 66 |  | 3.0 | 0.4 | 410.5 | . 74 |  | 0.0 | 0.0 | . 4.9 |
|  | >36.5 |  | 27.4 | 7.4 | 0.9 | 924.3 | 29 | 1 | 13.4 | 0.1 |  | 17.8 | 66 |  | 3.0 | 0.4 | . 10.5 | . 74 |  | 0.0 | 0.0 | . 4.9 |
|  | >37.0 |  | 27. | 7.4 | 0.9 | 924.3 | 29 | 1 | 13.4 | 0.1 |  | 17.8 | 66 |  | 3.0 | 0.4 | 410.5 | . 74 |  | 0.0 | 0.0 | . 4.9 |
|  | >37.5 | 270 | 00.0 | 0.0 | 0.0 | 012.8 | 291 | 1 | 13.4 | 0.1 |  | 17.8 | 66 |  | 1.5 | 0.0 | 08.2 | 74 |  | 0.0 | 0.0 | 04.9 |
|  | $>38.0$ | 270 | 00.0 | 0.0 | 0.0 | 012.8 | 291 | 1 | 13.4 | 0.1 |  | 17.8 | 66 | 0 | 0.0 | 0.0 | 05.4 | 74 |  | 0.0 | 0.0 | 04.9 |
|  | >38.5 |  | 00.0 | 0.0 | 0.0 | 012.8 | 290 | 0 | 0.0 | 0.0 |  | 11.9 | 66 |  | 0.0 | 0.0 | 05.4 | 74 |  | 0.0 | 0.0 | 04.9 |
|  | >39.0 | 270 | 00.0 | 0.0 | 0.0 | 012.8 | 290 | 0 | 0.0 | 0.0 |  | 1.9 | 66 |  | 0.0 | 0.0 | 05.4 | 74 |  | 0.0 | 0.0 | . 4.9 |
|  | >39.5 | 270 | 00.0 | 0.0 | 0.0 | 012.8 | 290 | 0 | 0.0 | 0.0 |  | 1.9 | 66 |  | 0.0 | 0.0 | 05.4 | 74 |  | 0.0 | 0.0 | . 4.9 |
|  | >40.0 | 270 | 00. | 0.0 | 0.0 | 012.8 | 290 | 0 | 0.0 | 0.0 |  | 1.9 | 66 |  | 0.0 | 0.0 | 05.4 | 74 |  | 0.0 | 0.0 | . 4.9 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 564 | 47. | 7.1 | 2.0 | 017.3 | 591 | 11 | 1.7 | 0.0 |  | 9.1 | 145 | 9 | 6.2 | 2.9 | 911.5 | 151 |  | 32.0 | 0.4 | . 45.7 |
|  | $\geq 35.5$ | 564 | 47. | 7.1 | 2.0 | 017.3 | 591 | 1 | 1.7 | 0.0 |  | 9.1 | 145 | 9 | 6.2 | 2.9 | 911.5 | 151 |  | 32.0 | 0.4 | . 4.7 |
|  | >36.0 | 564 | 47. | 7.1 | 2.0 | 017.3 | 59 | 1 | 1.7 | 0.0 |  | 9.1 | 145 | 9 | 6.2 | 2.9 | 911.5 | 151 |  | 32.0 | 0.4 | . 4.7 |
|  | >36.5 | 564 | 47. | 7.1 | 2.0 | 017.3 | 59 | 1 | 1.7 | 0.0 |  | 9.1 | 145 |  | 6.2 | 2.9 | 911.5 | 151 |  | 32.0 | 0.4 | 45.7 |


|  |  | 18-49ys |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  |  | 95 \% Cl |  |  |  |  | 95 \% CI |  |  |  | 95 \% Cl |  |  |  |  |  | 95 \% CI |  |  |  |
| Symptom | Type | N | n \% | \% | LL | UL | N | n \% | LL | UL | N |  | \% | LL | UL | N |  | \% | LL | UL |
|  | >37.0 | 56 | 47. | 7.1 | 2.0 | 17.3 | 591 | 11.7 | 70.0 | 0 9.1 | 145 | 9 | 6.2 | 2.9 | 11.5 | 151 |  | 2.0 | 0.4 | 5.7 |
|  | $>37.5$ | 56 | 23.6 | 3.6 | 0.4 | 412.3 | 591 | 11.7 | 70.0 | 09.1 | 145 | 6 | 4.1 | 1.5 | 8.8 | 151 |  | 2.0 | 0.4 | 5.7 |
|  | $>38.0$ | 56 |  | 0.0 | 0.0 | 6.4 | 591 | 11.7 | 70.0 | 9.1 | 145 | 2 | 1.4 | 0.2 | 4.9 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | $>38.5$ | 56 | 00.0 | 0.0 | 0.0 | 0.4 | 590 | 00.0 | 00.0 | 0.1 | 145 | 1 | 0.7 | 0.0 | 3.8 | 151 | 0 | 0.0 | 0.0 | 2.4 |
|  | >39.0 | 56 | 00.0 | 0.0 | 0.0 | 0. 6.4 | 590 | 00.0 | 00.0 | 0 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 |  | 0.0 | 0.0 | 2.4 |
|  | >39.5 | 56 | 00.0 | 0.0 | 0.0 | . 6.4 | 590 | 00.0 | 00.0 | . 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 |  | 0.0 | 0.0 | 2.4 |
|  | >40.0 | 56 | 00.0 | 0.0 | 0.0 | 6.4 | 590 | 00.0 | 00.0 | 6.1 | 145 | 0 | 0.0 | 0.0 | 2.5 | 151 |  | 0.0 | 0.0 | 2.4 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Axillary) ( ${ }^{\circ} \mathrm{C}$ ) | All | 29 | 413 | 13.8 | 3.9 | 31.7 | 301 | 13.3 | 30.1 | 17.2 | 79 | 9 | 11.4 | 5.3 | 20.5 | 77 |  | 3.9 | 0.8 | 11.0 |
|  | $\geq 35.5$ | 29 | 413 | 13.8 | 3.9 | 931.7 | 301 | 13.3 | 30.1 | . 117.2 | 79 | 9 | 11.4 | 5.3 | 20.5 | 77 | 3 | 3.9 | 0.8 | 11.0 |
|  | >36.0 | 29 | 413 | 13.8 | 3.9 | 931.7 | 301 | 13.3 | 30.1 | 117.2 | 79 | 9 | 11.4 | 5.3 | 20.5 | 77 | 3 | 3.9 | 0.8 | 11.0 |
|  | >36.5 | 29 | 413 | 13.8 | 3.9 | 931.7 | 301 | 13.3 | 30.1 | 117.2 | 79 | 9 | 11.4 | 5.3 | 20.5 | 77 | 3 | 3.9 | 0.8 | 11.0 |
|  | >37.0 | 29 | 413 | 13.8 | 3.9 | 931.7 | 301 | 13.3 | 30.1 | 117.2 | 79 | 9 | 11.4 | 5.3 | 20.5 | 77 | 3 | 3.9 | 0.8 | 11.0 |
|  | >37.5 | 29 |  | 6.9 | 0.8 | 822.8 | 301 | 13.3 | 30.1 | . 117.2 | 79 | 6 | 7.6 | 2.8 | 15.8 | 77 |  | 3.9 | 0.8 | 11.0 |
|  | >38.0 | 29 |  | 0.0 | 0.0 | 011.9 | 301 | 13.3 | 30.1 | 17.2 | 79 | 2 | 2.5 | 0.3 | 8.8 | 77 |  | 0.0 | 0.0 | 4.7 |
|  | >38.5 | 29 | 00.0 | 0.0 | 0.0 | 011.9 | 30 | 00.0 | 00.0 | 11.6 | 79 | 1 | 1.3 | 0.0 | 6.9 | 77 |  | 0.0 | 0.0 | 4.7 |
|  | >39.0 | 29 | 00.0 | 0.0 | 0.0 | 0 11.9 | 300 | 00.0 | 00.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 |  | 0.0 | 0.0 | 4.7 |
|  | >39.5 | 29 | 00.0 | 0.0 | 0.0 | 011.9 | 300 | 00.0 | 00.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 |  | 0.0 | 0.0 | 4.7 |
|  | >40.0 | 29 | 00.0 | 0.0 | 0.0 | 011.9 | 30 | 00.0 | 00.0 | 11.6 | 79 | 0 | 0.0 | 0.0 | 4.6 | 77 |  | 0.0 | 0.0 | 4.7 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
$95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; LL = lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for axillary route
Table 8.227 Number and percentage of subjects who reported temperature by half degree measured via tympanic route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  | 18-49ys |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |
|  |  | 95 \% Cl |  |  |  | 95 \% CI |  |  |  |  | 95 \% Cl |  |  |  |  |  |  |  | 95 \% Cl |
| Symptom | Type | N | n \% | LL | UL | N | n | \% | LL | UL | N |  | \% | LL | UL | N | n \% |  | LL UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Temperature/(Tympanic) ( ${ }^{\circ} \mathrm{C}$ ) | All | 29 | 00.0 | 0.0 | O 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 |  | 0.0 | 0.0 | 4.6 | 77 | 00. | . 0 | 0.04 .7 |
|  | $\geq 35.5$ | 29 | 00.0 | 0.0 | 0.011 .9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 |  | 0.0 | 0.0 | 4.6 | 77 | 00. | . 0 | 0.04 .7 |
|  | >36.0 | 29 | 00.0 | 0.0 | 0.011 .9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 |  | 0.0 | 0.0 | 4.6 | 77 | 00. | . 0 | 0.04 .7 |
|  | >36.5 | 29 | 00.0 | 0.0 | 0.011 .9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 |  | 0.0 | 0.0 | 4.6 | 77 | 00. | . 0 | 0.04 .7 |
|  | >37.0 | 29 | 00.0 | 0.0 | 0.011 .9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 |  | 0.0 | 0.0 | 4.6 | 77 | 00. | . 0 | 0.04 .7 |
|  | >37.5 | 29 | 00.0 | 0.0 | 0.011 .9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 |  | 0.0 | 0.0 | 4.6 | 77 | 00. | . 0 | 0.04 .7 |
|  | >38.0 | 29 | 00.0 | 0.0 | . 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 |  | 0.0 | 0.0 | 4.6 | 77 | 00. | . 0 | 0.04 .7 |
|  | >38.5 | 29 | 00.0 | 0.0 | 0.011 .9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 |  | 0.0 | 0.0 | 4.6 | 77 | 00. | . 0 | 0.04 .7 |
|  | >39.0 | 29 | 00.0 | 0.0 | 011.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 |  | 0.0 | 0.0 | 4.6 | 77 | 00. | . 0 | 0.04 .7 |
|  | >39.5 | 29 | 00.0 | 0.0 | .011.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 79 |  | 0.0 | 0.0 | 4.6 | 77 | 00. | . 0 | 0.04 .7 |



18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once For Overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
95\%CI = Exact 95\% confidence interval; LL = lower limit, UL = upper limit
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for tympanic route

Table 8.228 Number and percentage of subjects who reported temperature by half degree measured via rectal route during the 7 -day (Days 0-6) post-vaccination period following each dose (no conversion) by age strata (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)

No records exist in this table

Table 8.229 Number of days with grade 3 local symptoms during the solicited post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Pain | Dose 1 | 18-49ys | HZ/su | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 4 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Dose 2 | 18-49ys | HZ/su | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | $\geq 50 y s$ | HZ/su | 3 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
|  | Overall/dose | 18-49ys | HZ/su | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 7 | 1.9 | 1.0 | 1.0 | 1.0 | 3.0 | 3.0 |
| Redness | Dose 1 | $\geq 50 y s$ | HZ/su | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | $\geq 50 y s$ | HZ/su | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=25$ th percentile
Q3 $=75$ th percentile
Table 8.230 Number of days with grade 3 general symptoms during the solicited post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Fatigue | Dose 1 | 18-49ys | HZ/su | 5 | 2.0 | 1.0 | 1.0 | 2.0 | 2.0 | 4.0 |
|  |  |  | Placebo | 2 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 5 | 2.2 | 1.0 | 1.0 | 2.0 | 3.0 | 4.0 |
|  |  |  | Placebo | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  | Dose 2 | 18-49ys | HZ/su | 4 | 2.0 | 1.0 | 1.5 | 2.0 | 2.5 | 3.0 |
|  |  |  | Placebo | 3 | 2.7 | 1.0 | 1.0 | 3.0 | 4.0 | 4.0 |
|  |  | $\geq 50 y s$ | HZ/su | 5 | 4.2 | 1.0 | 2.0 | 4.0 | 7.0 | 7.0 |
|  |  |  | Placebo | 3 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | 18-49ys | HZ/su | 9 | 2.0 | 1.0 | 1.0 | 2.0 | 2.0 | 4.0 |
|  |  |  | Placebo | 5 | 2.4 | 1.0 | 2.0 | 2.0 | 3.0 | 4.0 |
|  |  | $\geq 50 y s$ | HZ/su | 10 | 3.2 | 1.0 | 1.0 | 2.5 | 4.0 | 7.0 |
|  |  |  | Placebo | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
| Gastrointestinal symptoms | Dose 1 | 18-49ys | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
|  |  | $\geq 50 y s$ | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  | Dose 2 | 18-49ys | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  |  | Placebo | 2 | 2.5 | 1.0 | 1.0 | 2.5 | 4.0 | 4.0 |
|  |  | $\geq 50 y s$ | HZ/su | 3 | 2.7 | 2.0 | 2.0 | 2.0 | 4.0 | 4.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |


| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Overall/dose | 18-49ys | HZ/su | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo 4 | 4 | 2.8 | 1.0 | 2.0 | 3.0 | 3.5 | 4.0 |
|  |  | $\geq 50 y s$ | HZ/su | 4 | 2.5 | 2.0 | 2.0 | 2.0 | 3.0 | 4.0 |
|  |  |  | Placebo | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
| Headache | Dose 1 | 18-49ys | HZ/su | 1 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Dose 2 | 18-49ys | HZ/su | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  |  | Placebo 2 | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  | Overall/dose | 18-49ys | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  |  | Placebo 2 | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 4 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Myalgia | Dose 1 | 18-49ys | HZ/su 4 | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
|  |  |  | Placebo 2 | 2 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
|  |  | $\geq 50 y s$ | HZ/su | 4 | 2.5 | 1.0 | 1.0 | 1.5 | 4.0 | 6.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Dose 2 | 18-49ys | Placebo | 1 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 |
|  |  | $\geq 50 y s$ | HZ/su | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  | Overall/dose | 18-49ys | HZ/su | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
|  |  |  | Placebo 3 | 3 | 3.7 | 3.0 | 3.0 | 3.0 | 5.0 | 5.0 |
|  |  | $\geq 50 y s$ | HZ/su | 7 | 2.1 | 1.0 | 1.0 | 2.0 | 2.0 | 6.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Shivering | Dose 1 | 18-49ys | HZ/su 2 | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 3 | 1.7 | 1.0 | 1.0 | 2.0 | 2.0 | 2.0 |
|  |  |  | Placebo 2 | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  | Dose 2 | $\geq 50 y s$ | HZ/su | 2 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  | Overall/dose | 18-49ys | HZ/su | 2 | 1.5 | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 5 | 1.4 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |
|  |  |  | Placebo 3 | 3 | 1.3 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=$ 25th percentile
Q3 $=75$ th percentile

Table 8.231 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=29 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ N=30 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=84 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=82 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 25 | 86.2 | 68.3 | 96.1 | 27 | 90.0 | 73.5 | 97.9 | 73 | 86.9 | 77.8 | 93.3 | 74 | 90.2 | 81.7 | 95.7 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 1 | 3.4 | 0.1 | 17.8 |  | 10.0 | 2.1 | 26.5 |  | 4.8 | 1.3 | 11.7 | 3 | 3.7 | 0.8 | 10.3 |
|  | Febrile neutropenia (10016288) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 4 | 4.8 | 1.3 | 11.7 | 2 | 2.4 | 0.3 | 8.5 |
|  | Iron deficiency anaemia (10022972) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Leukocytosis (10024378) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Leukopenia (10024384) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Lymphopenia (10025327) | 1 | 3.4 | 0.1 | 17.8 | - | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Neutropenia (10029354) | 2 | 6.9 | 0.8 | 22.8 | 3 | 10.0 | 2.1 | 26.5 | 9 | 10.7 | 5.0 | 19.4 | 12 | 14.6 | 7.8 | 24.2 |
|  | Thrombocytopenia (10043554) | 1 | 3.4 | 0.1 | 17.8 |  | 3.3 | 0.1 | 17.2 | 3 | 3.6 | 0.7 | 10.1 | 2 | 2.4 | 0.3 | 8.5 |
| Cardiac disorders (10007541) | Palpitations (10033557) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Tachycardia (10043071) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |
| Congenital, familial and genetic disorders (10010331) Ear and labyrinth disorders (10013993) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Neurosensory hypoacusis (10067587) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Tinnitus (10043882) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 3 | 3.7 | 0.8 | 10.3 |
| Eye disorders (10015919) | Eye discharge (10015915) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Eye irritation (10015946) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Eye swelling (10015967) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Lacrimation increased (10023644) | 2 | 6.9 | 0.8 | 22.8 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |
|  | Myopia (10028651) |  | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Visual acuity reduced (10047531) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 2 | 6.9 | 0.8 | 22.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Abdominal pain (10000081) | 2 | 6.9 | 0.8 | 22.8 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |
|  | Abdominal pain upper (10000087) | 1 | 3.4 | 0.1 | 17.8 | 1 | 3.3 | 0.1 | 17.2 | 3 | 3.6 | 0.7 | 10.1 | 2 | 2.4 | 0.3 | 8.5 |
|  | Aerophagia (10052813) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Aphthous ulcer (10002959) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Constipation (10010774) | 3 | 10.3 | 2.2 | 27.4 | 4 | 13.3 | 3.8 | 30.7 | 13 | 15.5 | 8.5 | 25.0 | 8 | 9.8 | 4.3 | 18.3 |
|  | Diarrhoea (10012735) | 3 | 10.3 | 2.2 | 27.4 | 0 | 0.0 | 0.0 | 11.6 | , | 6.0 | 2.0 | 13.3 | 10 | 12.2 | 6.0 | 21.3 |

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Report Final

|  |  | Report Final |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=29 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=30 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=84 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=82 \end{gathered}$ |  |  |  |
|  |  |  | 95\% Cl |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Dry mouth (10013781) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 2 | 2.4 | 0.3 | 8.3 | 2 | 2.4 | 0.3 | 8.5 |
|  | Dyspepsia (10013946) | 0 | 0.0 | 0.0 | 11.9 | 2 | 6.7 | 0.8 | 22.1 | 6 | 7.1 | 2.7 | 14.9 | 10 | 12.2 | 6.0 | 21.3 |
|  | Dysphagia (10013950) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |
|  | Epigastric discomfort (10053155) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Flatulence (10016766) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |
|  | Gastrointestinal disorder (10017944) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 3 | 3.7 | 0.8 | 10.3 |
|  | Gastrointestinal pain (10017999) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Gastrooesophageal reflux disease (10017885) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 2 | 2.4 | 0.3 | 8.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Gingival pain (10018286) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Glossitis (10018386) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Haemorrhoidal haemorrhage (10054787) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.0 | 11.9 | 2 | 6.7 | 0.8 | 22.1 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Hiatus hernia (10020028) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Nausea (10028813) | 12 | 41.4 | 23.5 | 61.1 | 9 | 30.0 | 14.7 | 49.4 | 19 | 22.6 | 14.2 | 33.0 | 19 | 23.2 | 14.6 | 33.8 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 3 | 3.7 | 0.8 | 10.3 |
|  | Oesophagitis (10030216) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Oral pain (10031009) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | - | 0.0 | 0.0 | 4.4 |
|  | Proctalgia (10036772) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 2 | 2.4 | 0.3 | 8.5 |
|  | Rectal tenesmus (10057071) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Stomatitis (10042128) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 4 | 4.8 | 1.3 | 11.7 | 2 | 2.4 | 0.3 | 8.5 |
|  | Swollen tongue (10042727) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Vomiting (10047700) | 1 | 3.4 | 0.1 | 17.8 | 6 | 20.0 | 7.7 | 38.6 | 9 | 10.7 | 5.0 | 19.4 | 8 | 9.8 | 4.3 | 18.3 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 13 | 44.8 | 26.4 | 64.3 | 4 | 13.3 | 3.8 | 30.7 | 16 | 19.0 | 11.3 | 29.1 | 24 | 29.3 | 19.7 | 40.4 |
|  | Axillary pain (10048750) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | O | 0.0 | 0.0 | 4.4 |
|  | Catheter site pain (10052268) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Chest pain (10008479) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Chills (10008531) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Fatigue (10016256) | 1 | 3.4 | 0.1 | 17.8 | 3 | 10.0 | 2.1 | 26.5 | 3 | 3.6 | 0.7 | 10.1 | 3 | 3.7 | 0.8 | 10.3 |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |

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|  |  |  |  |  | 18-4 | 9y |  |  |  |  |  |  | $\geq 5$ | Oy |  |  |  |
|  |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =29 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { ceb } \\ & =30 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =84 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { cebs } \\ & =82 \end{aligned}$ |  |
|  |  |  |  |  | CI |  |  |  | Cl |  |  |  | Cl |  |  |  | \% CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Generalised oedema (10018092) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Inflammation (10061218) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Influenza like illness (10022004) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 2 | 2.4 | 0.3 | 8.5 |
|  | Injection site pruritus (10022093) | 0 | 0.0 | 0.0 | 11.9 | - | 0.0 | 0.0 | 11.6 | 2 | 2.4 | 0.3 | 8.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Malaise (10025482) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 2 | 2.4 | 0.3 | 8.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Mucosal dryness (10028111) | 1 | 3.4 | 0.1 | 17.8 | - | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Mucosal inflammation (10028116) | 3 | 10.3 | 2.2 | 27.4 | - | 0.0 | 0.0 | 11.6 | 7 | 8.3 | 3.4 | 16.4 |  | 7.3 | 2.7 | 15.2 |
|  | Oedema peripheral (10030124) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 |  | 3.6 | 0.7 | 10.1 | 0 | 0.0 | 0.0 | 4.4 |
|  | Pain (10033371) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 2 | 2.4 | 0.3 | 8.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Peripheral swelling (10048959) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 11.9 | - | 0.0 | 0.0 | 11.6 | 2 | 2.4 | 0.3 | 8.3 | 5 | 6.1 | 2.0 | 13.7 |
|  | Temperature intolerance (10057040) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Hepatic steatosis (10019708) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Hepatomegaly (10019842) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Hyperbilirubinaemia (10020578) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 |  | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Hypersensitivity (10020751) | 1 | 3.4 | 0.1 | 17.8 |  | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Seasonal allergy (10048908) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 2 | 2.4 | 0.3 | 8.5 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Bacterial infection (10060945) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 2 | 2.4 | 0.3 | 8.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Bronchitis (10006451) | 0 | 0.0 | 0.0 | 11.9 | - | 0.0 | 0.0 | 11.6 |  | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 |  | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 1 | 1.2 | 0.0 | 6.5 |  | 1.2 | 0.0 | 6.6 |
|  | Erysipelas (10015145) | 0 | 0.0 | 0.0 | 11.9 | - | 0.0 | 0.0 | 11.6 |  | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Folliculitis (10016936) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 |  | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Gastroenteritis (10017888) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 |  | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |

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|  |  |  |  |  | 18-4 | 49y |  |  |  |  |  |  | $\geq 5$ | 0y |  |  |  |
|  |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =29 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { aceb } \\ & =30 \end{aligned}$ |  |  |  | $\begin{aligned} & I Z / s u \\ & I=84 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { cebs } \\ & =82 \end{aligned}$ |  |
|  |  |  |  | 95\% | CI |  |  |  | \% CI |  |  |  | Cl |  |  |  | \% CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Body temperature fluctuation (10063488) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Haemoglobin decreased (10018884) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Platelet count decreased (10035528) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 |  | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Weight decreased (10047895) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Weight increased (10047899) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) | 3 | 10.3 | 2.2 | 27.4 | 0 | 0.0 | 0.0 | 11.6 |  | 7.1 | 2.7 | 14.9 | 5 | 6.1 | 2.0 | 13.7 |
|  | Hypercholesterolaemia (10020603) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Hyperglycaemia (10020635) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 2 | 2.4 | 0.3 | 8.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Hypocalcaemia (10020947) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | - | 0.0 | 0.0 | 4.4 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Iron deficiency (10022970) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
| Musculoskeletal and connective tissue disorders | Arthralgia (10003239) | 1 | 3.4 | 0.1 | 17.8 | 1 | 3.3 | 0.1 | 17.2 | 2 | 2.4 | 0.3 | 8.3 | 2 | 2.4 | 0.3 | 8.5 |
|  | Back pain (10003988) | 2 | 6.9 | 0.8 | 22.8 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 2 | 2.4 | 0.3 | 8.5 |
|  | Bone pain (10006002) | 3 | 10.3 | 2.2 | 27.4 | 1 | 3.3 | 0.1 | 17.2 | - | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Groin pain (10018735) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Muscle contracture (10062575) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Muscle spasms (10028334) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Musculoskeletal discomfort (10053156) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Musculoskeletal pain (10028391) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 3 | 3.7 | 0.8 | 10.3 |
|  | Myalgia (10028411) | 2 | 6.9 | 0.8 | 22.8 | 2 | 6.7 | 0.8 | 22.1 | 2 | 2.4 | 0.3 | 8.3 | - | 3.7 | 0.8 | 10.3 |
|  | Neck pain (10028836) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 3 | 3.6 | 0.7 | 10.1 | 0 | 0.0 | 0.0 | 4.4 |
|  | Pain in extremity (10033425) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 2 | 2.4 | 0.3 | 8.3 | 2 | 2.4 | 0.3 | 8.5 |
| Neoplasms benign, malignant and unspecified (incl cysts | Adenocarcinoma of colon (10001167) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Prostate cancer (10060862) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 3 | 3.6 | 0.7 | 10.1 | 3 | 3.7 | 0.8 | 10.3 |
|  | Dizziness postural (10013578) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Dysaesthesia (10013886) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 |  | 1.2 | 0.0 | 6.5 | - | 0.0 | 0.0 | 4.4 |
|  | Dysgeusia (10013911) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 1 | 1.2 | 0.0 | 6.5 | 5 | 6.1 | 2.0 | 13.7 |

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|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=29 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=30 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=84 \end{aligned}$ |  |  |  | Placebo$N=82$ |  |  |  |
|  |  | 95\% Cl |  |  |  | - $95 \% \mathrm{Cl}$ |  |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Epistaxis (10015090) | 1 | 3.4 | 0.1 | 17.8 | 1 | 3.3 | 0.1 | 17.2 | 1 | 1.2 | 0.0 | 6.5 | 3 | 3.7 | 0.8 | 10.3 |
|  | Haemoptysis (10018964) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Hiccups (10020039) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 2 | 2.4 | 0.3 | 8.5 |
|  | Nasal congestion (10028735) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Oropharyngeal discomfort (10068318) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Oropharyngeal pain (10068319) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Pulmonary embolism (10037377) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 7 | 24.1 | 10.3 | 43.5 | 13 | 43.3 | 25.5 | 62.6 | 14 | 16.7 | 9.4 | 26.4 | 10 | 12.2 | 6.0 | 21.3 |
|  | Dermatitis (10012431) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Dry skin (10013786) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Erythema (10015150) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 3 | 3.6 | 0.7 | 10.1 | 1 | 1.2 | 0.0 | 6.6 |
|  | Nail dystrophy (10028698) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Onychalgia (10064251) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Palmar-plantar erythrodysaesthesia syndrome (10033553) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Pruritus (10037087) | 0 | 0.0 | 0.0 | 11.9 | 2 | 6.7 | 0.8 | 22.1 | 0 | 0.0 | 0.0 | 4.3 | 2 | 2.4 | 0.3 | 8.5 |
|  | Pruritus generalised (10052576) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Rash (10037844) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | - | 3.7 | 0.8 | 10.3 |
|  | Rash macular (10037867) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Scar pain (10049002) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Swelling face (10042682) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Urticaria (10046735) | 2 | 6.9 | 0.8 | 22.8 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | - | 0.0 | 0.0 | 4.4 |
| Social circumstances (10041244) | Menopause (10027308) | 1 | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Haematoma (10018852) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |
|  | Hot flush (10060800) | 0 | 0.0 | 0.0 | 11.9 | 2 | 6.7 | 0.8 | 22.1 | 0 | 0.0 | 0.0 | 4.3 | - | 0.0 | 0.0 | 4.4 |
|  | Hypotension (10021097) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |

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116427 (ZOSTER-028)
Report Final

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =29 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { cebs } \\ & =30 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =84 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { acebc } \\ & =82 \end{aligned}$ |  |
|  |  |  |  |  | CI |  |  |  | CI |  |  |  | CI |  |  |  | \% CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Lymphocele (10048642) | 0 | 0.0 | 0.0 | 11.90 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Phlebitis (10034879) | 0 | 0.0 | 0.0 | 11.90 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Thrombosis (10043607) | 0 | 0.0 | 0.0 | 11.90 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Vascular pain (10047095) | 0 | 0.0 | 0.0 | 11.90 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
n/\% = number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{CI}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.232 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=56 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=60 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=153 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=159 \end{aligned}$ |  |  |  |
|  |  | 95\% Cl |  |  |  |  |  | 95\% CI |  | 95\% CI |  |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 40 | 71.4 | 57.8 | 82.7 | 46 | 76.7 | 64.0 | 86.6 | 109 | 71.2 | 63.4 | 78.3 | 117 | 73.6 | 66.0 | 80.3 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 1 | 1.8 | 0.0 | 9.6 | 3 | 5.0 | 1.0 | 13.9 | 4 | 2.6 | 0.7 | 6.6 | 3 | 1.9 | 0.4 | 5.4 |
|  | Febrile neutropenia (10016288) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 4 | 2.6 | 0.7 | 6.6 | 3 | 1.9 | 0.4 | 5.4 |
|  | Iron deficiency anaemia (10022972) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Leukocytosis (10024378) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Leukopenia (10024384) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Lymphopenia (10025327) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Neutropenia (10029354) | 2 | 3.6 | 0.4 | 12.3 | 4 | 6.7 | 1.8 | 16.2 | 10 | 6.5 | 3.2 | 11.7 | 13 | 8.2 | 4.4 | 13.6 |
|  | Thrombocytopenia (10043554) | 1 | 1.8 | 0.0 | 9.6 | 2 | 3.3 | 0.4 | 11.5 | 3 | 2.0 | 0.4 | 5.6 | 2 | 1.3 | 0.2 | 4.5 |
| Cardiac disorders (10007541) | Palpitations (10033557) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Tachycardia (10043071) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Tinnitus (10043882) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 3 | 1.9 | 0.4 | 5.4 |
| Eye disorders (10015919) | Eye discharge (10015915) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Eye irritation (10015946) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Eye swelling (10015967) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Lacrimation increased (10023644) | 2 | 3.6 | 0.4 | 12.3 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Myopia (10028651) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Visual acuity reduced (10047531) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 |  | 0.6 | 0.0 | 3.5 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 2 | 3.6 | 0.4 | 12.3 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Abdominal pain (10000081) | 2 | 3.6 | 0.4 | 12.3 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Abdominal pain upper (10000087) | 1 | 1.8 | 0.0 | 9.6 | 1 | 1.7 | 0.0 | 8.9 | 4 | 2.6 | 0.7 | 6.6 | 2 | 1.3 | 0.2 | 4.5 |
|  | Aerophagia (10052813) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Aphthous ulcer (10002959) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Constipation (10010774) | 3 | 5.4 | 1.1 | 14.9 | 4 | 6.7 | 1.8 | 16.2 | 15 | 9.8 | 5.6 | 15.7 | 8 | 5.0 | 2.2 | 9.7 |
|  | Diarrhoea (10012735) | 4 | 7.1 | 2.0 | 17.3 | 0 | 0.0 | 0.0 | 6.0 | 6 | 3.9 | 1.5 | 8.3 | 10 | 6.3 | 3.1 | 11.3 |


|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=56 \end{aligned}$ |  |  |  | Placebo$N=60$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=153 \end{aligned}$ |  |  |  | $\begin{aligned} & \hline \text { Placebo } \\ & \mathrm{N}=159 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  | \| $95 \% \mathrm{Cl}$ |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Dry mouth (10013781) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 2 | 1.3 | 0.2 | 4.6 | 2 | 1.3 | 0.2 | 4.5 |
|  | Dyspepsia (10013946) | 0 | 0.0 | 0.0 | 6.4 | 2 | 3.3 | 0.4 | 11.5 | 6 | 3.9 | 1.5 | 8.3 | 10 | 6.3 | 3.1 | 11.3 |
|  | Dysphagia (10013950) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Epigastric discomfort (10053155) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | - | 0.0 | 0.0 | 2.3 |
|  | Flatulence (10016766) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Gastrointestinal disorder (10017944) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 |  | 1.9 | 0.4 | 5.4 |
|  | Gastrointestinal pain (10017999) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Gastrooesophageal reflux disease (10017885) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Gingival pain (10018286) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Glossitis (10018386) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 2 | 1.3 | 0.2 | 4.5 |
|  | Haemorrhoidal haemorrhage (10054787) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.0 | 6.4 | 2 | 3.3 | 0.4 | 11.5 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Hiatus hernia (10020028) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Nausea (10028813) | 15 | 26.8 | 15.8 | 40.3 | 13 | 21.7 | 12.1 | 34.2 | 20 | 13.1 | 8.2 | 19.5 | 19 | 11.9 | 7.4 | 18.0 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 3 | 1.9 | 0.4 | 5.4 |
|  | Oesophagitis (10030216) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Oral pain (10031009) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Proctalgia (10036772) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 2 | 1.3 | 0.2 | 4.5 |
|  | Rectal tenesmus (10057071) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Stomatitis (10042128) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 5 | 3.3 | 1.1 | 7.5 | 2 | 1.3 | 0.2 | 4.5 |
|  | Swollen tongue (10042727) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Vomiting (10047700) | 1 | 1.8 | 0.0 | 9.6 | 7 | 11.7 | 4.8 | 22.6 | 9 | 5.9 | 2.7 | 10.9 | 8 | 5.0 | 2.2 | 9.7 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 13 | 23.2 | 13.0 | 36.4 | 4 | 6.7 | 1.8 | 16.2 | 19 | 12.4 | 7.6 | 18.7 | 26 | 16.4 | 11.0 | 23.0 |
|  | Axillary pain (10048750) | 0 | 0.0 | 0.0 | 6.4 | 2 | 3.3 | 0.4 | 11.5 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Catheter site pain (10052268) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Chest pain (10008479) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Chills (10008531) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Fatigue (10016256) | 1 | 1.8 | 0.0 | 9.6 | 4 | 6.7 | 1.8 | 16.2 | 3 | 2.0 | 0.4 | 5.6 |  | 1.9 | 0.4 | 5.4 |


|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=56 \end{aligned}$ |  |  |  | Placebo$N=60$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=153 \end{aligned}$ |  |  | Placebo$N=159$ |  |  |  |
|  |  |  | 95\% CI |  |  |  |  | 95\% Cl |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Generalised oedema (10018092) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Inflammation (10061218) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Influenza like illness (10022004) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Injection site erythema (10022061) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Injection site pain (10022086) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 2 | 1.3 | 0.2 | 4.5 |
|  | Injection site pruritus (10022093) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Malaise (10025482) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 3 | 2.0 | 0.4 | 5.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Mucosal dryness (10028111) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Mucosal inflammation (10028116) |  | 5.4 | 1.1 | 14.9 | 0 | 0.0 | 0.0 | 6.0 | 8 | 5.2 | 2.3 | 10.0 | 8 | 5.0 | 2.2 | 9.7 |
|  | Oedema peripheral (10030124) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 3 | 2.0 | 0.4 | 5.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Pain (10033371) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Peripheral swelling (10048959) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.6 | 5 | 3.1 | 1.0 | 7.2 |
|  | Temperature intolerance (10057040) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Hepatic steatosis (10019708) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Hepatomegaly (10019842) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Hyperbilirubinaemia (10020578) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Hypersensitivity (10020751) |  | 1.8 | 0.0 | 9.6 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Seasonal allergy (10048908) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 2 | 1.3 | 0.2 | 4.5 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Bacterial infection (10060945) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Bronchitis (10006451) | - | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Erysipelas (10015145) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Folliculitis (10016936) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |


|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=56 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=60 \end{gathered}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=153 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=159 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% CI |  | 95\% CI |  |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Gastroenteritis (10017888) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Gingivitis (10018292) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Herpes zoster (10019974) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Infection (10021789) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | - | 0.0 | 0.0 | 2.3 |
|  | Influenza (10022000) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Nasopharyngitis (10028810) | 3 | 5.4 | 1.1 | 14.9 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Neutropenic sepsis (10049151) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 2 | 1.3 | 0.2 | 4.5 |
|  | Oral fungal infection (10061324) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Oral herpes (10067152) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Oral infection (10048685) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Pneumonia (10035664) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 3 | 2.0 | 0.4 | 5.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Post procedural infection (10067268) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Respiratory tract infection (10062352) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Sepsis (10040047) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Sinusitis (10040753) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Upper respiratory tract infection (10046306) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 3 | 2.0 | 0.4 | 5.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Urinary tract infection (10046571) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 3 | 1.9 | 0.4 | 5.4 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Injury, poisoning and procedural complications (10022117) | Arthropod bite (10003399) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Gastrostomy failure (10050056) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Ligament sprain (10024453) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Post procedural complication (10058046) | 0 | 0.0 | 0.0 | 6.4 | 3 | 5.0 | 1.0 | 13.9 | 2 | 1.3 | 0.2 | 4.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Post procedural diarrhoea (10057585) | 2 | 3.6 | 0.4 | 12.3 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Radiation skin injury (10063562) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 2 | 1.3 | 0.2 | 4.5 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |


|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=56 \end{aligned}$ |  |  |  | Placebo$N=60$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=153 \end{aligned}$ |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=159 \end{aligned}$ |  |  |  |
|  |  |  |  | 95\% CI |  |  |  | 95\% Cl |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| Investigations (10022891) | Blood iron decreased (10005619) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Body temperature fluctuation (10063488) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Haemoglobin decreased (10018884) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Platelet count decreased (10035528) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Weight decreased (10047895) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Weight increased (10047899) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) | 4 | 7.1 | 2.0 | 17.3 | 0 | 0.0 | 0.0 | 6.0 | 7 | 4.6 | 1.9 | 9.2 | 5 | 3.1 | 1.0 | 7.2 |
|  | Hypercholesterolaemia (10020603) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Hyperglycaemia (10020635) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Hypocalcaemia (10020947) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Iron deficiency (10022970) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) | 1 | 1.8 | 0.0 | 9.6 | 1 | 1.7 | 0.0 | 8.9 | 2 | 1.3 | 0.2 | 4.6 | 2 | 1.3 | 0.2 | 4.5 |
|  | Back pain (10003988) | 2 | 3.6 | 0.4 | 12.3 | - | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 2 | 1.3 | 0.2 | 4.5 |
|  | Bone pain (10006002) | 3 | 5.4 | 1.1 | 14.9 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Groin pain (10018735) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Muscle contracture (10062575) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Muscle spasms (10028334) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Musculoskeletal discomfort (10053156) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Musculoskeletal pain (10028391) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 3 | 1.9 | 0.4 | 5.4 |
|  | Myalgia (10028411) | 2 | 3.6 | 0.4 | 12.3 | 2 | 3.3 | 0.4 | 11.5 | 2 | 1.3 | 0.2 | 4.6 | 3 | 1.9 | 0.4 | 5.4 |
|  | Neck pain (10028836) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 3 | 2.0 | 0.4 | 5.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Pain in extremity (10033425) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.6 | 2 | 1.3 | 0.2 | 4.5 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Prostate cancer (10060862) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 3 | 2.0 | 0.4 | 5.6 | 3 | 1.9 | 0.4 | 5.4 |
|  | Dizziness postural (10013578) | 0 | 0.0 | 0.0 | 6.4 | - | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Dysaesthesia (10013886) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |


|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=56 \end{aligned}$ |  |  |  | Placebo$N=60$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=153 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=159 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Dysgeusia (10013911) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 1 | 0.7 | 0.0 | 3.6 | 5 | 3.1 | 1.0 | 7.2 |
|  | Headache (10019211) | 1 | 1.8 | 0.0 | 9.6 | 2 | 3.3 | 0.4 | 11.5 | 3 | 2.0 | 0.4 | 5.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Hepatic encephalopathy (10019660) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Hypoaesthesia (10020937) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Motor dysfunction (10061296) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Muscle contractions involuntary (10028293) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Neuropathy peripheral (10029331) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 4 | 2.6 | 0.7 | 6.6 | 5 | 3.1 | 1.0 | 7.2 |
|  | Neurotoxicity (10029350) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 2 | 1.3 | 0.2 | 4.5 |
|  | Paraesthesia (10033775) | 3 | 5.4 | 1.1 | 14.9 | 1 | 1.7 | 0.0 | 8.9 | 4 | 2.6 | 0.7 | 6.6 | 4 | 2.5 | 0.7 | 6.3 |
|  | Paresis (10033985) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Peripheral sensory neuropathy (10034620) | 3 | 5.4 | 1.1 | 14.9 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 2 | 1.3 | 0.2 | 4.5 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Syncope (10042772) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Tremor (10044565) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 3 | 1.9 | 0.4 | 5.4 |
| Psychiatric disorders (10037175) | Aggression (10001488) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Anxiety (10002855) | 3 | 5.4 | 1.1 | 14.9 | 0 | 0.0 | 0.0 | 6.0 | 3 | 2.0 | 0.4 | 5.6 | 2 | 1.3 | 0.2 | 4.5 |
|  | Depression (10012378) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Insomnia (10022437) | 1 | 1.8 | 0.0 | 9.6 | 1 | 1.7 | 0.0 | 8.9 | 3 | 2.0 | 0.4 | 5.6 | 1 | 0.6 | 0.0 | 3.5 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) |  | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 |  | 1.3 | 0.2 | 4.5 |
|  | Bladder spasm (10048994) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Chronic kidney disease (10064848) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Dysuria (10013990) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 |  | 0.6 | 0.0 | 3.5 |
|  | Renal impairment (10062237) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Urinary retention (10046555) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Reproductive system and breast disorders (10038604) | Oedema genital (10030104) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 |  | 0.0 | 0.0 | 2.3 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Asthma (10003553) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Catarrh (10007774) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Cough (10011224) | 2 | 3.6 | 0.4 | 12.3 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Dysaesthesia pharynx (10062665) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |


|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=56 \end{aligned}$ |  |  |  | Placebo$N=60$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=153 \end{aligned}$ |  |  |  | $\begin{aligned} & \hline \text { Placebo } \\ & \mathrm{N}=159 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  | - $95 \% \mathrm{Cl}$ |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Dysphonia (10013952) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Dyspnoea (10013968) | 2 | 3.6 | 0.4 | 12.3 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Epistaxis (10015090) | 1 | 1.8 | 0.0 | 9.6 | 1 | 1.7 | 0.0 | 8.9 | 1 | 0.7 | 0.0 | 3.6 | 3 | 1.9 | 0.4 | 5.4 |
|  | Haemoptysis (10018964) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Hiccups (10020039) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 3 | 1.9 | 0.4 | 5.4 |
|  | Nasal congestion (10028735) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Oropharyngeal discomfort (10068318) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Oropharyngeal pain (10068319) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Pulmonary embolism (10037377) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
| Skin and subcutaneous tissue disorders (10040785) | Alopecia (10001760) | 7 | 12.5 | 5.2 | 24.1 | 13 | 21.7 | 12.1 | 34.2 | 14 | 9.2 | 5.1 | 14.9 | 10 | 6.3 | 3.1 | 11.3 |
|  | Dermatitis (10012431) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Dry skin (10013786) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Erythema (10015150) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 4 | 2.6 | 0.7 | 6.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Nail dystrophy (10028698) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Onychalgia (10064251) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 |  | 0.6 | 0.0 | 3.5 |
|  | Palmar-plantar erythrodysaesthesia syndrome (10033553) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Pruritus (10037087) | 0 | 0.0 | 0.0 | 6.4 | 2 | 3.3 | 0.4 | 11.5 | 0 | 0.0 | 0.0 | 2.4 | 2 | 1.3 | 0.2 | 4.5 |
|  | Pruritus generalised (10052576) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Rash (10037844) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 |  | 1.9 | 0.4 | 5.4 |
|  | Rash macular (10037867) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | - | 0.0 | 0.0 | 2.3 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Scar pain (10049002) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | - | 0.0 | 0.0 | 2.3 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | - | 0.0 | 0.0 | 2.3 |
|  | Swelling face (10042682) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Urticaria (10046735) | 2 | 3.6 | 0.4 | 12.3 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
| Social circumstances (10041244) | Menopause (10027308) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Haematoma (10018852) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |

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18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
$95 \% \mathrm{CI}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.233 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the $\mathbf{3 0}$-day (Days $0-29$ ) post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)


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18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \%$ CI $=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.234 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the $\mathbf{3 0 - d a y}$ (Days 0-29) post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=56 \end{aligned}$ |  |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=60 \end{aligned}$ |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=153 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=159 \end{aligned}$ |  |  |  |
|  |  |  | 95\% CI |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) |  | \% | LL | UL |  | \% |  | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  |  | 7.1 | 2.0 | . 17.3 |  | 6.7 | 1.8 | 816.2 | 18 | 11.8 | 7.1 | 18.0 | 11 | 6.9 | 3.5 | 12.0 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) |  | 0.0 | 0.0 | 06.4 |  | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Febrile neutropenia (10016288) | 0 | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 4 | 2.6 | 0.7 | 6.6 | 2 | 1.3 | 0.2 | 4.5 |
|  | Neutropenia (10029354) |  | 0.0 | 0.0 | 06.4 | 1 | 1.7 | 0.0 | 08.9 | 4 | 2.6 | 0.7 | 6.6 | 2 | 1.3 | 0.2 | 4.5 |
|  | Thrombocytopenia (10043554) |  | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Gastrointestinal disorders (10017947) | Abdominal pain (10000081) |  | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Constipation (10010774) |  | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Haemorrhoids (10019022) |  | 0.0 | 0.0 | 06.4 | 1 | 1.7 | 0.0 | 08.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 0 | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Malaise (10025482) | 0 | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) |  | 1.8 | 0.0 | 09.6 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Kidney infection (10023424) |  | 0.0 | 0.0 | 06.4 |  | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Lower respiratory tract infection (10024968) |  | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Nasopharyngitis (10028810) |  | 1.8 | 0.0 | 09.6 |  | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Sepsis (10040047) |  | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
| Injury, poisoning and procedural complications (10022117) | Post procedural diarrhoea (10057585) |  | 3.6 | 0.4 | 412.3 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
| Investigations (10022891) | Platelet count decreased (10035528) | 0 | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 1 | 0.7 | 0.0 | 3.6 |  | 0.0 | 0.0 | 2.3 |
|  | Weight increased (10047899) |  | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104) | Adenocarcinoma of colon (10001167) |  | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Prostate cancer (10060862) |  | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Nervous system disorders (10029205) | Hepatic encephalopathy (10019660) |  | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Seizure (10039906) |  | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
| Psychiatric disorders (10037175) | Insomnia (10022437) |  | 0.0 | 0.0 | 06.4 | 1 | 1.7 | 0.0 | 08.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) |  | 0.0 | 0.0 | 06.4 | 0 | 0.0 | 0.0 | 06.0 | 0 | 0.0 | 0.0 | 2.4 | 2 | 1.3 | 0.2 | 4.5 |
|  | Hydronephrosis (10020524) |  | 0.0 | 0.0 | 06.4 |  | 0.0 |  | 06.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |

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18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of administered doses
n/\% = number/percentage of doses with the symptom
$95 \% \mathrm{CI}=$ exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.235 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30 -day (Days 0-29) postvaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  | 18-49ys |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=29 \end{aligned}$ |  |  |  | Placebo$N=30$ |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=84 \end{aligned}$ |  |  |  | Placebo$N=82$ |  |  |  |
|  |  |  | 95\% CI |  |  | 95\% CI |  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) |  | \% | LL | UL | n \% | LL | UL | . | \% | LL | UL |  | \% | LL | UL |
| At least one symptom |  | , | 13.8 | 3.9 | 31.7 | 26.7 | 0.8 | 22.1 | 6 | 7.1 | 2.7 | 14.9 | 7 | 8.5 | 3.5 | 16.8 |
| Blood and lymphatic system disorders (10005329) | Neutropenia (10029354) | 0 | 0.0 | 0.0 | 11.9 | 00.0 | 0.0 | . 11.6 | 0 | 0.0 | 0.0 | 4.3 |  | 1.2 | 0.0 | 6.6 |
| Cardiac disorders (10007541) | Tachycardia (10043071) |  | 3.4 | 0.1 | 17.8 | 00.0 | 0.0 | . 11.6 | 0 | 0.0 | 0.0 | 4.3 |  | 1.2 | 0.0 | 6.6 |
| Gastrointestinal disorders (10017947) | Swollen tongue (10042727) |  | 3.4 | 0.1 | 17.8 | 00.0 | 0.0 | . 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) |  | 6.9 | 0.8 | 22.8 | 00.0 | 0.0 | . 11.6 | 0 | 0.0 | 0.0 | 4.3 |  | 1.2 | 0.0 | 6.6 |
|  | Axillary pain (10048750) |  | 0.0 | 0.0 | 11.9 | 13.3 | 0.1 | 117.2 | 0 | 0.0 | 0.0 | 4.3 |  | 0.0 | 0.0 | 4.4 |
|  | Feeling hot (10016334) | 0 | 0.0 | 0.0 | 11.9 | 00.0 | 0.0 | 0.011.6 | 0 | 0.0 | 0.0 | 4.3 |  | 1.2 | 0.0 | 6.6 |
|  | Injection site bruising (10022052) | 0 | 0.0 | 0.0 | 11.9 | 13.3 | 0.1 | 117.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Injection site erythema (10022061) |  | 0.0 | 0.0 | 11.9 | 13.3 | 0.1 | 117.2 | 0 | 0.0 | 0.0 | 4.3 |  | 0.0 | 0.0 | 4.4 |
|  | Injection site mass (10022081) |  | 0.0 | 0.0 | 11.9 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 |  | 1.2 | 0.0 | 6.6 |
|  | Injection site pain (10022086) |  | 0.0 | 0.0 | 11.90 | 00.0 | 0.0 | . 11.6 | 0 | 0.0 | 0.0 | 4.3 |  | 2.4 | 0.3 | 8.5 |
|  | Injection site pruritus (10022093) | 0 | 0.0 | 0.0 | 11.9 | 00.0 | 0.0 | . 11.6 | 2 | 2.4 | 0.3 | 8.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Malaise (10025482) |  | 0.0 | 0.0 | 11.9 | 00.0 | 0.0 | . 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Pyrexia (10037660) |  | 0.0 | 0.0 | 11.9 | 00.0 | 0.0 | . 11.6 | 0 | 0.0 | 0.0 | 4.3 |  | 1.2 | 0.0 | 6.6 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) |  | 3.4 | 0.1 | 17.8 | 00.0 | 0.0 | . 11.6 | 0 | 0.0 | 0.0 | 4.3 |  | 0.0 | 0.0 | 4.4 |
|  | Oral herpes (10067152) |  | 0.0 | 0.0 | 11.9 | 00.0 | 0.0 | . 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) |  | 0.0 | 0.0 | 11.9 | 00.0 | 0.0 | . 11.6 | 0 | 0.0 | 0.0 | 4.3 |  | 1.2 | 0.0 | 6.6 |
| Musculoskeletal and connective tissue disorders (10028395) | Arthralgia (10003239) |  | 3.4 | 0.1 | 17.8 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 |  | 1.2 | 0.0 | 6.6 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 0 | 0.0 | 0.0 | 11.9 | 00.0 | 0.0 | . 11.6 | 0 | 0.0 | 0.0 | 4.3 |  | 1.2 | 0.0 | 6.6 |
|  | Muscle contractions involuntary (10028293) |  | 0.0 | 0.0 | 11.9 | 00.0 | 0.0 | . 11.6 | 1 | 1.2 | 0.0 | 6.5 |  | 0.0 | 0.0 | 4.4 |
| Skin and subcutaneous tissue disorders (10040785) | Erythema (10015150) |  | 0.0 | 0.0 | 11.90 | 00.0 | 0.0 | . 11.6 |  | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Rash pruritic (10037884) |  | 0.0 | 0.0 | 11.9 | 00.0 | 0.0 | . 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Urticaria (10046735) |  | 0.0 | 0.0 | 11.9 | 13.3 |  | 117.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group

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At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.236 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)


18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

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116427 (ZOSTER-028)
Report Final
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of administered doses
n/\% = number/percentage of doses with the symptom
$95 \% \mathrm{CI}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.237 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the $\mathbf{3 0 - d a y}$ (Days $\mathbf{0 - 2 9}$ ) post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  | 18-49ys |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=29 \end{aligned}$ |  |  | Placebo$N=30$ |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=84 \end{aligned}$ |  |  |  | Placebo$N=82$ |  |  |  |
|  |  | 95\% CI |  |  | 95\% CI |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n $\%$ | LL | UL | n \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 13.4 | 0.1 | 17.8 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
| Infections and infestations (10021881) | Gastroenteritis (10017888) | 13.4 | 0.1 | 17.8 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit
Table 8.238 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  | 18-49ys |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=56 \end{aligned}$ |  |  | Placebo |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=153 \end{aligned}$ |  |  |  | Placebo$N=159$ |  |  |
|  |  |  | $\begin{gathered} 95 \% \\ \mathrm{CI} \end{gathered}$ |  | $\begin{gathered} 95 \% \\ \mathrm{CI} \end{gathered}$ |  |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL | UL n | n\% |  | L UL | JL | \% | LL | UL | L | \% |  |  |
| At least one symptom |  | 11.8 | 80.0 | 09.60 | 0.0 | 0.0 |  | 6.0 | 0.0 | 0.0 | 02.4 | 4 | 0.0 | 0. | 2.3 |
| Infections and infestations (10021881) | $\begin{aligned} & \text { Gastroenteritis } \\ & (10017888) \end{aligned}$ | 11.8 | 80.0 | 09.60 | 0.0 | 0.0 |  | 6.00 | 0.0 | 0.0 | 02.4 | 40 | 0.0 |  | 02.3 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.239 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 30-day (Days 0-29) post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  | 18-49ys |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=29 \end{aligned}$ |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=30 \end{gathered}$ |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=84 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=82 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  | N $\quad 95 \% \mathrm{Cl}$ |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL | UL | n \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 931.0 | 15.3 | 50.8 | 826.7 | 12.3 | 45.9 | 22 | 26.2 | 17.2 | 36.9 | 24 | 29.3 | 19.7 | 40.4 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 00.0 | 0.0 | 11.9 | 13.3 | 0.1 | 17.2 | 2 | 2.4 | 0.3 | 8.3 | 2 | 2.4 | 0.3 | 8.5 |
|  | Febrile neutropenia (10016288) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 4 | 4.8 | 1.3 | 11.7 | 2 | 2.4 | 0.3 | 8.5 |
|  | Neutropenia (10029354) | 00.0 | 0.0 | 11.9 | 13.3 | 0.1 | 17.2 | 2 | 2.4 | 0.3 | 8.3 | 2 | 2.4 | 0.3 | 8.5 |
|  | Thrombocytopenia (10043554) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 13.4 | 0.1 | 17.80 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 13.4 | 0.1 | 17.80 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Abdominal pain (10000081) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Abdominal pain upper (10000087) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |
|  | Constipation (10010774) | 00.0 | 0.0 | 11.9 | 13.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 2 | 2.4 | 0.3 | 8.5 |
|  | Diarrhoea (10012735) | 13.4 | 0.1 | 17.8 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Dyspepsia (10013946) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Dysphagia (10013950) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Gastrooesophageal reflux disease (10017885) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Haemorrhoids (10019022) | 00.0 | 0.0 | 11.9 | 13.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Mouth ulceration (10028034) | 00.0 | 0.0 | 11.9 | 13.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Nausea (10028813) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 3 | 3.6 | 0.7 | 10.1 | 0 | 0.0 | 0.0 | 4.4 |
|  | Odynophagia (10030094) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Stomatitis (10042128) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Swollen tongue (10042727) | 13.4 | 0.1 | 17.8 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Vomiting (10047700) | 00.0 | 0.0 | 11.93 | 310.0 | 2.1 | 26.5 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 3 | 3.6 | 0.7 | 10.1 | 0 | 0.0 | 0.0 | 4.4 |
|  | Injection site mass (10022081) | 00.0 | 0.0 | 11.90 | 00.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |

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$18-49 y s=$ Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.240 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 30-day (Days 0-29) post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=56 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=60 \end{aligned}$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=153 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=159 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 10 | 17.9 | 8.9 | 30.4 | 11 | 18.3 | 9.5 | 30.4 | 26 | 17.0 | 11.4 | 23.9 | 30 | 18.9 | 13.1 | 25.8 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | .0.9 | 2 | 1.3 | 0.2 | 4.6 | 2 | 1.3 | 0.2 | 4.5 |
|  | Febrile neutropenia (10016288) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 4 | 2.6 | 0.7 | 6.6 | 3 | 1.9 | 0.4 | 5.4 |
|  | Neutropenia (10029354) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 3 | 2.0 | 0.4 | 5.6 | 2 | 1.3 | 0.2 | 4.5 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Cardiac disorders (10007541) | Tachycardia (10043071) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 0.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Congenital, familial and genetic disorders (10010331) | Hypertrophic cardiomyopathy (10020871) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Ear and labyrinth disorders (10013993) | Neurosensory hypoacusis (10067587) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
| Gastrointestinal disorders (10017947) | Abdominal discomfort (10000059) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Abdominal pain (10000081) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 0.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Abdominal pain upper (10000087) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Constipation (10010774) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 2 | 1.3 | 0.2 | 4.5 |
|  | Diarrhoea (10012735) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Dyspepsia (10013946) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 0.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Dysphagia (10013950) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Gastrooesophageal reflux disease (10017885) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Haemorrhoids (10019022) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Nausea (10028813) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | . 6.0 | 3 | 2.0 | 0.4 | 5.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | - | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Stomatitis (10042128) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Swollen tongue (10042727) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Vomiting (10047700) | 0 | 0.0 | 0.0 | 6.4 | 3 | 5.0 | 1.0 | 1.013.9 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
| General disorders and administration site conditions (10018065) | Asthenia (10003549) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | 0.0 | 3 | 2.0 | 0.4 | 5.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Injection site mass (10022081) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |

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|  |  | 18-49ys |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=56 \end{aligned}$ |  |  |  | Placebo$N=60$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=153 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Placebo } \\ & \mathrm{N}=159 \end{aligned}$ |  |  |  |
|  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  |  | 95\% CI |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% |  |  | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Mucosal inflammation (10028116) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0. | . 06 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0. | . 06 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
| Hepatobiliary disorders (10019805) | Hepatic pain (10019705) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | . 06 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Hepatomegaly (10019842) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | . 06 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0. | . 08 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
| Infections and infestations (10021881) | Abdominal abscess (10060921) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0. | . 06 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Candida infection (10074170) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | . 06 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Cellulitis (10007882) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 |  | . 08 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Gastroenteritis (10017888) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 |  | . 06 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Infected dermal cyst (10071367) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | . 06 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Kidney infection (10023424) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | . 06 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Lower respiratory tract infection (10024968) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | . 06 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Nasopharyngitis (10028810) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 |  |  | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Neutropenic sepsis (10049151) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 |  | . 06 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 2 | 1.3 | 0.2 | 4.5 |
|  | Oropharyngeal candidiasis (10050346) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | . 06 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Post procedural infection (10067268) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 |  | . 06 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Respiratory tract infection (10062352) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | . 06 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Sepsis (10040047) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | . 06 | 6.0 | 2 | 1.3 | 0.2 | 4.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Subcutaneous abscess (10042343) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 |  | . 08 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Upper respiratory tract infection (10046306) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | . 06 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Urosepsis (10048709) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | . 06 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Injury, poisoning and procedural complications (10022117) | Gastrostomy failure (10050056) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 |  | . 06 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Radius fracture (10037802) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  |  | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Seroma (10040102) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  |  | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Investigations (10022891) | Electrocardiogram abnormal (10014363) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  |  | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Platelet count decreased (10035528) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | . 06 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
| Metabolism and nutrition disorders (10027433) | Decreased appetite (10061428) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  |  | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Hypomagnesaemia (10021027) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  |  | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Musculoskeletal and connective tissue disorders (10028395) | Back pain (10003988) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 |  | . 06 |  | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |

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|  |  |  |  |  |  |  |  |  |  |  |  |  |  | 0y |  |  |  |
|  |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =56 \end{aligned}$ |  |  |  | $\begin{aligned} & \text { ceb } \\ & == \end{aligned}$ |  |  |  | $\begin{aligned} & \text { Z/su } \\ & =15 \end{aligned}$ |  |  |  |  |  |
|  |  |  |  |  | \% CI |  |  |  | \% Cl |  |  |  | CI |  |  |  | \% CI |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Muscle spasms (10028334) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Neck pain (10028836) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Pain in extremity (10033425) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 2 | 1.3 | 0.2 | 4.6 | 0 | 0.0 | 0.0 | 2.3 |
| Neoplasms benign, malignant and unspecified (incl cysts and | Adenocarcinoma of colon (10001167) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
| polyps) (10029104) | Prostate cancer (10060862) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 |  | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
| Nervous system disorders (10029205) | Dizziness (10013573) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Headache (10019211) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Hepatic encephalopathy (10019660) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Motor dysfunction (10061296) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Neuropathy peripheral (10029331) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Paraesthesia (10033775) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Seizure (10039906) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 1 | 0.6 | 0.0 | 3.5 |
|  | Syncope (10042772) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
| Psychiatric disorders (10037175) | Anxiety (10002855) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 2 | 1.3 | 0.2 | 4.5 |
|  | Hydronephrosis (10020524) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Cough (10011224) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
|  | Epistaxis (10015090) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Hiccups (10020039) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Pleural effusion (10035598) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Pulmonary embolism (10037377) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |
| Skin and subcutaneous tissue disorders (10040785) | Erythema (10015150) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Rash maculo-papular (10037868) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Rash pruritic (10037884) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 1 | 0.6 | 0.0 | 3.5 |
|  | Scar pain (10049002) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Skin haemorrhage (10064265) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Urticaria (10046735) | 1 | 1.8 | 0.0 | 9.6 | 0 | 0.0 | 0.0 | 6.0 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
| Vascular disorders (10047065) | Embolism (10061169) | 0 | 0.0 | 0.0 | 6.4 | 1 | 1.7 | 0.0 | 8.9 | 0 | 0.0 | 0.0 | 2.4 | 0 | 0.0 | 0.0 | 2.3 |
|  | Thrombosis (10043607) | 0 | 0.0 | 0.0 | 6.4 | 0 | 0.0 | 0.0 | 6.0 | 1 | 0.7 | 0.0 | 3.6 | 0 | 0.0 | 0.0 | 2.3 |

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18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses with the symptom
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.241 Global Summary of unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | 18-49ys |  | $\geq 50 y s$ |  | All |  |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |
| Number of subjects with at least one unsolicited symptom reported | 25 | 27 | 73 | 74 | 98 | 101 |
| Number of doses followed by at least one unsolicited symptom | 40 | 46 | 109 | 117 | 149 | 163 |
| Number of unsolicited symptoms classified by MedDRA Preferred Term* | 130 | 100 | 276 | 288 | 406 | 388 |
| Number of unsolicited symptoms reported** | 136 | 103 | 285 | 297 | 421 | 400 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.242 Global Summary of grade 3 unsolicited signs and symptoms reported within the 30 -day (Days $0-29$ ) post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  | 18-49ys |  | $\geq$ 50ys |  | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su |
|  | Placebo |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 3 | 4 | 15 | 11 | 18 |
| Number of doses followed by at least one unsolicited symptom | 4 | 4 | 18 | 11 | 22 |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 4 | 5 | 19 | 17 | 23 |
| Number of unsolicited symptoms reported** | 4 | 5 | 19 | 17 | 22 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once ** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.243 Global Summary of unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  | 18-49ys |  |  | $\geq$ 50ys |  |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su |
|  | Placebo |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 4 | 2 | 6 | 7 | 10 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.244 Global Summary of grade 3 unsolicited signs and symptoms reported with causal relationship to vaccination, within the 30-day (Days 0-29) post-vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | 18-49ys |  | $\geq$ 50ys |  | All |  |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |
| Number of subjects with at least one unsolicited symptom reported | 1 | 0 | 0 | 0 | 1 | 0 |
| Number of doses followed by at least one unsolicited symptom | 1 | 0 | 0 | 0 | 1 | 0 |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 1 | 0 | 0 | 0 | 1 | 0 |
| Number of unsolicited symptoms reported** | 1 | 0 | 0 | 0 | 1 | 0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.245 Global Summary of unsolicited signs and symptoms reported with medically attended visit, within the 30-day (Days 0-29) postvaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  | Group |  |  |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :---: | :---: | :---: | :---: | :---: | :---: |
|  | 18-49ys |  |  |  |  |  |  |  |  | $\geq$ 50ys |  | All |
|  | HZ/su | Placebo | HZ/su | Placebo | HZ/su | Placebo |  |  |  |  |  |  |
| Number of subjects with at least one unsolicited symptom reported | 9 | 8 | 22 | 24 | 31 | 32 |  |  |  |  |  |  |
| Number of doses followed by at least one unsolicited symptom | 10 | 11 | 26 | 30 | 36 | 41 |  |  |  |  |  |  |
| Number of unsolicited symptoms classified by MedDRA Preferred <br> Term* | 12 | 17 | 48 | 43 | 60 | 60 |  |  |  |  |  |  |
| Number of unsolicited symptoms reported** | 12 | 17 | 48 | 43 | 60 | 60 |  |  |  |  |  |  |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 8.246 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to 30 days post last vaccination by age strata (ATP cohort for safety up to 30 days post last vaccination)

No records exist in this table

Table 8.247 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from 30 days post last vaccination up to the study end by age strata (ATP cohort for safety up to the study end)

|  |  | 18-49ys |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=29 \end{aligned}$ |  | Placebo$N=30$ |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=84 \end{aligned}$ |  |  |  | Placebo$N=82$ |  |  |
|  |  | 95\% CI |  | 95\% CI |  |  |  | $\begin{aligned} & 95 \% \\ & \hline \end{aligned}$ |  |  | $\begin{aligned} & 95 \% \\ & \hline \end{aligned}$ |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL UL | n $\%$ |  | UL | n\% |  | L UL | L n | \% |  | UL |
| At least one symptom |  | 00.0 | 0.011 .90 | 00.0 | 00.0 | 011.6 | 00.0 | 0.0 | . 4.3 | . 31 | 1.2 | 0.0 | 06.6 |
| $\begin{aligned} & \text { Endocrine disorders } \\ & \text { (10014698) } \end{aligned}$ | Autoimmune thyroiditis $(10049046)$ | 00.0 | 0.011 .90 |  | 0.0 | 011.6 | 00.0 |  |  | . 31 | 1.2 | 0.0 | 06.6 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.248 Percentage of subjects reporting the occurrence of potential Immune Mediated Diseases classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to the study end by age strata (ATP cohort for safety up to the study end)

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=29 \end{aligned}$ |  |  |  | Placebo$N=30$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=84 \end{aligned}$ |  |  |  | Placebo$N=82$ |  |  |  |
|  |  |  | 95\% CI |  |  | 95\% CI |  |  |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |  |  | $\begin{gathered} 95 \% \\ \mathrm{Cl} \end{gathered}$ |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) |  | \% | LL | UL |  | \% | LL | UL |  | \% | LL | UL |  | \% | LL | UL |
| At least one symptom |  | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 |  | 1.2 | 0.0 | 6.6 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.249 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from the first vaccination up to 30 days post last vaccination by age strata (ATP cohort for safety up to 30 days post last vaccination)


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|  |  | 18-49ys |  |  |  | $\geq 50 y s$ |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=29 \end{aligned}$ |  | Placebo$N=30$ |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=84 \end{aligned}$ |  |  | Placebo$N=82$ |  |  |
|  |  | 95\% CI |  | 95\% CI |  |  | 95\% CI |  | 95\% CI |  |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) | n \% | LL UL | n \% | LL UL | n | \% | LL UL | n | \% | LL UL |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 00.0 | 0.011 .9 | 00.0 | 0.011 .6 | 0 | 0.0 | 0.04 .3 | 2 | 2.4 | 0.38 .5 |
|  | Hydronephrosis (10020524) | 00.0 | 0.011 .9 | 00.0 | 0.011 .6 | 0 | 0.0 | 0.04 .3 | 1 | 1.2 | 0.06 .6 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Pleural effusion (10035598) | 00.0 | 0.011 .9 | 00.0 | 0.011 .6 | 0 | 0.0 | 0.04 .3 | 1 | 1.2 | 0.06 .6 |
|  | Pulmonary embolism (10037377) | 00.0 | 0.011 .9 | 00.0 | 0.011 .6 | - | 1.2 | 0.06 .5 | 0 | 0.0 | 0.04 .4 |
| Skin and subcutaneous tissue disorders (10040785) | Skin haemorrhage (10064265) | 00.0 | 0.011 .9 | 13.3 | 0.117 .2 |  | 0.0 | 0.04 .3 | 0 | 0.0 | 0.04 .4 |
| Vascular disorders (10047065) | Thrombosis (10043607) | 00.0 | 0.011 .9 | 00.0 | 0.011 .6 | 1 | 1.2 | 0.06 .5 | 0 | 0.0 | 0.04 .4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.250 Global Summary of serious adverse events reported from the first vaccination up to 30 days post last vaccination by age strata (ATP cohort for safety up to $\mathbf{3 0}$ days post last vaccination)


Table 8.251 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relation to vaccination from first vaccination up to 30 days post last vaccination by age strata (ATP cohort for safety up to 30 days post last vaccination)

No records exist in this table

Table 8.252 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from 30 days post last vaccination up to the study end by age strata (ATP cohort for safety up to the study end)


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|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=29 \end{aligned}$ |  |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=30 \end{gathered}$ |  |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=84 \end{aligned}$ |  |  | $\begin{gathered} \text { Placebo } \\ \mathrm{N}=82 \end{gathered}$ |  |  |  |
|  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) |  | \% | LL | UL |  | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
|  | Lung neoplasm malignant (10058467) |  | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |
|  | Malignant melanoma (10025650) |  | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Metastases to central nervous system (10059282) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Metastases to liver (10027457) |  | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Non-small cell lung cancer (10061873) |  | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Ovarian cancer (10033128) |  | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Prostate cancer (10060862) |  | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Rectal cancer metastatic (10055097) |  | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Squamous cell carcinoma of lung (10041826) |  | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Tongue neoplasm malignant stage unspecified (10043966) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Tumour haemorrhage (10049750) |  | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Uterine leiomyosarcoma (10046799) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
| Renal and urinary disorders (10038359) | Acute kidney injury (10069339) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
| Respiratory, thoracic and mediastinal disorders (10038738) | Bronchial obstruction (10006440) |  | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 |  | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Pleural effusion (10035598) |  | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |
|  | Pulmonary embolism (10037377) |  | 0.0 | 0.0 | 11.9 | 2 | 6.7 | 0.8 | 22.1 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Respiratory failure (10038695) |  | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 |  | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
| Surgical and medical procedures (10042613) | Abdominal hernia repair (10060802) |  | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
| Vascular disorders (10047065) | Superior vena cava occlusion (10058988) |  | 0.0 | 0.0 | 11.9 |  | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50$ ys $=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%$ = number/percentage of subjects reporting the symptom at least once
95\% CI = exact 95\% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.253 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, from 30 days post last vaccination up to the study end by age strata (ATP cohort for safety up to the study end)

No records exist in this table

Table 8.254 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term from first vaccination up to the study end by age strata (ATP cohort for safety up to the study end)

|  |  | 18-49ys |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=29 \end{aligned}$ |  |  |  | Placebo$N=30$ |  |  |  | $\begin{aligned} & \mathrm{HZ} / \mathrm{su} \\ & \mathrm{~N}=84 \end{aligned}$ |  |  |  | Placebo$N=82$ |  |  |  |
|  |  |  | 95\% CI |  |  | 95\% CI |  |  |  | 95\% CI |  |  |  |  |  | 95\% CI |  |
| Primary System Organ Class (CODE) | Preferred Term (CODE) |  | \% | LL | UL |  | \% | LL | UL | n | \% | LL | UL | n | \% | LL | UL |
| At least one symptom |  | 5 | 17.2 | 5.8 | 35.8 | 9 | 30.0 | 14.7 | 49.4 | 31 | 36.9 | 26.6 | 48.1 | 32 | 39.0 | 28.4 | 50.4 |
| Blood and lymphatic system disorders (10005329) | Anaemia (10002034) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 2 | 2.4 | 0.3 | 8.3 | 3 | 3.7 | 0.8 | 10.3 |
|  | Febrile neutropenia (10016288) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 6 | 7.1 | 2.7 | 14.9 | 2 | 2.4 | 0.3 | 8.5 |
|  | Neutropenia (10029354) |  | 3.4 | 0.1 | 17.8 | 1 | 3.3 | 0.1 | 17.2 | 1 | 1.2 | 0.0 | 6.5 | 3 | 3.7 | 0.8 | 10.3 |
|  | Pancytopenia (10033661) |  | 3.4 | 0.1 | 17.8 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Thrombocytopenia (10043554) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 2 | 2.4 | 0.3 | 8.5 |
| Cardiac disorders (10007541) | Cardiac arrest (10007515) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Cardiac failure (10007554) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Cardiac failure congestive (10007559) | 0 | 0.0 | 0.0 | 11.9 | 1 | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Myocardial infarction (10028596) | 0 | 0.0 | 0.0 | 11.9 |  | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
| Endocrine disorders (10014698) | Autoimmune thyroiditis (10049046) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
| Gastrointestinal disorders (10017947) | Constipation (10010774) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 2 | 2.4 | 0.3 | 8.5 |
|  | Diarrhoea (10012735) | 0 | 0.0 | 0.0 | 11.9 |  | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Dysphagia (10013950) |  | 0.0 | 0.0 | 11.9 |  | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Enteritis (10014866) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Mouth ulceration (10028034) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Nausea (10028813) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Odynophagia (10030094) | 0 | 0.0 | 0.0 | 11.9 |  | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Oesophagitis (10030216) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
| General disorders and administration site conditions (10018065) | Death (10011906) | 0 | 0.0 | 0.0 | 11.9 | 0 | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
|  | Mucosal inflammation (10028116) | 0 | 0.0 | 0.0 | 11.9 |  | 0.0 | 0.0 | 11.6 | 2 | 2.4 | 0.3 | 8.3 | 0 | 0.0 | 0.0 | 4.4 |
|  | Pyrexia (10037660) | 0 | 0.0 | 0.0 | 11.9 |  | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 1 | 1.2 | 0.0 | 6.6 |
| Hepatobiliary disorders (10019805) | Cholangitis acute (10008605) | 0 | 0.0 | 0.0 | 11.9 |  | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |
| Immune system disorders (10021428) | Drug hypersensitivity (10013700) | 0 | 0.0 | 0.0 | 11.9 |  | 3.3 | 0.1 | 17.2 | 0 | 0.0 | 0.0 | 4.3 | 0 | 0.0 | 0.0 | 4.4 |
| Infections and infestations (10021881) | Anal abscess (10048946) |  | 0.0 | 0.0 | 11.9 |  | 0.0 | 0.0 | 11.6 | 0 | 0.0 | 0.0 | 4.3 | 1 | 1.2 | 0.0 | 6.6 |
|  | Bacteraemia (10003997) | 0 | 0.0 | 0.0 | 11.9 |  | 0.0 | 0.0 | 11.6 | 1 | 1.2 | 0.0 | 6.5 | 0 | 0.0 | 0.0 | 4.4 |

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18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
$\mathrm{N}=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval; LL = Lower Limit, UL = Upper Limit

Table 8.255 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, from first vaccination up to the study end by age strata (ATP cohort for safety up to the study end)

No records exist in this table

Table 8.256 Global Summary of potential immune mediated diseases reported from the first vaccination up to 30 days post last vaccination by age strata (ATP cohort for safety up to 30 days post last vaccination)

No records exist in this table

Table 8.257 Number and percentage of subjects with fatal outcome reported up to the study end by age strata (ATP cohort for safety up to the study end)

|  | 18-49ys |  | $\geq$ 50ys |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | HZ/su | Placebo | HZ/su | Placebo |  |  |
|  | $\mathrm{N}=\mathbf{2 9}$ | $\mathrm{N}=\mathbf{3 0}$ | $\mathrm{N}=\mathbf{8 4}$ | $\mathrm{N}=\mathbf{8 2}$ |  |  |
| Characteristics | n | $\%$ | n | $\%$ | n | $\%$ |
| n | $\%$ |  |  |  |  |  |
| Fatalities | 1 | 3.4 | 2 | 6.7 | 11 | 13.1 |

$18-49 y s=$ Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of subjects with at least one administered dose
$\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once

Table 8.258 Percentage of subjects with concomitant medication during the 30day (Day 0-29) post vaccination period by age strata (ATP cohort for safety up to 30 days post last vaccination)

|  | 18-49ys |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HZ/su |  |  |  |  | Placebo |  |  |  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |
|  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |  |  |  |
|  | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL | N | $n$ | \% | LL | UL |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 29 | 27 | 93.1 | 77.2 | 99.2 | 30 | 29 | 96.7 | 82.8 | 99.9 | 84 | 81 | 96.4 | 89.9 | 99.3 | 82 | 77 | 93.9 | 86.3 | 98.0 |
| Steroids to prevent chemotherapy nausea and vomiting | 29 | 25 | 86.2 | 68.3 | 96.1 | 30 | 26 | 86.7 | 69.3 | 96.2 | 84 | 73 | 86.9 | 77.8 | 93.3 | 82 | 69 | 84.1 | 74.4 | 91.3 |
| Any in anticipation of study vaccine reaction | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 84 | 0 | 0.0 | 0.0 | 4.3 | 82 | 0 | 0.0 | 0.0 | 4.4 |
| Any chronic use | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 1 | 3.3 | 0.1 | 17.2 | 84 | 4 | 4.8 | 1.3 | 11.7 | 82 | 6 | 7.3 | 2.7 | 15.2 |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 27 | 22 | 81.5 | 61.9 | 93.7 | 30 | 27 | 90.0 | 73.5 | 97.9 | 69 | 64 | 92.8 | 83.9 | 97.6 | 77 | 64 | 83.1 | 72.9 | 90.7 |
| Steroids to prevent chemotherapy nausea and vomiting | 27 | 21 | 77.8 | 57.7 | 91.4 | 30 | 23 | 76.7 | 57.7 | 90.1 | 69 | 57 | 82.6 | 71.6 | 90.7 | 77 | 56 | 72.7 | 61.4 | 82.3 |
| Any in anticipation of study vaccine reaction | 27 | 0 | 0.0 | 0.0 | 12.8 | 30 | 0 | 0.0 | 0.0 | 11.6 | 69 | 0 | 0.0 | 0.0 | 5.2 | 77 | 0 | 0.0 | 0.0 | 4.7 |
| Any chronic use | 27 |  | 3.7 | 0.1 | 19.0 | 30 | 1 | 3.3 | 0.1 | 17.2 | 69 | 1 | 1.4 | 0.0 | 7.8 | 77 | 6 | 7.8 | 2.9 | 16.2 |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 56 | 49 | 87.5 | 75.9 | 94.8 | 60 | 56 | 93.3 | 83.8 | 98.2 | 153 | 145 | 94.8 | 90.0 | 97.7 | 159 | 141 | 88.7 | 82.7 | 93.2 |
| Steroids to prevent chemotherapy nausea and vomiting | 56 | 46 | 82.1 | 69.6 | 91.1 | 60 | 49 | 81.7 | 69.6 | 90.5 | 153 | 130 | 85.0 | 78.3 | 90.2 | 159 | 125 | 78.6 | 71.4 | 84.7 |
| Any in anticipation of study vaccine reaction | 56 | 0 | 0.0 | 0.0 | 6.4 | 60 | 0 | 0.0 | 0.0 | 6.0 | 153 | 0 | 0.0 | 0.0 | 2.4 | 159 | 0 | 0.0 | 0.0 | 2.3 |
| Any chronic use | 56 |  | 1.8 | 0.0 | 9.6 | 60 | 2 | 3.3 | 0.4 | 11.5 | 153 | 5 | 3.3 | 1.1 | 7.5 | 159 | 12 | 7.5 | 4.0 | 12.8 |
| Overall/subject |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Any | 29 | 28 | 96.6 | 82.2 | 99.9 | 30 | 30 | 100 | 88.4 | 100 | 84 | 81 | 96.4 | 89.9 | 99.3 | 82 | 80 | 97.6 | 91.5 | 99.7 |
| Steroids to prevent chemotherapy nausea and vomiting | 29 | 27 | 93.1 | 77.2 | 99.2 | 30 | 28 | 93.3 | 77.9 | 99.2 | 84 | 73 | 86.9 | 77.8 | 93.3 | 82 | 70 | 85.4 | 75.8 | 92.2 |
| Any in anticipation of study vaccine reaction | 29 | 0 | 0.0 | 0.0 | 11.9 | 30 | 0 | 0.0 | 0.0 | 11.6 | 84 | 0 | 0.0 | 0.0 | 4.3 | 82 | 0 | 0.0 | 0.0 | 4.4 |
| Any chronic use | 29 | 1 | 3.4 | 0.1 | 17.8 | 30 | 2 | 6.7 | 0.8 | 22.1 | 84 | 5 | 6.0 | 2.0 | 13.3 | 82 | 10 | 12.2 | 6.0 | 21.3 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one administered dose
$n / \%=$ number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
$\mathrm{N}=$ number of administered doses
$\mathrm{n} / \%=$ number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
$95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, $\mathrm{LL}=$ Lower Limit, UL = Upper Limit

## Table 8.259 Number of days with local symptoms during the solicited postvaccination period by age strata (Total Vaccinated Cohort)

| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Pain | Dose 1 | 18-49ys | HZ/su | 26 | 2.9 | 1.0 | 2.0 | 2.0 | 4.0 | 7.0 |
|  |  |  | Placebo | 2 | 2.0 | 1.0 | 1.0 | 2.0 | 3.0 | 3.0 |
|  |  | $\geq 50 y s$ | HZ/su | 57 | 2.8 | 1.0 | 2.0 | 2.0 | 3.0 | 7.0 |
|  | Dose 2 | 18-49ys | HZ/su | 19 | 2.5 | 1.0 | 1.0 | 2.0 | 3.0 | 6.0 |
|  |  |  | Placebo | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 33 | 2.8 | 1.0 | 2.0 | 2.0 | 4.0 | 7.0 |
|  |  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |
|  | Overall/dose | 18-49ys | HZ/su | 45 | 2.7 | 1.0 | 1.0 | 2.0 | 4.0 | 7.0 |
|  |  |  | Placebo | 6 | 1.5 | 1.0 | 1.0 | 1.0 | 2.0 | 3.0 |
|  |  | $\geq 50 y s$ | HZ/su | 90 | 2.8 | 1.0 | 2.0 | 2.0 | 4.0 | 7.0 |
|  |  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |
| Redness | Dose 1 | 18-49ys | HZ/su | 11 | 4.0 | 1.0 | 3.0 | 4.0 | 6.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 22 | 3.4 | 1.0 | 2.0 | 3.0 | 5.0 | 7.0 |
|  | Dose 2 | 18-49ys | HZ/su | 8 | 3.4 | 1.0 | 1.0 | 2.5 | 6.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 12 | 3.7 | 1.0 | 2.5 | 4.0 | 4.5 | 6.0 |
|  | Overall/dose | 18-49ys | HZ/su | 19 | 3.7 | 1.0 | 2.0 | 3.0 | 6.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 34 | 3.5 | 1.0 | 2.0 | 4.0 | 5.0 | 7.0 |
| Swelling | Dose 1 | 18-49ys | HZ/su | 6 | 3.8 | 2.0 | 2.0 | 3.5 | 5.0 | 7.0 |
|  |  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 9 | 3.7 | 2.0 | 2.0 | 4.0 | 5.0 | 6.0 |
|  | Dose 2 | 18-49ys | HZ/su | 4 | 3.3 | 1.0 | 1.5 | 2.5 | 5.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 4 | 4.3 | 2.0 | 3.0 | 4.0 | 5.5 | 7.0 |
|  | Overall/dose | 18-49ys | HZ/su | 10 | 3.6 | 1.0 | 2.0 | 2.5 | 5.0 | 7.0 |
|  |  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 13 | 3.8 | 2.0 | 2.0 | 4.0 | 5.0 | 7.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.260 Number of days with local symptoms by age strata (Total Vaccinated Cohort)

| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Pain | Dose 1 | 18-49ys | HZ/su | 26 | 3.2 | 1.0 | 2.0 | 2.0 | 4.0 | 15.0 |
|  |  |  | Placebo | 2 | 2.0 | 1.0 | 1.0 | 2.0 | 3.0 | 3.0 |
|  |  | $\geq 50 y s$ | HZ/su | 57 | 2.8 | 1.0 | 2.0 | 2.0 | 3.0 | 7.0 |
|  | Dose 2 | 18-49ys | HZ/su | 19 | 2.5 | 1.0 | 1.0 | 2.0 | 3.0 | 6.0 |
|  |  |  | Placebo | 4 | 1.3 | 1.0 | 1.0 | 1.0 | 1.5 | 2.0 |
|  |  | $\geq 50 y s$ | HZ/su | 33 | 3.1 | 1.0 | 2.0 | 2.0 | 4.0 | 11.0 |
|  |  |  | Placebo | 1 | 17.0 | 17.0 | 17.0 | 17.0 | 17.0 | 17.0 |
|  | Overall/dose | 18-49ys | HZ/su | 45 | 2.9 | 1.0 | 1.0 | 2.0 | 4.0 | 15.0 |
|  |  |  | Placebo | 6 | 1.5 | 1.0 | 1.0 | 1.0 | 2.0 | 3.0 |
|  |  | $\geq 50 y s$ | HZ/su | 90 | 2.9 | 1.0 | 2.0 | 2.0 | 4.0 | 11.0 |
|  |  |  | Placebo | 1 | 17.0 | 17.0 | 17.0 | 17.0 | 17.0 | 17.0 |
| Redness | Dose 1 | 18-49ys | HZ/su | 11 | 5.1 | 1.0 | 3.0 | 4.0 | 7.0 | 15.0 |
|  |  | $\geq 50 y s$ | HZ/su | 22 | 3.7 | 1.0 | 2.0 | 3.0 | 5.0 | 10.0 |
|  | Dose 2 | 18-49ys | HZ/su | 8 | 4.0 | 1.0 | 1.0 | 2.5 | 7.0 | 10.0 |
|  |  | $\geq 50 y s$ | HZ/su | 12 | 4.5 | 1.0 | 2.5 | 4.0 | 5.0 | 11.0 |
|  | Overall/dose | 18-49ys | HZ/su | 19 | 4.6 | 1.0 | 2.0 | 3.0 | 7.0 | 15.0 |
|  |  | $\geq 50 y s$ | HZ/su | 34 | 4.0 | 1.0 | 2.0 | 4.0 | 5.0 | 11.0 |
| Swelling | Dose 1 | 18-49ys | HZ/su | 6 | 6.3 | 2.0 | 2.0 | 3.5 | 13.0 | 14.0 |
|  |  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 9 | 4.0 | 2.0 | 2.0 | 4.0 | 5.0 | 9.0 |
|  | Dose 2 | 18-49ys | HZ/su | 4 | 4.0 | 1.0 | 1.5 | 2.5 | 6.5 | 10.0 |
|  |  | $\geq 50 y s$ | HZ/su | 4 | 5.0 | 2.0 | 3.0 | 4.0 | 7.0 | 10.0 |
|  | Overall/dose | 18-49ys | HZ/su | 10 | 5.4 | 1.0 | 2.0 | 2.5 | 10.0 | 14.0 |
|  |  |  | Placebo | 1 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 13 | 4.3 | 2.0 | 2.0 | 4.0 | 5.0 | 10.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom (during the solicited post-vaccination period and beyond)
Q1 $=25$ th percentile
Q3 $=75$ th percentile

## Table 8.261 Solicited local symptoms ongoing beyond the 7-day (Days 0-6) post-vaccination period by age strata (Total

 Vaccinated Cohort)|  |  | 18-49ys |  |  |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  |  | Placebo |  |  |  |  |  | HZ/su |  |  |  |  |  | Placebo |  |  |  |  |
|  |  | Time to resolution (days) |  |  |  |  |  | Time to resolution (days) |  |  |  |  |  | Time to resolution (days) |  |  |  |  |  | Time to resolution (days) |  |  |  |  |
| Symptoms | Type | N |  | s n | q1 | median | q3 |  |  | s n | q1 | median | q3 | N | N | Ns n | n $q 1$ | median | q3 | N |  |  | median | q3 |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | Any |  | 126 | 61 | 8 | 8 | 8 | 30 | 2 | 0 | - | - | - | 81 | 57 | 570 | -- | - | - | 80 | 0 | 0- | - | - |
|  | Grade 3 | 31 | 14 | 0 | - | - | - | 30 | 0 | 0 | - | - | - | 81 | 4 | 40 | -- | - | - | 80 | 0 | 0- | - | - |
| Redness | Any | 31 | 111 | 12 | 3 | 6 | 9 | 30 | 0 | 0 | - | - | - | 81 |  | 222 | 23 | 3 | 3 | 80 | 0 | 0- | - | - |
|  | Grade 3 | 31 | 10 | 0 | - | - | - | 30 | 0 | 0 | - | - | - | 81 | 2 | 20 | - | - | - | 80 | 0 | 0 - |  | - |
| Swelling | Any | 31 | 16 | 2 | 6 | 7.5 | 9 | 30 | 1 | 0 | - | - | - | 81 | 9 | 91 | 13 | 3 | 3 | 80 | 0 | 0 - | - | - |
|  | Grade 3 | 31 | 10 | 0 | - | - | - | 30 | 0 | 0 | - | - | - | 81 | 0 | 0 | -- | - | - | 80 | 0 | 0 - |  | - |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | Any | 29 | 19 | 90 | - | - | - | 29 | 4 | 0 | - | - | - | 69 | 33 | 332 | 23 | 5 | 7 | 76 | 1 | 110 | 10 | 10 |
|  | Grade 3 | 29 | 1 | 0 | - | - | - | 29 | 0 | 0 | - | - | - | 69 | 3 | 32 | 23 | 5 | 7 | 76 | 0 | 0 - |  | - |
| Redness | Any | 29 | 8 | 2 | 2 | 2.5 | 3 | 29 | 0 | 0 | - | - | - | 69 |  | 122 | 23 | 5 | 7 | 76 | 0 | 0 - | - | - |
|  | Grade 3 | 29 | 0 | 0 | - | - | - | 29 | 0 | 0 | - | - | - | 69 | 0 | 0 | - | - | - | 76 | 0 | 0 - | - | - |
| Swelling | Any | 29 | 4 | 1 | 3 | 3 | 3 | 29 | 0 | 0 | - | - | - | 69 | 4 | 41 | 13 | 3 | 3 | 76 | 0 | 0 - |  | - |
|  | Grade 3 | 29 | 0 | 0 | - | - | - | 29 | 0 | 0 | - | - | - | 69 | 0 | 0 | -- | - | - | 76 | 0 | 0 - | - | - |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pain | Any | 60 | 45 | 51 | 8 | 8 | 8 | 59 | 6 | 0 | - |  | - |  |  |  | 23 | 5 | 7 | 156 | 1 | 110 | 10 | 10 |
|  | Grade 3 | 60 | 5 | 0 | - | - | - | 59 | 0 | 0 | - | - | - | 150 | 507 | 72 | 23 | 5 | 7 | 156 | 0 | 0 - |  | - |
| Redness | Any | 60 | 19 | 94 | 2.5 | 3 | 6 | 59 | 0 | 0 | - | - | - | 150 | 5034 | 344 | 43 | 3 | 5 | 156 | 0 | 0- | - | - |
|  | Grade 3 | 60 | 0 | 0 | - | - | - | 59 | 0 | 0 | - | - | - |  | 502 | 20 | - | - | - | 156 | 0 | 0 - | - | - |
| Swelling | Any | 60 | 10 | 03 | 3 | 6 | 9 | 59 | 1 | 0 | - | - | - |  | 5013 | 132 | 23 | 3 | 3 | 156 | 0 | 0 - | - | - |
|  | Grade 3 | 60 | 0 | 0 | - | - | - | 59 | 0 | 0 | - | - | - |  | 50 | 0 | 0- | - | - | 156 | 0 | 0 - | - | - |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of documented doses
Ns = total number of reports for a given symptom
$\mathrm{n}=$ number of symptoms that were ongoing after the follow-up period

## CONFIDENTIAL

Time to resolution : number of days beyond the end of the follow-up period q1 $=25$ th percentile
q3 $=75$ th percentile

## Table 8.262 Number of days with general symptoms during the solicited postvaccination period by age strata (Total Vaccinated Cohort)

| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Fatigue | Dose 1 | 18-49ys | HZ/su | 17 | 3.3 | 1.0 | 2.0 | 3.0 | 4.0 | 7.0 |
|  |  |  | Placebo | 14 | 4.1 | 1.0 | 2.0 | 5.0 | 6.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 39 | 3.7 | 1.0 | 1.0 | 4.0 | 6.0 | 7.0 |
|  |  |  | Placebo | 30 | 4.4 | 1.0 | 2.0 | 5.0 | 6.0 | 7.0 |
|  | Dose 2 | 18-49ys | HZ/su | 18 | 4.8 | 1.0 | 4.0 | 5.0 | 7.0 | 7.0 |
|  |  |  | Placebo | 18 | 4.0 | 1.0 | 2.0 | 4.0 | 6.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 39 | 4.4 | 1.0 | 2.0 | 5.0 | 7.0 | 7.0 |
|  |  |  | Placebo | 39 | 4.8 | 1.0 | 4.0 | 5.0 | 7.0 | 7.0 |
|  | Overall/dose | 18-49ys | HZ/su | 35 | 4.1 | 1.0 | 2.0 | 4.0 | 6.0 | 7.0 |
|  |  |  | Placebo | 32 | 4.0 | 1.0 | 2.0 | 4.0 | 6.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 78 | 4.1 | 1.0 | 2.0 | 4.0 | 7.0 | 7.0 |
|  |  |  | Placebo | 69 | 4.7 | 1.0 | 3.0 | 5.0 | 7.0 | 7.0 |
| Gastrointestinal symptoms | Dose 1 | 18-49ys | HZ/su | 8 | 3.1 | 1.0 | 2.0 | 2.5 | 4.0 | 7.0 |
|  |  |  | Placebo | 6 | 5.0 | 1.0 | 4.0 | 5.5 | 7.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 24 | 3.0 | 1.0 | 1.0 | 2.5 | 4.5 | 7.0 |
|  |  |  | Placebo | 15 | 3.8 | 1.0 | 2.0 | 4.0 | 6.0 | 7.0 |
|  | Dose 2 | 18-49ys | HZ/su | 16 | 4.6 | 1.0 | 3.0 | 4.5 | 6.5 | 7.0 |
|  |  |  | Placebo | 13 | 3.6 | 2.0 | 2.0 | 3.0 | 4.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 25 | 4.6 | 2.0 | 2.0 | 4.0 | 7.0 | 7.0 |
|  |  |  | Placebo | 26 | 4.3 | 1.0 | 2.0 | 4.0 | 7.0 | 7.0 |
|  | Overall/dose | 18-49ys | HZ/su | 24 | 4.1 | 1.0 | 2.5 | 4.0 | 6.0 | 7.0 |
|  |  |  | Placebo | 19 | 4.1 | 1.0 | 2.0 | 3.0 | 6.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 49 | 3.8 | 1.0 | 2.0 | 3.0 | 6.0 | 7.0 |
|  |  |  | Placebo | 41 | 4.1 | 1.0 | 2.0 | 4.0 | 6.0 | 7.0 |
| Headache | Dose 1 | 18-49ys | HZ/su | 10 | 2.2 | 1.0 | 1.0 | 2.0 | 3.0 | 5.0 |
|  |  |  | Placebo | 9 | 2.6 | 1.0 | 1.0 | 2.0 | 3.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 18 | 3.2 | 1.0 | 1.0 | 2.0 | 6.0 | 7.0 |
|  |  |  | Placebo | 15 | 3.3 | 1.0 | 2.0 | 2.0 | 5.0 | 6.0 |
|  | Dose 2 | 18-49ys | HZ/su | 9 | 3.3 | 1.0 | 2.0 | 2.0 | 6.0 | 7.0 |
|  |  |  | Placebo | 12 | 2.6 | 1.0 | 1.0 | 2.0 | 3.5 | 6.0 |
|  |  | $\geq 50 y s$ | HZ/su | 20 | 3.4 | 1.0 | 1.5 | 3.0 | 5.5 | 7.0 |
|  |  |  | Placebo | 13 | 3.4 | 1.0 | 2.0 | 2.0 | 5.0 | 7.0 |
|  | Overall/dose | 18-49ys | HZ/su | 19 | 2.7 | 1.0 | 1.0 | 2.0 | 3.0 | 7.0 |
|  |  |  | Placebo | 21 | 2.6 | 1.0 | 1.0 | 2.0 | 3.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 38 | 3.3 | 1.0 | 1.0 | 2.0 | 6.0 | 7.0 |
|  |  |  | Placebo | 28 | 3.4 | 1.0 | 2.0 | 2.0 | 5.0 | 7.0 |
| Myalgia | Dose 1 | 18-49ys | HZ/su | 15 | 2.3 | 1.0 | 1.0 | 2.0 | 3.0 | 5.0 |
|  |  |  | Placebo | 3 | 6.7 | 6.0 | 6.0 | 7.0 | 7.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 35 | 3.2 | 1.0 | 2.0 | 3.0 | 5.0 | 7.0 |
|  |  |  | Placebo | 14 | 2.8 | 1.0 | 1.0 | 2.0 | 5.0 | 6.0 |
|  | Dose 2 | 18-49ys | HZ/su | 11 | 3.1 | 1.0 | 2.0 | 3.0 | 4.0 | 7.0 |
|  |  |  | Placebo | 6 | 4.7 | 1.0 | 3.0 | 5.5 | 6.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 21 | 4.0 | 1.0 | 2.0 | 4.0 | 7.0 | 7.0 |
|  |  |  | Placebo | 17 | 4.5 | 1.0 | 3.0 | 5.0 | 7.0 | 7.0 |
|  | Overall/dose | 18-49ys | HZ/su | 26 | 2.7 | 1.0 | 1.0 | 2.5 | 3.0 | 7.0 |
|  |  |  | Placebo | 9 | 5.3 | 1.0 | 5.0 | 6.0 | 7.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 56 | 3.5 | 1.0 | 2.0 | 3.0 | 5.0 | 7.0 |
|  |  |  | Placebo | 31 | 3.7 | 1.0 | 2.0 | 3.0 | 6.0 | 7.0 |
| Shivering | Dose 1 | 18-49ys | HZ/su | 9 | 1.6 | 1.0 | 1.0 | 1.0 | 2.0 | 3.0 |
|  |  |  | Placebo | 5 | 2.4 | 1.0 | 1.0 | 1.0 | 2.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 18 | 2.2 | 1.0 | 1.0 | 2.0 | 3.0 | 5.0 |
|  |  |  | Placebo | 8 | 2.1 | 1.0 | 1.0 | 2.0 | 2.5 | 5.0 |


| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Dose 2 | 18-49ys | HZ/su | 7 | 2.6 | 1.0 | 1.0 | 2.0 | 4.0 | 7.0 |
|  |  |  | Placebo | 8 | 2.4 | 1.0 | 1.0 | 2.0 | 3.0 | 6.0 |
|  |  | $\geq 50 y s$ | HZ/su | 13 | 3.9 | 1.0 | 2.0 | 3.0 | 7.0 | 7.0 |
|  |  |  | Placebo | 9 | 3.1 | 1.0 | 1.0 | 3.0 | 4.0 | 7.0 |
|  | Overall/dose | 18-49ys | HZ/su | 16 | 2.0 | 1.0 | 1.0 | 1.0 | 2.5 | 7.0 |
|  |  |  | Placebo | 13 | 2.4 | 1.0 | 1.0 | 2.0 | 2.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 31 | 2.9 | 1.0 | 1.0 | 2.0 | 4.0 | 7.0 |
|  |  |  | Placebo | 17 | 2.6 | 1.0 | 1.0 | 2.0 | 4.0 | 7.0 |
| Temperature | Dose 1 | 18-49ys | HZ/su | 4 | 2.5 | 1.0 | 1.0 | 1.5 | 4.0 | 6.0 |
|  |  | $\geq 50 y s$ | HZ/su | 9 | 1.8 | 1.0 | 1.0 | 1.0 | 1.0 | 5.0 |
|  |  |  | Placebo | 4 | 2.0 | 1.0 | 1.0 | 1.0 | 3.0 | 5.0 |
|  | Dose 2 | 18-49ys | HZ/su | 4 | 1.8 | 1.0 | 1.0 | 1.0 | 2.5 | 4.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | $\geq 50 y s$ | HZ/su | 4 | 2.0 | 1.0 | 1.5 | 2.0 | 2.5 | 3.0 |
|  | Overall/dose | 18-49ys | HZ/su | 8 | 2.1 | 1.0 | 1.0 | 1.0 | 3.0 | 6.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | $\geq 50 y s$ | HZ/su | 13 | 1.8 | 1.0 | 1.0 | 1.0 | 2.0 | 5.0 |
|  |  |  | Placebo | 4 | 2.0 | 1.0 | 1.0 | 1.0 | 3.0 | 5.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of doses with the symptom
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.263 Number of days with general symptoms by age strata (Total Vaccinated Cohort)

| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Fatigue | Dose 1 | 18-49ys | HZ/su | 17 | 7.4 | 1.0 | 2.0 | 3.0 | 4.0 | 49.0 |
|  |  |  | Placebo | 14 | 4.5 | 1.0 | 2.0 | 5.0 | 7.0 | 8.0 |
|  |  | $\geq 50 y s$ | HZ/su | 39 | 9.0 | 1.0 | 1.0 | 4.0 | 6.0 | 105.0 |
|  |  |  | Placebo | 30 | 11.0 | 1.0 | 2.0 | 5.5 | 7.0 | 76.0 |
|  | Dose 2 | 18-49ys | HZ/su | 18 | 13.9 | 1.0 | 4.0 | 5.0 | 7.0 | 161.0 |
|  |  |  | Placebo | 18 | 6.7 | 1.0 | 2.0 | 4.5 | 6.0 | 43.0 |
|  |  | $\geq 50 y s$ | HZ/su | 39 | 5.2 | 1.0 | 2.0 | 5.0 | 7.0 | 24.0 |
|  |  |  | Placebo | 39 | 12.3 | 1.0 | 4.0 | 6.0 | 7.0 | 139.0 |
|  | Overall/dose | 18-49ys | HZ/su | 35 | 10.7 | 1.0 | 2.0 | 4.0 | 7.0 | 161.0 |
|  |  |  | Placebo | 32 | 5.8 | 1.0 | 2.0 | 5.0 | 7.0 | 43.0 |
|  |  | $\geq 50 y s$ | HZ/su | 78 | 7.1 | 1.0 | 2.0 | 4.0 | 7.0 | 105.0 |
|  |  |  | Placebo | 69 | 11.8 | 1.0 | 3.0 | 6.0 | 7.0 | 139.0 |
| Gastrointestinal symptoms | Dose 1 | 18-49ys | HZ/su | 8 | 3.3 | 1.0 | 2.0 | 2.5 | 4.0 | 8.0 |
|  |  |  | Placebo 6 | 6 | 10.2 | 1.0 | 4.0 | 5.5 | 7.0 | 38.0 |
|  |  | $\geq 50 y s$ | HZ/su | 24 | 3.6 | 1.0 | 1.0 | 3.0 | 5.5 | 11.0 |
|  |  |  | Placebo | 15 | 9.6 | 1.0 | 2.0 | 4.0 | 14.0 | 60.0 |
|  | Dose 2 | 18-49ys | HZ/su | 16 | 11.4 | 1.0 | 3.0 | 4.5 | 7.0 | 104.0 |
|  |  |  | Placebo | 13 | 5.1 | 2.0 | 2.0 | 3.0 | 4.0 | 18.0 |
|  |  | $\geq 50 y s$ | HZ/su | 25 | 5.3 | 2.0 | 2.0 | 5.0 | 7.0 | 21.0 |
|  |  |  | Placebo | 26 | 7.2 | 1.0 | 3.0 | 5.5 | 7.0 | 55.0 |
|  | Overall/dose | 18-49ys | HZ/su | 24 | 8.7 | 1.0 | 2.5 | 4.0 | 6.5 | 104.0 |
|  |  |  | Placebo | 19 | 6.7 | 1.0 | 2.0 | 3.0 | 7.0 | 38.0 |
|  |  | $\geq 50 y s$ | HZ/su | 49 | 4.5 | 1.0 | 2.0 | 3.0 | 7.0 | 21.0 |
|  |  |  | Placebo | 41 | 8.0 | 1.0 | 2.0 | 5.0 | 7.0 | 60.0 |
| Headache | Dose 1 | 18-49ys | HZ/su | 10 | 2.2 | 1.0 | 1.0 | 2.0 | 3.0 | 5.0 |
|  |  |  | Placebo 9 | 9 | 2.6 | 1.0 | 1.0 | 2.0 | 3.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 18 | 6.8 | 1.0 | 1.0 | 2.0 | 7.0 | 66.0 |
|  |  |  | Placebo | 15 | 12.4 | 1.0 | 2.0 | 2.0 | 6.0 | 75.0 |
|  | Dose 2 | 18-49ys | HZ/su | 9 | 3.9 | 1.0 | 2.0 | 2.0 | 7.0 | 11.0 |
|  |  |  | Placebo | 12 | 2.6 | 1.0 | 1.0 | 2.0 | 3.5 | 6.0 |
|  |  | $\geq 50 y s$ | HZ/su 20 | 20 | 4.7 | 1.0 | 1.5 | 3.0 | 5.5 | 29.0 |
|  |  |  | Placebo | 13 | 5.5 | 1.0 | 2.0 | 2.0 | 7.0 | 25.0 |
|  | Overall/dose | 18-49ys | HZ/su | 19 | 3.0 | 1.0 | 1.0 | 2.0 | 3.0 | 11.0 |
|  |  |  | Placebo 2 | 21 | 2.6 | 1.0 | 1.0 | 2.0 | 3.0 | 7.0 |
|  |  | $\geq 50 y s$ | HZ/su | 38 | 5.7 | 1.0 | 1.0 | 2.0 | 6.0 | 66.0 |
|  |  |  | Placebo | 28 | 9.2 | 1.0 | 2.0 | 2.0 | 6.5 | 75.0 |
| Myalgia | Dose 1 | 18-49ys | HZ/su | 15 | 2.3 | 1.0 | 1.0 | 2.0 | 3.0 | 5.0 |
|  |  |  | Placebo 3 | 3 | 7.3 | 6.0 | 6.0 | 7.0 | 9.0 | 9.0 |
|  |  | $\geq 50 y s$ | HZ/su | 35 | 6.0 | 1.0 | 2.0 | 3.0 | 5.0 | 105.0 |
|  |  |  | Placebo | 14 | 3.6 | 1.0 | 1.0 | 2.0 | 6.0 | 11.0 |
|  | Dose 2 | 18-49ys | HZ/su 11 | 11 | 3.8 | 1.0 | 2.0 | 3.0 | 5.0 | 10.0 |
|  |  |  | Placebo 6 | 6 | 10.7 | 1.0 | 3.0 | 5.5 | 6.0 | 43.0 |
|  |  | $\geq 50 y s$ | HZ/su | 21 | 4.2 | 1.0 | 2.0 | 4.0 | 7.0 | 9.0 |
|  |  |  | Placebo | 17 | 11.3 | 1.0 | 3.0 | 5.0 | 7.0 | 112.0 |
|  | Overall/dose | 18-49ys | HZ/su | 26 | 3.0 | 1.0 | 1.0 | 3.0 | 4.0 | 10.0 |
|  |  |  | Placebo 9 | 9 | 9.6 | 1.0 | 5.0 | 6.0 | 7.0 | 43.0 |
|  |  | $\geq 50 y s$ | HZ/su | 56 | 5.3 | 1.0 | 2.0 | 3.0 | 5.0 | 105.0 |
|  |  |  | Placebo | 31 | 7.8 | 1.0 | 2.0 | 3.0 | 6.0 | 112.0 |
| Shivering | Dose 1 | 18-49ys | HZ/su | 9 | 1.6 | 1.0 | 1.0 | 1.0 | 2.0 | 3.0 |
|  |  |  | Placebo 5 | 5 | 8.6 | 1.0 | 1.0 | 1.0 | 2.0 | 38.0 |
|  |  | $\geq 50 y s$ | HZ/su | 18 | 2.3 | 1.0 | 1.0 | 2.0 | 3.0 | 7.0 |
|  |  |  | Placebo 8 | 8 | 2.1 | 1.0 | 1.0 | 2.0 | 2.5 | 5.0 |


| Solicited symptom | Dose | Sub-group | Group | N | Mean | Min | Q1 | Median | Q3 | Max |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Dose 2 | 18-49ys | HZ/su | 7 | 4.0 | 1.0 | 1.0 | 2.0 | 4.0 | 17.0 |
|  |  |  | Placebo 8 | 8 | 2.6 | 1.0 | 1.0 | 2.0 | 3.0 | 8.0 |
|  |  | $\geq 50 y s$ | HZ/su | 13 | 4.0 | 1.0 | 2.0 | 3.0 | 7.0 | 8.0 |
|  |  |  | Placebo | 9 | 3.6 | 1.0 | 1.0 | 3.0 | 4.0 | 9.0 |
|  | Overall/dose | 18-49ys | HZ/su | 16 | 2.6 | 1.0 | 1.0 | 1.0 | 2.5 | 17.0 |
|  |  |  | Placebo | 13 | 4.9 | 1.0 | 1.0 | 2.0 | 2.0 | 38.0 |
|  |  | $\geq 50 y s$ | HZ/su | 31 | 3.0 | 1.0 | 1.0 | 2.0 | 4.0 | 8.0 |
|  |  |  | Placebo | 17 | 2.9 | 1.0 | 1.0 | 2.0 | 4.0 | 9.0 |
| Temperature* | Dose 1 | 18-49ys | HZ/su | 4 | 2.5 | 1.0 | 1.0 | 1.5 | 4.0 | 6.0 |
|  |  | $\geq 50 y s$ | HZ/su | 9 | 1.8 | 1.0 | 1.0 | 1.0 | 1.0 | 5.0 |
|  |  |  | Placebo 4 | 4 | 9.8 | 1.0 | 1.0 | 7.0 | 18.5 | 24.0 |
|  | Dose 2 | 18-49ys | HZ/su | 4 | 1.8 | 1.0 | 1.0 | 1.0 | 2.5 | 4.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | $\geq 50 y s$ | HZ/su | 4 | 2.0 | 1.0 | 1.5 | 2.0 | 2.5 | 3.0 |
|  | Overall/dose | 18-49ys | HZ/su | 8 | 2.1 | 1.0 | 1.0 | 1.0 | 3.0 | 6.0 |
|  |  |  | Placebo | 1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
|  |  | $\geq 50 y s$ | HZ/su | 13 | 1.8 | 1.0 | 1.0 | 1.0 | 2.0 | 5.0 |
|  |  |  | Placebo | 4 | 9.8 | 1.0 | 1.0 | 7.0 | 18.5 | 24.0 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$N=$ number of doses with the symptom (during the solicited post-vaccination period and beyond)
Q1 $=25$ th percentile
Q3 $=75$ th percentile

Table 8.264 Solicited general symptoms ongoing beyond the 7-day (Days 0-6) post-vaccination period by age strata (Total Vaccinated Cohort)

|  |  | 18-49ys |  |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  | Placebo |  |  |  |  |  | HZ/su |  |  |  |  |  |  | Placebo |  |  |  |  |  |
|  |  | Time to resolution (days) |  |  |  |  | Time to resolution (days) |  |  |  |  |  | Time to resolution (days) |  |  |  |  |  |  | Time to resolution (days) |  |  |  |  |  |
| Symptoms | Type | N N | Ns n | q1 | median | q3 |  | Ns |  | q1 | median | q3 | N |  | Ns n |  | q1 | median | q3 | N | Ns |  | q1 | median | q3 |
| Dose 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | Any | 3117 | 174 | 26 | 34.5 | 43 |  | 14 | 4 | 1 | 2 | 3 | 81 |  | 396 | 6 | 3 | 22.5 | 57 | 80 | 30 | 10 | 19 | 23 | 28 |
|  | Grade 3 | 315 | 51 |  | - | - | 30 | 2 | 0 | - | - | - | 81 | 5 | 5 | 1 | 2 | 2 | 2 | 80 | 1 | 0 | - | - |  |
| Gastrointestinal symptoms | Any | 318 | 81 | 1 | 1 | 1 | 30 | 6 | 1 | 31 | 31 | 31 | 81 |  | 244 | 4 | 2 | 2 | 9 | 80 | 15 | 6 | 8 | 8 | 16 |
|  | Grade 3 | 311 | 10 | - | - | - | 30 | 2 | 1 | 31 | 31 | 31 | 81 | 1 | 1 | 1 | 2 | 2 | 2 | 80 | 3 | 1 | - | - | - |
| Headache | Any | 3110 | 101 | - | - | - | 30 | 9 | 0 | - | - | - | 81 |  | 183 | 3 | 2 | 32 | 62 | 80 | 15 | 3 | 10 | 57 | 69 |
|  | Grade 3 | 311 | 10 | - | - | - | 30 | 0 | 0 | - | - | - | 81 | 2 | 21 | 1 | - | - | - | 80 | 1 | 1 | 69 | 69 | 69 |
| Myalgia | Any |  | 151 | - | - | - | 30 | 3 |  | 2 | 2 | 2 | 81 |  | 353 | 3 | 2 | 50 | 98 | 80 | 14 | 2 | 2 | 5.5 | 9 |
|  | Grade 3 | 314 | 41 | - | - | - | 30 | 2 |  | 2 | 2 | 2 | 81 | 4 | 41 | 1 | 2 | 2 | 2 | 80 | 1 | 1 | 2 | 2 | 2 |
| Shivering | Any | 319 | 90 | - | - | - | 30 | 5 | 1 | 31 | 31 | 31 | 81 |  | 18 | 1 | 2 | 2 | 2 | 80 | 8 | 0 | - | - | - |
|  | Grade 3 | 312 | 20 | - | - | - | 30 | 0 | 0 | - | - | - | 81 | 3 | 3 | 1 | 2 | 2 | 2 | 80 | 2 | 0 | - | - | - |
| Temperature | Any | 314 | 40 | - | - | - | 30 | 0 | 0 | - | - | - | 81 | 9 | 9 | 0 | - | - | - | 80 | 4 | 2 | 12 | 15.5 | 19 |
|  | Grade 3 | 310 | 0 | - | - | - | 30 | 0 | 0 | - | - | - | 81 | 0 | 0 | 0 | - | - | - | 80 | 0 | 0 | - | - | - |
| Dose 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | Any 2 | 2918 | 184 | 4 | 6 | 154 |  | 18 | 5 | 5 | 8 | 36 | 68 |  | 395 | 5 | 1.5 | 6.5 | 14 | 75 | 39 | 13 | 5.5 | 8.5 | 63 |
|  | Grade 3 | 294 | 42 | 4 | 79 | 154 | 29 | 3 | 2 | 5 | 5 | 5 | 68 | 5 | 51 | 1 | 11 | 11 | 11 | 75 | 3 | 1 | 105 | 105 | 105 |
| Gastrointestinal symptoms | Any 29 | 2916 | 163 | 4 | 6 | 98 |  | 13 |  | 2 | 6 | 11 | 68 |  | 255 | 5 | 1.5 | 2 | 8 | 75 | 26 | 9 | 1 | 4 | 11 |
|  | Grade 3 | 292 | 20 | - | - | - | 29 | 2 | 1 | 11 | 11 | 11 | 68 | 3 | 1 | 1 | 14 | 14 | 14 | 75 | 1 | 1 | - | - | - |
| Headache | Any | 299 | 93 | 5 | 5 | 5 |  | 12 | 1 | - | - | - | 68 |  | 20 | 3 | 1 | 2 | 23 | 75 | 13 | 2 | 8 | 14 | 20 |
|  | Grade 3 | 291 | 11 | - |  | - | 29 | 2 | 0 | - | - | - | 68 | 2 | 2 | 0 | - | - | - | 75 | 0 | 0 | - | - | - |
| Myalgia | Any 29 | 291 | 113 | 3 | 4 | 5 | 29 | 6 |  | 36 | 36 | 36 | 68 |  | 21 | 3 | 1 | 1.5 | 2 | 75 | 17 | 3 | 10 | 57.5 | 105 |
|  | Grade 3 | 291 | 10 | - | - | - | 29 | 1 | 0 | - | - | - | 68 | 3 | 3 | 1 | 1 | 1 | 1 | 75 | 0 | 0 | - | - | - |
| Shivering | Any | 297 | 71 | 10 | 10 | 10 | 29 | 8 |  | 2 | 2 | 2 | 68 |  | 13 |  | 1 | 1 | 1 | 75 | 9 | 1 | 4 | 4 | 4 |
|  | Grade 3 | 291 | 10 |  | - | - | 29 | 0 | 0 | - | - | - | 68 | 2 | 2 | 0 | - | - | - | 75 | 1 | 0 | - | - | - |
| Temperature | Any 29 | 294 | 40 | - | - | - | 29 | 1 | 0 | - | - | - | 68 | 4 | 4 | 0 | - | - | - | 75 | 0 | 0 | - | - | - |
|  | Grade 3 | 290 | 0 | - | - | - | 29 | 0 | 0 | - | - | - | 68 | 0 | 0 | 0 | - | - | - | 75 | 0 | 0 | - | - | - |
| Overall/dose |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fatigue | Any 6 |  | 358 | 6 | 26 | 43 |  | 32 |  | 2 | 4 | 8 |  | 149 | 8 | 112 | 2 | 11.5 | 33 |  | 69 | 23 | 8 | 21 | 28 |


|  |  | 18-49ys |  |  |  |  |  |  |  |  |  |  |  |  | $\geq 50 y s$ |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/su |  |  |  |  |  | Placebo |  |  |  |  |  |  | HZ/su |  |  |  |  |  | Placebo |  |  |  |  |  |
|  |  | Time to resolution (days) |  |  |  |  |  | Time to resolution (days) |  |  |  |  |  |  | Time to resolution (days) |  |  |  |  |  | Time to resolution (days) |  |  |  |  |  |
| Symptoms | Type | N | Ns |  | q1 | median | q3 | N | N | S | q1 |  | median | q3 | N | Ns | n | q1 | median | q3 | N | Ns | n | q1 | median | q3 |
|  | Grade 3 | 60 | 9 | 3 | 4 | 79 | 154 | 59 | 5 | 2 | 5 | 5 | 5 | 5 | 149 | 10 | 2 | 2 | 6.5 | 11 | 155 | 4 | 1 | 105 | 105 | 105 |
| Gastrointestinal symptoms | Any | 60 | 24 | 4 | 2.5 | 5 | 52 | 59 | 19 | 9 | 4 |  | 8.5 | 21 | 149 | 49 | 9 | 2 | 2 | 9 | 155 | 41 | 15 | 2 | 6.5 | 13.5 |
|  | Grade 3 | 60 | 3 | 0 |  | - | - | 59 | 4 | 2 | 11 |  | 21 | 31 | 149 | 4 | 2 | 2 | 8 | 14 | 155 | 4 | 2 | - | - | - |
| Headache | Any | 60 | 19 | 4 | 5 | 5 | 5 | 59 | 21 | 1 | - |  |  | - | 149 | 38 | 6 | 2 | 2 | 23 | 155 | 28 | 5 | 10 | 20 | 57 |
|  | Grade 3 | 60 | 2 | 1 |  | - | - | 59 | 2 | 0 |  |  |  | - | 149 | 4 | 1 | - | - | - | 155 | 1 | 1 | 69 | 69 | 69 |
| Myalgia | Any | 60 | 26 | 4 | 3 | 4 | 5 | 59 | 9 | 5 | 2 |  | 19 | 36 | 149 | 56 | 6 | 1.5 | 2 | 50 | 155 | 31 | 5 | 5.5 | 9.5 | 57.5 |
|  | Grade 3 | 60 | 5 | 1 |  | - | - | 59 | 3 | 1 | 2 | 2 | 2 | 2 | 149 | 7 | 2 | 1 | 1.5 | 2 | 155 | 1 | 1 | 2 | 2 | 2 |
| Shivering | Any | 60 | 16 | 1 | 10 | 10 | 10 | 59 | 13 | 32 | 2 |  | 16.5 | 31 | 149 | 31 | 2 | 1 | 1.5 | 2 | 155 | 17 | 1 | 4 | 4 | 4 |
|  | Grade 3 | 60 | 3 | 0 |  | - | - | 59 | 0 | 0 | - |  |  | - | 149 | 5 | 1 | 2 | 2 | 2 | 155 | 3 | 0 | - | - | - |
| Temperature | Any | 60 | 8 | 0 |  | - | - | 59 | 1 | 0 | - |  |  | - | 149 | 13 | 0 | - | - | - | 155 | 4 | 2 | 12 | 15.5 | 19 |
|  | Grade 3 | 60 | 0 | 0 |  | - | - | 59 | 0 | 0 |  | - |  | - | 149 | 0 | 0 | - | - | - | 155 | 0 | 0 | - | - | - |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
$\mathrm{N}=$ number of documented doses
Ns = total number of reports for a given symptom
$\mathrm{n}=$ number of symptoms that were ongoing after the follow-up period
Time to resolution : number of days beyond the end of the follow-up period
q1 $=25$ th percentile
q3 $=75$ th percentile

Table 8.265 Incidence and nature of symptoms (solicited only) reported during the 7-day (Days 0-6) post-vaccination period and lasting beyond this period following each dose and overall (Total Vaccinated Cohort)

|  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | 95\% Cl |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | HZ/su | 112 | 19 | 17.0 | 10.5 | 25.2 | 112 | 15 | 13.4 | 7.7 | 21.1 | 112 | 6 | 5.4 | 2.0 | 11.3 |
|  | Placebo | 110 | 18 | 16.4 | 10.0 | 24.6 | 110 | 18 | 16.4 | 10.0 | 24.6 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Dose 2 | HZ/su | 98 | 14 | 14.3 | 8.0 | 22.8 | 97 | 12 | 12.4 | 6.6 | 20.6 | 98 | 4 | 4.1 | 1.1 | 10.1 |
|  | Placebo | 105 | 24 | 22.9 | 15.2 | 32.1 | 104 | 24 | 23.1 | 15.4 | 32.4 | 105 | 1 | 1.0 | 0.0 | 5.2 |
| Overall/dose | HZ/su | 210 | 33 | 15.7 | 11.1 | 21.4 | 209 | 27 | 12.9 | 8.7 | 18.2 | 210 | 10 | 4.8 | 2.3 | 8.6 |
|  | Placebo | 215 | 42 | 19.5 | 14.5 | 25.5 | 214 | 42 | 19.6 | 14.5 | 25.6 | 215 | 1 | 0.5 | 0.0 | 2.6 |
| Overall/subject | HZ/su | 112 | 27 | 24.1 | 16.5 | 33.1 | 112 | 22 | 19.6 | 12.7 | 28.2 | 112 | 9 | 8.0 | 3.7 | 14.7 |
|  | Placebo | 110 | 34 | 30.9 | 22.4 | 40.4 | 110 | 34 | 30.9 | 22.4 | 40.4 | 110 | 1 | 0.9 | 0.0 | 5.0 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.266 Incidence and nature of symptoms grade 3 (solicited only) reported during the 7-day (Days 0-6) post-vaccination period and lasting beyond this period following each dose and overall (Total Vaccinated Cohort)

|  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 95\% Cl |  |  |  |  | 95\% Cl |  |  |  |  | 95\% Cl |  |  |  |  |
|  | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N |  | \% | LL | UL |
| Dose 1 | HZ/su | 112 | 3 | 2.7 | 0.6 | 7.6 | 112 | 3 | 2.7 | 0.6 | 7.6 | 112 | 0 | 0.0 | 0.0 | 3.2 |
|  | Placebo | 110 | 5 | 4.5 | 1.5 | 10.3 | 110 | 5 | 4.5 | 1.5 | 10.3 | 110 | 0 | 0.0 | 0.0 | 3.3 |
| Dose 2 | HZ/su | 98 | 4 | 4.1 | 1.1 | 10.1 | 97 | 4 | 4.1 | 1.1 | 10.2 | 98 | 2 | 2.0 | 0.2 | 7.2 |
|  | Placebo | 105 | 5 | 4.8 | 1.6 | 10.8 | 104 | 5 | 4.8 | 1.6 | 10.9 | 105 | 0 | 0.0 | 0.0 | 3.5 |
| Overall/dose | HZ/su | 210 | 7 | 3.3 | 1.4 | 6.7 | 209 | 7 | 3.3 | 1.4 | 6.8 | 210 | 2 | 1.0 | 0.1 | 3.4 |
|  | Placebo | 215 | 10 | 4.7 | 2.3 | 8.4 | 214 | 10 | 4.7 | 2.3 | 8.4 | 215 | 0 | 0.0 | 0.0 | 1.7 |
| Overall/subject | HZ/su | 112 | 7 | 6.3 | 2.5 | 12.5 | 112 | 7 | 6.3 | 2.5 | 12.5 | 112 | 2 | 1.8 | 0.2 | 6.3 |
|  | Placebo | 110 |  | 8.2 |  | 15.0 | 110 | 9 | 8.2 | 3.8 | 15.0 | 110 |  |  |  | 3.3 |

HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered 95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.267 Incidence and nature of symptoms (solicited only) reported during the 7 -day (Days 0-6) post-vaccination period and lasting beyond this period following each dose and overall by age strata (Total Vaccinated Cohort)

|  |  |  | Any symptom |  |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  |  |  |  |  | 95\% Cl |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n | \% | LL | UL | N | n | \% | LL | UL | N |  | \% | LL | UL |
| Dose 1 | 18-49ys | HZ/su | 31 | 7 | 22.6 | 9.6 | 41.1 | 31 | 5 | 16.1 | 5.5 | 33.7 | 31 | 3 | 9.7 | 2.0 | 25.8 |
|  |  | Placebo | 30 | 4 | 13.3 | 3.8 | 30.7 | 30 | 4 | 13.3 | 3.8 | 30.7 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 81 | 12 | 14.8 | 7.9 | 24.4 | 81 | 10 | 12.3 | 6.1 | 21.5 | 81 | 3 | 3.7 | 0.8 | 10.4 |
|  |  | Placebo | 80 | 14 | 17.5 | 9.9 | 27.6 | 80 | 14 | 17.5 | 9.9 | 27.6 | 80 | 0 | 0.0 | 0.0 | 4.5 |
| Dose 2 | 18-49ys | HZ/su | 29 | 6 | 20.7 | 8.0 | 39.7 | 29 | 4 | 13.8 | 3.9 | 31.7 | 29 | 2 | 6.9 | 0.8 | 22.8 |
|  |  | Placebo | 29 | 7 | 24.1 | 10.3 | 43.5 | 29 | 7 | 24.1 | 10.3 | 43.5 | 29 | 0 | 0.0 | 0.0 | 11.9 |
|  | $\geq 50 y s$ | HZ/su | 69 | 8 | 11.6 | 5.1 | 21.6 | 68 | 8 | 11.8 | 5.2 | 21.9 | 69 | 2 | 2.9 | 0.4 | 10.1 |
|  |  | Placebo | 76 | 17 | 22.4 | 13.6 | 33.4 | 75 | 17 | 22.7 | 13.8 | 33.8 | 76 | 1 | 1.3 | 0.0 | 7.1 |
| Overall/dose | 18-49ys | HZ/su | 60 | 13 | 21.7 | 12.1 | 34.2 | 60 | 9 | 15.0 | 7.1 | 26.6 | 60 | 5 | 8.3 | 2.8 | 18.4 |
|  |  | Placebo | 59 | 11 | 18.6 | 9.7 | 30.9 | 59 | 11 | 18.6 | 9.7 | 30.9 | 59 | 0 | 0.0 | 0.0 | 6.1 |
|  | $\geq 50 y s$ | HZ/su | 150 | 20 | 13.3 | 8.3 | 19.8 | 149 | 18 | 12.1 | 7.3 | 18.4 | 150 | 5 | 3.3 | 1.1 | 7.6 |
|  |  | Placebo | 156 | 31 | 19.9 | 13.9 | 27.0 | 155 | 31 | 20.0 | 14.0 | 27.2 | 156 | 1 | 0.6 | 0.0 | 3.5 |
| Overall/subject | 18-49ys | HZ/su | 31 | 10 | 32.3 | 16.7 | 51.4 | 31 | 7 | 22.6 | 9.6 | 41.1 | 31 | 4 | 12.9 | 3.6 | 29.8 |
|  |  | Placebo | 30 | 8 | 26.7 | 12.3 | 45.9 | 30 | 8 | 26.7 | 12.3 | 45.9 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 81 | 17 | 21.0 | 12.7 | 31.5 | 81 | 15 | 18.5 | 10.8 | 28.7 | 81 | 5 | 6.2 | 2.0 | 13.8 |
|  |  | Placebo | 80 | 26 | 32.5 | 22.4 | 43.9 | 80 | 26 | 32.5 | 22.4 | 43.9 | 80 | 1 | 1.3 | 0.0 | 6.8 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered $95 \% \mathrm{Cl}=$ exact $95 \%$ confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.268 Incidence and nature of symptoms grade 3 (solicited only) reported during the 7 -day (Days 0-6) post-vaccination period and lasting beyond this period following each dose and overall by age strata (Total Vaccinated Cohort)

|  |  |  | Any symptom |  |  |  | General symptoms |  |  |  |  | Local symptoms |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 95\% CI |  |  |  |  |  |  | 95\% CI |  |  |  |  | 95\% CI |  |
|  | Sub-group | Group | N | n \% | LL | UL | N |  | \% | LL | UL | N | n | \% | LL | UL |
| Dose 1 | 18-49ys | HZ/su | 31 | 13.2 | 0.1 | 16.7 | 31 |  | 3.2 | 0.1 | 16.7 | 31 | 0 | 0.0 | 0.0 | 11.2 |
|  |  | Placebo | 30 | 26.7 | 0.8 | 22.1 | 30 | 2 | 6.7 | 0.8 | 22.1 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 81 | 22.5 | 0.3 | 8.6 | 81 | 2 | 2.5 | 0.3 | 8.6 | 81 | 0 | 0.0 | 0.0 | 4.5 |
|  |  | Placebo | 80 | 33.8 | 0.8 | 10.6 | 80 | 3 | 3.8 | 0.8 | 10.6 | 80 | 0 | 0.0 | 0.0 | 4.5 |
| Dose 2 | 18-49ys | HZ/su | 29 | 26.9 | 0.8 | 22.8 | 29 | 2 | 6.9 | 0.8 | 22.8 | 29 | 0 | 0.0 | 0.0 | 11.9 |
|  |  | Placebo | 29 | 310.3 | 2.2 | 27.4 | 29 | 3 | 10.3 | 2.2 | 27.4 | 29 | 0 | 0.0 | 0.0 | 11.9 |
|  | $\geq 50 y s$ | HZ/su | 69 | 22.9 | 0.4 | . 10.1 | 68 | 2 | 2.9 | 0.4 | 10.2 | 69 | 2 | 2.9 | 0.4 | 10.1 |
|  |  | Placebo | 76 | 22.6 | 0.3 | 9.2 | 75 | 2 | 2.7 | 0.3 | 9.3 | 76 | 0 | 0.0 | 0.0 | 4.7 |
| Overall/dose | 18-49ys | HZ/su | 60 | 35.0 | 1.0 | 13.9 | 60 | 3 | 5.0 | 1.0 | 13.9 | 60 | 0 | 0.0 | 0.0 | 6.0 |
|  |  | Placebo | 59 | 58.5 | 2.8 | 18.7 | 59 | 5 | 8.5 | 2.8 | 18.7 | 59 | 0 | 0.0 | 0.0 | 6.1 |
|  | $\geq 50 y s$ | HZ/su | 150 | 42.7 | 0.7 | 6.7 | 149 | 4 | 2.7 | 0.7 | 6.7 | 150 | 2 | 1.3 | 0.2 | 4.7 |
|  |  | Placebo | 156 | 53.2 | 1.0 | 7.3 | 155 | 5 | 3.2 | 1.1 | 7.4 | 156 | 0 | 0.0 | 0.0 | 2.3 |
| Overall/subject | 18-49ys | HZ/su | 31 | 39.7 | 2.0 | 25.8 | 31 | 3 | 9.7 | 2.0 | 25.8 | 31 | 0 | 0.0 | 0.0 | 11.2 |
|  |  | Placebo | 30 | 413.3 | 3.8 | 30.7 | 30 | 4 | 13.3 | 3.8 | 30.7 | 30 | 0 | 0.0 | 0.0 | 11.6 |
|  | $\geq 50 y s$ | HZ/su | 81 | 44.9 | 1.4 | 12.2 | 81 | 4 | 4.9 | 1.4 | 12.2 | 81 | 2 | 2.5 | 0.3 | 8.6 |
|  |  | Placebo | 80 | 56.3 | 2.1 | 14.0 | 80 | 5 | 6.3 | 2.1 | 14.0 | 80 | 0 | 0.0 | 0.0 | 4.5 |

18-49ys = Subjects aged between 18 and 49 years
$\geq 50 y s=$ Subjects aged 50 years and older
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
For each dose and overall/subject:
$\mathrm{N}=$ number of subjects with at least one documented dose
$\mathrm{n} / \%=$ number/percentage of subjects presenting at least one type of symptom whatever the study vaccine
administered
For overall/dose:
$\mathrm{N}=$ number of documented doses
$n / \%=$ number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered 95\% CI = exact 95\% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 8.269 Listing of withdrawn due to AEs, SAEs and solicited symptoms (Total Vaccinated Cohort)

| Sub-group | Group | StudySubject No. | Country | Gender | Race | AE Description | SAE | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PreChemo | HZ/su | PPD | France | M |  | PROGRESSION OF PROSTATE CANCER | Y | N | Fatal |
|  |  |  | United Kingdom | F | White - caucasian / european heritage | TACHYCARDIA | N | Y | Recovered / resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | ACUTE GASTROENTERITIS | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | HEPATIC ENCEPHALOPATHY | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | MUGUET CANDIDIASIS | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | PROTEIN CALORIC MALNUTRITION | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | DYSPHAGIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | ANEMIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | ODYNOPHAGIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | ESOPHAGITIS | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | RENAL FAILURE ACUTE | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | PROGRESSION OF COLORECTAL CARCINOMA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | BRAIN METASTASIS | Y | N | Not recovered / not resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | NEUTROPENIA FEBRILE | Y | N | Recovered / resolved |
|  |  |  | Spain | F | White - caucasian / european heritage | SEPSIS | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | STAGE IV COLON ADENOCARCINOMA PROGRESSION | Y | N | Fatal |


| Sub-group | Group | StudySubject No. | Country | Gender | Race | AE Description | SAE | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | Spain | M | White - caucasian / european heritage | DEATH, NOS | Y | N | Fatal |
|  |  |  | Spain | F | White - caucasian / european heritage | SUSPECIOUS INFECTION BY ZOSTER HERPES | N | N | Recovered / resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | RESPIRATORY INFECTION | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | LUNG SQUAMOUS CELL CARCINOMA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | BLADDER CARCINOMA PROGRESSION | Y | N | Fatal |
|  | Placebo |  | Canada | M | African heritage / african american | PROGRESSIVE NON SMALL CELL LUNG CANCER | Y | N | Fatal |
|  |  |  | France | M |  | PROGRESSIVE DISEASE OF TONG CANCER | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | NEUTROPENIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | ANEMIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | RESPIRATORY INFECTION | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | THROMBOCYTOPENIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | RENAL FAILURE ACUTE | Y | N | Recovered / resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | BILATERAL HYDRONEPHROSIS | Y | N | Recovered / resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | ANEMIA | Y | N | Not recovered / not resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | PULMONARY PROGRESSION OF THE PROSTATIC CANCER | Y | N | Not recovered / not resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | PLEURAL EFFUSION | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | SKIN BLEDDING | Y | N | Fatal |

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| Sub-group | Group | StudySubject No. | Country | Gender | Race | AE Description | SAE | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | Spain | M | White - caucasian / european heritage | LUNG CANCER PROGRESION | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | SUPERIOR CAVA VEIN COMPRESSION | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | LIPOSARCOMA DISEASE PROGRESSION | Y | N | Fatal |
|  |  |  | Spain | F | White - caucasian / european heritage | PNEUMONIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | RECTAL CANCER METASTATIC | Y | N | Fatal |
|  |  |  | Spain | F | White - caucasian / european heritage | DISEASE PROGRESSION (OVARIAN CANCER PROGRESSION | Y | N | Fatal |
| OnChemo | HZ/su |  | France | M |  | BLEEDING FROM HIS PRIMARY TUMOR | Y | N | Fatal |
|  |  |  | United Kingdom | F | White - caucasian / european heritage | LIVER METASTASES | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | PROGRESSION OF THE LUNG CANCER | Y | N | Fatal |
|  | Placebo |  | France | F |  | UTERINE LEIOMYOSARCOMA WORSENING | Y | N | Fatal |


| Sub-group | Group | StudySubject No. | Type of discontinuation |
| :---: | :---: | :---: | :---: |
| PreChemo | HZ/su | PPD | Study |
|  |  |  | Treatment <br> Dose : 2 at visit: VISIT 2 - M1 |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
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|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Treatment <br> Dose : 2 at visit: VISIT 2 - M1 |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  | Placebo |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |


| Sub-group | Group | StudySubject No. | Type of discontinuation |
| :---: | :---: | :---: | :---: |
|  |  | PPD | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
| OnChemo | HZ/su |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  | Placebo |  | Study |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
Missing = Missing
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group
Table 8.270 Details of potential immune-mediated disorders (pIMDs) reported as identified by predefined list of preferred terms and/or by investigator assessment up to study end (Total Vaccinated Cohort)

| Subgroup | Group | Patient ID | Country | Age <br> at <br> onset <br> (Y) | Gender | Race | Primary System Organ Class | Preferred term | Dose | Day of onset | Relation | Serious pIMD based on Investigator? | SAE <br> (Y/N) | Outcome | pIMD <br> Source |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| OnChemo | Placebo | PPD | Spain | 51 | Female | WHITE CAUCASIAN / EUROPEAN HERITAGE | Endocrine disorders | Autoimmune thyroiditis | 2 | 252 | N | Y | Y | Recovering / resolving | MedDRA and investigator |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
Missing = Missing
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Table 8.271 Listing of All SAEs (Total Vaccinated Cohort)

| Sub group | Group | Sub. <br> No. |  | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PreChemo | HZ/su | PPD | F | Korea Republic of | Asian - <br> East Asian <br> Heritage | 40 | Cancer recurrence in uoq of the right breast | Breast cancer recurrent | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | MD | 2 | 109 | 23 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 40 | Right breast tumor recurrence | Breast cancer recurrent | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | MD | 2 | 295 | 140 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 40 | Acute nasopharyngitis | Nasopharyngitis | Infections and infestations | HO | 2 | 21 | 6 | 3 | N | Recovered / resolved |
|  |  |  | F | Canada | White Caucasian / European Heritage | 69 | Pulmonary embolism | Pulmonary embolism | Respiratory, thoracic and mediastinal disorders | ER | 2 | 6 | 44 | 3 | N | Recovered / resolved |
|  |  |  | M | France |  | 83 | Progression of prostate cancer | Prostate cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | MD | 2 | 280 | 20 | 3 | N | Fatal |
|  |  |  | M | United Kingdom | White Caucasian / European Heritage | 65 | Left pleural effusion | Pleural effusion | Respiratory, thoracic and mediastinal disorders | HO | 2 | 59 | -7 | 2 | N | Recovered / resolved |
|  |  |  |  |  |  | 65 | Infection of pleural fluid | Pleural infection | Infections and infestations | HO | 2 | 66 | 17 | 2 | N | Recovered / resolved |

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| Sub group | Group | Sub. No. | Sex | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | M | Spain | White Caucasian / European Heritage | 68 | Brain metastasis | Metastases to central nervous system | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 259 |  | 3 | N | Not recovered / not resolved |
|  |  |  |  |  |  | 69 | Neutropenia febrile | Febrile neutropenia | Blood and lymphatic system disorders | HO | 2 | 366 | 10 | 2 | N | Recovered / resolved |
|  |  |  | F | Spain | White Caucasian / European Heritage | 52 | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | HO | 1 | 25 | 16 | 3 | N | Recovered / resolved |
|  |  |  | F | Spain | White Caucasian / European Heritage | 64 | Sepsis | Sepsis | Infections and infestations | MD | 2 | 4 | 1 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 72 | Epiglottitis | Epiglotitis | Infections and infestations | HO | 2 | 219 | 14 | 2 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 74 | Stage iv colon adenocarcinoma progression | Adenocarcinoma of colon | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 1 | 4 | 76 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 63 | Death, nos | Death | General disorders and administration site conditions | MD | 1 | 37 | 1 | 3 | N | Fatal |


| Sub group | Group | Sub. <br> No. | Sex | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{array}{\|c\|} \hline \text { MED } \\ \text { type } \end{array}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | M | Spain | White Caucasian / European Heritage | 59 | Buccal mucosa ulceration | Mouth ulceration | Gastrointestinal disorders | HO | 2 | 119 | 8 | 2 | N | Recovered / resolved |
|  |  |  |  |  |  | 59 | Cardiac infarction killip ii | Myocardial infarction | Cardiac disorders | HO | 2 | 148 | 21 | 2 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 74 | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | HO | 1 | 12 | 14 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 74 | Respiratory infection | Respiratory tract infection | Infections and infestations | HO | 2 | 157 | 17 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 69 | Lung squamous cell carcinoma | Squamous cell carcinoma of lung | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | MD | 2 | 148 | 95 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 45 | Non invasive bladder carcinoma | Bladder cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 99 | 58 | 1 | N | Recovered / resolved |
|  |  |  | F | Spain | White Caucasian / European Heritage | 60 | Diverticulitis | Diverticulitis | Infections and infestations | HO | 2 | 361 | 18 | 2 | N | Recovered / resolved |
|  |  |  | F | Spain | White Caucasian / European Heritage | 48 | Neutropenia | Neutropenia | Blood and lymphatic system disorders | HO | 2 | 75 | 4 | 2 | N | Recovered / resolved |

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| Sub group | Group | Sub. No. | Sex | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Placebo ${ }^{\text {PF }}$ | PPD | F | Korea Republic of | Asian - <br> South East <br> Asian <br> Heritage | 54 | Arthralgia | Arthralgia | Musculoskeletal and connective tissue disorders | HO | 2 | 205 | 84 | 2 | N | Recovered / resolved |
|  |  |  | F | Korea Republic of | Asian East Asian Heritage | 50 | Upper respiratory infection | Upper respiratory tract infection | Infections and infestations | HO | 2 | 241 | 6 | 3 | N | Recovered / resolved |
|  |  |  | F | Korea Republic of | Asian East Asian Heritage | 49 | Congestive heart failure | Cardiac failure congestive | Cardiac disorders | HO | 2 | 114 | 63 | 3 | N | Recovered / resolved |
|  |  |  | M | Korea Republic of | Asian East Asian Heritage | 54 | Colon cancer progress disease | Colon cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 145 |  | 2 | N | Not recovered / not resolved |
|  |  |  | M | Canada | White Caucasian / European Heritage | 69 | Melanoma malignant | Malignant melanoma | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | MD | 2 | 372 | 346 | 2 | N | Recovered / resolved with sequelae |
|  |  |  | M | Canada | African Heritage / African American | 70 | Progressive non small cell lung cancer | Non-small cell lung cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 186 | 50 | 3 | N | Fatal |

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| Sub group | Group | Sub. No. | Sex | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | M | France |  | 73 | Progressive disease of tong cancer | Tongue neoplasm malignant stage unspecified | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | MD | 2 | 159 | 1 |  | N | Fatal |
|  |  |  | M | United Kingdom | White Caucasian / European Heritage | 76 | Constipation | Constipation | Gastrointestinal disorders | MD | 2 | 110 | 15 | 2 | N | Recovered / resolved |
|  |  |  | F | United Kingdom | White Caucasian / European Heritage | 65 | Neutropenic sepsis | Neutropenic sepsis | Infections and infestations | HO | 1 | 24 | 5 | 2 | N | Recovered / resolved |
|  |  |  |  |  |  | 65 | Neutropenic sepsis | Neutropenic sepsis | Infections and infestations | HO | 2 | 12 | 10 | 2 | N | Recovered / resolved |
|  |  |  | M | United Kingdom | White Caucasian / European Heritage | 69 | Neutropenic sepsis | Neutropenic sepsis | Infections and infestations | HO | 2 | 67 | 13 | 3 | N | Recovered / resolved |
|  |  |  | F | United Kingdom | White Caucasian / European Heritage | 54 | Metastatic colorectal carcinoma | Colorectal cancer metastatic | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 264 | 29 | 3 | N | Recovered / resolved |
|  |  |  | F | United Kingdom | White Caucasian / European Heritage | 66 | Urinary sepsis | Urosepsis | Infections and infestations | HO | 2 | 8 | 6 |  | N | Recovered / resolved |

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| Sub group | Group | Sub. No. |  | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{array}{\|l\|} \hline \text { MED } \\ \text { type } \end{array}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | F | United Kingdom | White Caucasian / European Heritage | 62 | Skin rash | Rash | Skin and subcutaneous tissue disorders | HO | 2 | 6 | 41 | 1 | N | Recovered / resolved |
|  |  |  |  |  |  | 63 | Sepsis - origin unknown | Sepsis | Infections and infestations | HO | 2 | 69 | 11 | 1 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 69 | Anemia | Anaemia | Blood and lymphatic system disorders | HO | 2 | 259 | 4 | 3 | N | Fatal |
|  |  |  |  |  |  | 69 | Neutropenia | Neutropenia | Blood and lymphatic system disorders | HO | 2 | 259 | 4 | 3 | N | Fatal |
|  |  |  |  |  |  | 69 | Respiratory infection | Respiratory tract infection | Infections and infestations | HO | 2 | 259 | 4 | 3 | N | Fatal |
|  |  |  |  |  |  | 69 | Thrombocytopenia | Thrombocytopenia | Blood and lymphatic system disorders | HO | 2 | 259 | 4 | 2 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European | 87 | Renal failure acute | Acute kidney injury | Renal and urinary disorders | HO | 2 | 25 | 24 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 87 | Anemia | Anaemia | Blood and lymphatic system disorders | HO | 2 | 25 |  | 3 | N | Not recovered / not resolved |
|  |  |  |  |  |  | 87 | Bilateral hydronephrosis | Hydronephrosis | Renal and urinary disorders | HO | 2 | 7 | 40 | 3 | N | Recovered / resolved |

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| Sub group | Group | Sub. No. | Sex | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | F | Spain | White Caucasian / European Heritage | 45 | Pulmonary thromboembolism | Pulmonary embolism | Respiratory, thoracic and mediastinal disorders | HO | 2 | 207 | 593 | 2 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 63 | Right bronchi obstruction | Bronchial obstruction | Respiratory, thoracic and mediastinal disorders | HO | 2 | 266 | 68 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 63 | Pneumonia | Pneumonia | Infections and infestations | HO | 2 | 266 | 45 | 3 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 71 | Lung cancer progresion | Lung neoplasm malignant | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 128 | 8 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 71 | Seizures | Seizure | Nervous system disorders | HO | 2 | 3 | 13 | 2 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 47 | Liposarcoma disease progression | Liposarcoma | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 224 | 79 | 3 | N | Fatal |
|  |  |  |  |  |  | 47 | Superior cava vein compression | Superior vena cava occlusion | Vascular disorders | HO | 2 | 224 | 79 | 3 | N | Fatal |
|  |  |  | F | Spain | White Caucasian / European Heritage | 78 | Lung infection | Lung infection | Infections and infestations | ER | 2 | 138 | 17 | 3 | N | Recovered / resolved |

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| Sub group | Group | Sub. <br> No. |  | Country | Race | Age <br> at <br> onset <br> (Year) | Verbatim | Preferred term | Primary <br> System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD |  |  |  | 78 | Neutropenia | Neutropenia | Blood and lymphatic system disorders | ER | 2 | 138 | 17 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 78 | Pneumonia | Pneumonia | Infections and infestations | ER | 2 | 186 | 5 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 52 | Pleural effusion secondary to pneumoniae | Pleural effusion | Respiratory, thoracic and mediastinal disorders | HO | 2 | 348 | 46 | 1 | N | Recovered / resolved |
|  |  |  | F | Spain | White Caucasian / European Heritage | 58 | Anemia | Anaemia | Blood and lymphatic system disorders | HO | 1 | 21 | 7 | 2 | N | Recovered / resolved |
|  |  |  |  |  |  | 58 | Neutropenia | Neutropenia | Blood and lymphatic system disorders | HO | 1 | 21 | 7 | 2 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 68 | rectal cancer metastatic | Rectal cancer metastatic | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 213 | 108 | 2 | N | Fatal |
|  |  |  | F | Spain | White Caucasian / European Heritage | 57 | Clostridium bacteremia | Clostridium bacteraemia | Infections and infestations | HO | 2 | 379 | 9 | 2 | N | Recovered / resolved |


| Sub group | Group | Sub. <br> No. |  | Country | Race | Age <br> at <br> onset <br> (Year) | Verbatim | Preferred term | Primary <br> System Organ <br> Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 57 | Disease progression (ovarian cancer progression | Ovarian cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 338 | 88 | 3 | N | Fatal |
|  |  | PPD | F | Spain | White Caucasian / European Heritage | 40 | Neutropenia | Neutropenia | Blood and lymphatic system disorders | HO | 2 | 144 | 4 | 2 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 60 | Cecoileitis | Enteritis | Gastrointestinal disorders | HO | 2 | 282 | 7 | 2 | N | Recovered / resolved |
|  |  |  | M | Czech Republic | White Caucasian / European Heritage | 39 | Erbitux allergic reaction | Drug hypersensitivity | Immune system disorders | HO | 2 | 4 | 2 | 1 | N | Recovered / resolved |
| OnChemo | HZ/su | F |  | Korea Republic of | Asian East Asian Heritage | 58 | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | HO | 1 | 13 | 8 | 3 | N | Recovered / resolved |
|  |  |  |  | 59 |  | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | HO | 2 | 33 | 4 | 3 | N | Recovered / resolved |
|  |  |  |  | 59 |  | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | HO | 2 | 80 | 5 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | France | 48 | Gastrostomy failure | Gastrostomy failure | Injury, poisoning and procedural complications | HO | 1 | 28 | 9 | 1 | N | Recovered / resolved |

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| Sub group | Group | Sub. No. |  | Country | Race | Age <br> at <br> onset <br> (Year) | Verbatim | Preferred term | Primary <br> System Organ Class | MED <br> type | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD |  |  |  | 61 | Liver metastases | Metastases to liver | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 224 | 33 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 68 | Clostridium difficile infection | Clostridium difficile infection | Infections and infestations | HO | 1 | 39 | 16 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Clostridium difficile infection | Clostridium difficile infection | Infections and infestations | ER | 1 | 76 | 22 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Diarrhea | Diarrhoea | Gastrointestinal disorders | ER | 1 | 33 | 18 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Diarrhea | Diarrhoea | Gastrointestinal disorders | ER | 1 | 66 | 32 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | ER | 1 | 39 | 3 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Hypokalemia | Hypokalaemia | Metabolism and nutrition disorders | ER | 1 | 39 | 13 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Hyponatremia | Hyponatraemia | Metabolism and nutrition disorders | ER | 1 | 39 | 13 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | protein malnutrition | Malnutrition | Metabolism and nutrition disorders | HO | 1 | 91 | 14 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Mucositis | Mucosal inflammation | General disorders and administration site conditions | ER | 1 | 33 | 23 | 3 | N | Recovered / resolved |

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| Sub group | Group | Sub. No. | Sex | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | M | Spain | White Caucasian / European Heritage | 68 | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | HO | 2 | 8 | 15 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Gastroenteritis | Gastroenteritis | Infections and infestations | HO | 1 | 9 | 17 | 2 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Respiratory infectio | Respiratory tract infection | Infections and infestations | HO | 1 | 20 | 16 | 2 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European | 71 | Seizures cerebral | Seizure | Nervous system disorders | HO | 1 | 4 | 1 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 72 | Progression of the lung cancer | Lung neoplasm malignant | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 247 | 3 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 51 | Candidiasis | Candida infection | Infections and infestations | HO | 2 | 39 | 7 | 2 | N | Recovered / resolved |
|  |  |  |  |  |  | 51 | Mucositis | Mucosal inflammation | General disorders and administration site conditions | HO | 1 | 21 | 59 | 2 | N | Recovered / resolved |
|  |  |  |  |  |  | 51 | Neutropenia | Neutropenia | Blood and lymphatic system disorders | HO | 2 | 39 | 7 | 2 | N | Recovered / resolved |

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| Sub group | Group | Sub. No. | Sex | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 51 | Toxic pancytopenia | Pancytopenia | Blood and lymphatic system disorders | HO | 2 | 39 | 7 | 2 | N | Recovered / resolved |
|  | Placebo ${ }^{\text {P }}$ |  | M | Canada | White Caucasian / European Heritage | 63 | Compression fracture of 14 vertebra | Lumbar vertebral fracture | Injury, poisoning and procedural complications | HO | 2 | 59 |  | 2 | N | Not recovered / not resolved |
|  |  |  | F | France |  | 60 | Sepsis | Sepsis | Infections and infestations | HO | 2 | 173 | 34 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 61 | Uterine leiomyosarcoma worsening | Uterine leiomyosarcoma | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 344 | 1 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 84 | Acute renal failure | Acute kidney injury | Renal and urinary disorders | HO | 1 | 15 | 8 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 84 | Constipation | Constipation | Gastrointestinal disorders | HO | 1 | 6 | 13 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 84 | Thrombocytopenia | Thrombocytopenia | Blood and lymphatic system disorders | HO | 1 | 11 | 11 | 3 | N | Recovered / resolved |
|  |  |  | F | Spain | White Caucasian / European Heritage | 51 | Autoinmune thyroiditis | Autoimmune thyroiditis | Endocrine disorders | MD | 2 | 252 |  | 1 | N | Recovering / resolving |

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| Sub group | Group | Sub. No. | Sex | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 51 | Fever unknown origin | Pyrexia | General disorders and administration site conditions | HO | 1 | 16 | 14 | 2 | N | Recovered / resolved |
|  |  | PPD | M | Spain | White Caucasian / European Heritage | 54 | Virus hepatitis c (reactivation) | Hepatitis C | Infections and infestations | HO | 1 | 45 | 16 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 55 | Disease progresion (head and neck cancer) | Head and neck cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 123 |  | 2 | N | Not recovered / not resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 78 | Right costal pain | Musculoskeletal chest pain | Musculoskeletal and connective tissue disorders | HO | 2 | 69 | 142 | 2 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 73 | Neutropenic fever | Febrile neutropenia | Blood and lymphatic system disorders | HO | 1 | 6 | 13 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 73 | Neutropenic fever | Febrile neutropenia | Blood and lymphatic system disorders | HO | 2 | 10 | 4 | 1 | N | Recovered / resolved |
|  |  |  |  |  |  | 73 | Scrotal sebaceous cyst infected | Infected dermal cyst | Infections and infestations | ER | 1 | 28 | 9 | 1 | N | Recovered / resolved |
|  |  |  | F | Spain | White Caucasian / European Heritage | 60 | Abdominal hernia repair | Abdominal hernia repair | Surgical and medical procedures | HO | 2 | 265 | 1 | 1 | N | Recovered / resolved |

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PreChemo $=$ first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
Missing = Missing
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
MED = Medical Advice type (HO: hospitalisation, ER: emergency room visit, MD: medical practice visit)

Table 8.272 Listing of withdrawn due to AEs, SAEs and solicited symptoms (ATP cohort for safety up to the study end)

| Subgroup | Group | StudySubject No. | Country | Gender | Race | AE Description | SAE | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PreChemo | HZ/su | PPD | France | M |  | PROGRESSION OF PROSTATE CANCER | Y | N | Fatal |
|  |  |  | United Kingdom | F | White - caucasian / european heritage | TACHYCARDIA | N | Y | Recovered / resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | ACUTE GASTROENTERITIS | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | HEPATIC ENCEPHALOPATHY | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | MUGUET CANDIDIASIS | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | PROTEIN CALORIC MALNUTRITION | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | DYSPHAGIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | ANEMIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | ODYNOPHAGIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | ESOPHAGITIS | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | RENAL FAILURE ACUTE | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | PROGRESSION OF COLORECTAL CARCINOMA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | BRAIN METASTASIS | Y | N | Not recovered / not resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | NEUTROPENIA FEBRILE | Y | N | Recovered / resolved |
|  |  |  | Spain | F | White - caucasian / european heritage | SEPSIS | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | STAGE IV COLON ADENOCARCINOMA PROGRESSION | Y | N | Fatal |


| Subgroup | Group | Study- <br> Subjec No. | Country | Gender | Race | AE Description | SAE | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | Spain | M | White - caucasian / european heritage | DEATH, NOS | Y | N | Fatal |
|  |  |  | Spain | F | White - caucasian / european heritage | SUSPECIOUS INFECTION BY ZOSTER HERPES | N | N | Recovered / resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | RESPIRATORY INFECTION | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | LUNG SQUAMOUS CELL CARCINOMA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | BLADDER CARCINOMA PROGRESSION | Y | N | Fatal |
|  | Placebo |  | Canada | M | African heritage / african american | PROGRESSIVE NON SMALL CELL LUNG CANCER | Y | N | Fatal |
|  |  |  | France | M |  | PROGRESSIVE DISEASE OF TONG CANCER | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | NEUTROPENIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | ANEMIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | RESPIRATORY INFECTION | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | THROMBOCYTOPENIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | RENAL FAILURE ACUTE | Y | N | Recovered / resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | BILATERAL HYDRONEPHROSIS | Y | N | Recovered / resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | ANEMIA | Y | N | Not recovered / not resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | PULMONARY PROGRESSION OF THE PROSTATIC CANCER | Y | N | Not recovered / not resolved |
|  |  |  | Spain | M | White - caucasian / european heritage | PLEURAL EFFUSION | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | SKIN BLEDDING | Y | N | Fatal |


| Subgroup | Group | StudySubjec No. | Country | Gender | Race | AE Description | SAE | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | Spain | M | White - caucasian / european heritage | LUNG CANCER PROGRESION | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | SUPERIOR CAVA VEIN COMPRESSION | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | LIPOSARCOMA DISEASE PROGRESSION | Y | N | Fatal |
|  |  |  | Spain | F | White - caucasian / european heritage | PNEUMONIA | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | RECTAL CANCER METASTATIC | Y | N | Fatal |
|  |  |  | Spain | F | White - caucasian / european heritage | DISEASE PROGRESSION (OVARIAN CANCER PROGRESSION | Y | N | Fatal |
| OnChemo | HZ/su |  | France | M |  | BLEEDING FROM HIS PRIMARY TUMOR | Y | N | Fatal |
|  |  |  | United Kingdom | F | White - caucasian / european heritage | LIVER METASTASES | Y | N | Fatal |
|  |  |  | Spain | M | White - caucasian / european heritage | PROGRESSION OF THE LUNG CANCER | Y | N | Fatal |
|  | Placebo |  | France | F |  | UTERINE LEIOMYOSARCOMA WORSENING | Y | N | Fatal |


| Sub-group | Group | StudySubject No. | Type of discontinuation |
| :---: | :---: | :---: | :---: |
| PreChemo | HZ/su | PPD | Study |
|  |  |  | Treatment <br> Dose : 2 at visit: VISIT 2 - M1 |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Treatment <br> Dose : 2 at visit: VISIT 2 - M1 |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  | Placebo |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |


| Sub-group | Group | Study- <br> Subiect No. | Type of discontinuation |
| :---: | :---: | :---: | :---: |
|  |  | PPD | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  |  |  | Study |
| OnChemo | HZ/su |  | Study |
|  |  |  | Study |
|  |  |  | Study |
|  | Placebo |  | Study |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
Missing = Missing
HZ/su = Herpes Zoster sub-unit vaccine group
Placebo $=$ Placebo group
Table 8.273 Details of potential immune-mediated disorders (pIMDs) reported as identified by predefined list of preferred terms and/or by investigator assessment up to study end (ATP cohort for safety up to the study end)

| Subgroup | Group | Patient ID | Country | Age <br> at <br> onset <br> (Y) | Gender | Race | Primary System Organ Class | Preferred term | Dose | Day of onset | Relation | Serious pIMD based on Investigator? | SAE <br> (Y/N) | Outcome | pIMD Source |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| OnChemo | Placebo | PPD | Spain | 51 | Female | WHITE CAUCASIAN / EUROPEAN HERITAGE | Endocrine disorders | Autoimmune thyroiditis | 2 | 252 | N | Y | Y | Recovering / resolving | MedDRA and investigator |

PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
Missing = Missing
$\mathrm{HZ} /$ su $=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group

Table 8.274 Listing of All SAEs (ATP cohort for safety up to the study end)

| Sub group | Group | Sub. No. |  | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PreChemo | HZ/su | PPD | F | Korea Republic of | Asian - <br> East Asian <br> Heritage | 40 | Cancer recurrence in uoq of the right breast | Breast cancer recurrent | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | MD | 2 | 109 | 23 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 40 | Right breast tumor recurrence | Breast cancer recurrent | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | MD | 2 | 295 | 140 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 40 | Acute nasopharyngitis | Nasopharyngitis | Infections and infestations | HO | 2 | 21 | 6 | 3 | N | Recovered / resolved |
|  |  |  | F | Canada | White Caucasian / European Heritage | 69 | Pulmonary embolism | Pulmonary embolism | Respiratory, thoracic and mediastinal disorders | ER | 2 | 6 | 44 | 3 | N | Recovered / resolved |
|  |  |  | M | France |  | 83 | Progression of prostate cancer | Prostate cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | MD | 2 | 280 | 20 | 3 | N | Fatal |
|  |  |  | M | United Kingdom | White Caucasian / European Heritage | 65 | Left pleural effusion | Pleural effusion | Respiratory, thoracic and mediastinal disorders | HO | 2 | 59 | -7 | 2 | N | Recovered / resolved |
|  |  |  |  |  |  | 65 | Infection of pleural fluid | Pleural infection | Infections and infestations | HO | 2 | 66 | 17 | 2 | N | Recovered / resolved |

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| Sub group | Group | Sub. <br> No. | Sex | Country | Race | Age <br> at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | MED <br> type | Dose | Day of onse | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 68 | Acute gastroenteritis | Gastroenteritis | Infections and infestations | HO | 2 | 41 | 13 | 3 | N | Fatal |
|  |  |  |  |  |  | 68 | Hepatic encephalopathy | Hepatic encephalopathy | Nervous system disorders | HO | 2 | 21 | 33 | 3 | N | Fatal |
|  |  |  |  |  |  | 68 | Protein caloric malnutrition | Malnutrition | Metabolism and nutrition disorders | HO | 2 | 44 | 10 | 2 | N | Fatal |
|  |  |  |  |  |  | 68 | Odynophagia | Odynophagia | Gastrointestinal disorders | HO | 2 | 47 | 7 | 2 | N | Fatal |
|  |  |  |  |  |  | 68 | Esophagitis | Oesophagitis | Gastrointestinal disorders | HO | 2 | 47 | 7 | 2 | N | Fatal |
|  |  |  |  |  |  | 68 | Muguet candidiasis | Oral candidiasis | Infections and infestations | HO | 2 | 47 | 7 | 2 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 64 | Progression of colorectal carcinoma | Colorectal cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | MD | 2 | 144 | 75 | 3 | N | Fatal |
|  |  |  | F | Spain | White Caucasian / European Heritage | 85 | Anemia | Anaemia | Blood and lymphatic system disorders | HO | 2 | 65 | 3 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 85 | Respiratory insuficience | Respiratory failure | Respiratory, thoracic and mediastinal disorders | HO | 2 | 44 | 7 | 2 | N | Recovered / resolved |
|  |  |  |  |  |  | 85 | Rerpiratory insufficiency | Respiratory failure | Respiratory, thoracic and mediastinal disorders | HO | 2 | 64 | 5 | 2 | N | Recovered / resolved |

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| Sub group | Group | Sub. No. | Sex | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | M | Spain | White Caucasian / European Heritage | 68 | Brain metastasis | Metastases to central nervous system | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 259 |  | 3 | N | Not recovered / not resolved |
|  |  |  |  |  |  | 69 | Neutropenia febrile | Febrile neutropenia | Blood and lymphatic system disorders | HO | 2 | 366 | 10 | 2 | N | Recovered / resolved |
|  |  |  | F | Spain | White Caucasian / European Heritage | 52 | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | HO | 1 | 25 | 16 | 3 | N | Recovered / resolved |
|  |  |  | F | Spain | White Caucasian / European Heritage | 64 | Sepsis | Sepsis | Infections and infestations | MD | 2 | 4 | 1 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 72 | Epiglotitis | Epiglottitis | Infections and infestations | HO | 2 | 219 | 14 | 2 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 74 | Stage iv colon adenocarcinoma progression | Adenocarcinoma of colon | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 1 | 4 | 76 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 63 | Death, nos | Death | General disorders and administration site conditions | MD | 1 | 37 | 1 | 3 | N | Fatal |


| Sub group | Group | Sub. No. | Sex | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{array}{\|c\|} \hline \text { MED } \\ \text { type } \end{array}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | M | Spain | White Caucasian / European Heritage | 59 | Buccal mucosa ulceration | Mouth ulceration | Gastrointestinal disorders | HO | 2 | 119 | 8 | 2 | N | Recovered / resolved |
|  |  |  |  |  |  | 59 | Cardiac infarction killip ii | Myocardial infarction | Cardiac disorders | HO | 2 | 148 | 21 | 2 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 74 | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | HO | 1 | 12 | 14 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 74 | Respiratory infection | Respiratory tract infection | Infections and infestations | HO | 2 | 157 | 17 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 69 | Lung squamous cell carcinoma | Squamous cell carcinoma of lung | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | MD | 2 | 148 | 95 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 45 | Non invasive bladder carcinoma | Bladder cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 99 | 58 | 1 | N | Recovered / resolved |
|  |  |  | F | Spain | White Caucasian / European Heritage | 60 | Diverticulitis | Diverticulitis | Infections and infestations | HO | 2 | 361 | 18 | 2 | N | Recovered / resolved |
|  |  |  | F | Spain | White Caucasian / European Heritage | 48 | Neutropenia | Neutropenia | Blood and lymphatic system disorders | HO | 2 | 75 | 4 | 2 | N | Recovered / resolved |

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| Sub group | Group | Sub. No. | Sex | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Placebo ${ }^{\text {PP }}$ |  | F | Korea Republic of | Asian - <br> South East <br> Asian <br> Heritage | 54 | Arthralgia | Arthralgia | Musculoskeletal and connective tissue disorders | HO | 2 | 205 | 84 | 2 | N | Recovered / resolved |
|  |  |  | F | Korea Republic of | Asian East Asian Heritage | 50 | Upper respiratory infection | Upper respiratory tract infection | Infections and infestations | HO | 2 | 241 | 6 | 3 | N | Recovered / resolved |
|  |  |  | F | Korea Republic of | Asian East Asian Heritage | 49 | Congestive heart failure | Cardiac failure congestive | Cardiac disorders | HO | 2 | 114 | 63 | 3 | N | Recovered / resolved |
|  |  |  | M | Korea Republic of | Asian East Asian Heritage | 54 | Colon cancer progress disease | Colon cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 145 |  | 2 | N | Not recovered / not resolved |
|  |  |  | M | Canada | White Caucasian / European Heritage | 69 | Melanoma malignant | Malignant melanoma | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | MD | 2 | 372 | 346 | 2 | N | Recovered / resolved with sequelae |
|  |  |  | M | Canada | African Heritage / African American | 70 | Progressive non small cell lung cancer | Non-small cell lung cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 186 | 50 | 3 | N | Fatal |

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| Sub group | Group | Sub. No. |  | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{array}{\|l\|} \hline \text { MED } \\ \text { type } \end{array}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | M <br>  | Spain | White Caucasian / European Heritage | 69 | Anemia | Anaemia | Blood and lymphatic system disorders | HO | 2 | 259 | 4 | 3 | N | Fatal |
|  |  |  |  |  |  | 69 | Neutropenia | Neutropenia | Blood and lymphatic system disorders | HO | 2 | 259 | 4 | 3 | N | Fatal |
|  |  |  |  |  |  | 69 | Respiratory infection | Respiratory tract infection | Infections and infestations | HO | 2 | 259 | 4 | 3 | N | Fatal |
|  |  |  |  |  |  | 69 | Thrombocytopenia | Thrombocytopenia | Blood and lymphatic system disorders | HO | 2 | 259 | 4 | 2 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 87 | Renal failure acute | Acute kidney injury | Renal and urinary disorders | HO | 2 | 25 | 24 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | $87$ | Anemia | Anaemia | Blood and lymphatic system disorders | HO | 2 | 25 |  | 3 | N | Not recovered / not resolved |
|  |  |  |  |  |  |  | Bilateral hydronephrosis | Hydronephrosis | Renal and urinary disorders | HO | 2 | 7 | 40 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 87 | Pulmonary progression of the prostatic cancer | Prostate cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 25 |  | 3 | N | Not recovered / not resolved |

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| Sub group | Group | Sub. No. | Sex | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | M | Spain | White Caucasian / European Heritage | 67 | Perianal abscess | Anal abscess | Infections and infestations | HO | 2 | 108 | 124 | 3 | N | Recovered / resolved |
|  |  |  | F | Spain | White Caucasian / European Heritage | 41 | Bacterial infection (s. aureus) | Staphylococcal infection | Infections and infestations | HO | 2 | 124 | 10 | 2 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 78 | Pleural effusion | Pleural effusion | Respiratory, thoracic and mediastinal disorders | HO | 1 | 21 | 6 | 3 | N | Fatal |
|  |  |  | F | Spain | White Caucasian / European Heritage | 73 | Febrile neutrophenia | Febrile neutropenia | Blood and lymphatic system disorders | HO | 1 | 21 | 46 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 73 | Renal infection | Kidney infection | Infections and infestations | HO | 1 | 19 | 48 | 3 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 36 | Skin bledding | Skin haemorrhage | Skin and subcutaneous tissue disorders | HO | 2 | 0 | 58 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 48 | Embolism pulmonary | Pulmonary embolism | Respiratory, thoracic and mediastinal disorders | HO | 2 | 76 | 45 | 1 | N | Recovered / resolved |
|  |  |  | F | Spain | White Caucasian / European Heritage | 45 | Pulmonary thromboembolism | Pulmonary embolism | Respiratory, thoracic and mediastinal disorders | HO | 2 | 207 | 593 | 2 | N | Recovered / resolved |

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| Sub group | Group | Sub. No. |  | Country | Race | Age <br> at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | M | Spain | White Caucasian / European Heritage | 63 | Right bronchi obstruction | Bronchial obstruction | Respiratory, thoracic and mediastinal disorders | HO | 2 | 266 | 68 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 63 | Pneumonia | Pneumonia | Infections and infestations | HO | 2 | 266 | 45 | 3 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 71 | Lung cancer progresion | Lung neoplasm malignant | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 128 | 8 | 3 | N | Fatal |
|  |  |  | M | Spain | White Caucasian / European Heritage | 71 | Seizures | Seizure | Nervous system disorders | HO | 2 | 3 | 13 | 2 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 47 | Liposarcoma disease progression | Liposarcoma | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 224 | 79 | 3 | N | Fatal |
|  |  |  |  |  |  | 47 | Superior cava vein compression | Superior vena cava occlusion | Vascular disorders | HO | 2 | 224 | 79 | 3 | N | Fatal |
|  |  |  | F | Spain | White Caucasian / European Heritage | 78 | Lung infection | Lung infection | Infections and infestations | ER | 2 | 138 | 17 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 78 | Neutropenia | Neutropenia | Blood and lymphatic system disorders | ER | 2 | 138 | 17 | 3 | N | Recovered / resolved |

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| Sub group | Group | Sub. No. | Sex | Country | Race | Age at onset (Year) | Verbatim | Preferred term | Primary System Organ Class | $\begin{aligned} & \text { MED } \\ & \text { type } \end{aligned}$ | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | PPD | F | Spain | White Caucasian / European Heritage | 40 | Neutropenia | Neutropenia | Blood and lymphatic system disorders | HO | 2 | 144 | 4 | 2 | N | Recovered / resolved |
|  |  |  | M | Spain | White Caucasian / European Heritage | 60 | Cecoileitis | Enteritis | Gastrointestinal disorders | HO | 2 | 282 | 7 | 2 | N | Recovered / resolved |
|  |  |  | M | Czech Republic | White Caucasian / European Heritage | 39 | Erbitux allergic reaction | Drug hypersensitivity | Immune system disorders | HO | 2 | 4 | 2 | 1 | N | Recovered / resolved |
| OnChemo | HZ/su |  | F | Korea Republic of | Asian East Asian Heritage | 58 | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | HO | 1 | 13 | 8 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 59 | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | HO | 2 | 33 | 4 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 59 | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | HO | 2 | 80 | 5 | 3 | N | Recovered / resolved |
|  |  |  | M | France |  | 48 | Gastrostomy failure | Gastrostomy failure | Injury, poisoning and procedural complications | HO | 1 | 28 | 9 | 1 | N | Recovered / resolved |
|  |  |  |  |  |  | 49 | Bleeding from his primary tumor | Tumour haemorrhage | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | HO | 2 | 48 | 3 | 3 | N | Fatal |

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| Sub group | Group | Sub. <br> No. |  | Country | Race | Age <br> at <br> onset <br> (Year) | Verbatim | Preferred term | Primary <br> System Organ Class | MED <br> type | Dose | Day of onset | Duration | Intensity | Causality | Outcome |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | 68 | Clostridium difficile infection | Clostridium difficile infection | Infections and infestations | ER | 1 | 76 | 22 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Diarrhea | Diarrhoea | Gastrointestinal disorders | ER | 1 | 33 | 18 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Diarrhea | Diarrhoea | Gastrointestinal disorders | ER | 1 | 66 | 32 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | $68$ | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | ER | 1 | 39 | 3 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | $68$ | Hypokalemia | Hypokalaemia | Metabolism and nutrition disorders | ER | 1 | 39 | 13 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | $68$ | Hyponatremia | Hyponatraemia | Metabolism and nutrition disorders | ER | 1 | 39 | 13 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | $68$ | protein malnutrition | Malnutrition | Metabolism and nutrition disorders | HO | 1 | 91 | 14 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Mucositis | Mucosal inflammation | General disorders and administration site conditions | ER | 1 | 33 | 23 | 3 | N | Recovered / resolved |
|  |  | PPD | M | Spain | White Caucasian / European Heritage | 68 | Febrile neutropenia | Febrile neutropenia | Blood and lymphatic system disorders | HO | 2 | 8 | 15 | 3 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Gastroenteritis | Gastroenteritis | Infections and infestations | HO | 1 | 9 | 17 | 2 | N | Recovered / resolved |
|  |  |  |  |  |  | 68 | Respiratory infectio | Respiratory tract infection | Infections and infestations | HO | 1 | 20 | 16 | 2 | N | Recovered / resolved |

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PreChemo = first vaccination 8 days or more prior to the start of a chemotherapy cycle
OnChemo = first vaccination at the start of a chemotherapy cycle (+ or - 1 day)
Missing = Missing
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster sub-unit vaccine group
Placebo = Placebo group
MED = Medical Advice type (HO: hospitalisation, ER: emergency room visit, MD: medical practice visit)

## MODULAR APPENDICES

List of modular appendices available for the study report and ICH-specific appendices - Study Information equivalent numbering

| Modular appendices | ICH numbering |
| :--- | :--- |
| Protocol and protocol amendments. | 16.1 .1 |
| Sample Case Report form (unique pages only). | 16.1 .2 |
| List of IECs or IRBs \& List of Investigators and other important <br> participants in the study | 16.1 .3 \& 16.1.4 |
| Representative written information for patient and sample consent <br> forms. | 16.1 .3 |
| Investigator CVs or equivalent summaries of training and <br> experience relevant to the performance of the clinical study | 16.1 .4 |
| Signatures of principal or coordinating investigator(s) or sponsor's <br> responsible medical officer, depending on the regulatory <br> authority's requirement | 16.1 .5 |
| Listings of patients receiving test drug(s) /investigational <br> product(s) from specific batches, where more than one batch was <br> used | 16.1 .6 |
| Randomization list (patient identification and treatment assigned). | 16.1 .7 |
| Audit certificates | 16.1 .8 |
| Documentation of statistical methods | 16.1 .9 |
| Documentation of inter-laboratory standardization methods and <br> quality assurance procedures | 16.1 .10 |
| Publications based on the study. | 16.1 .11 |
| Important publications referenced in the report | 16.1 .12 |
| Individual listings | 16.2 |
| Case report forms (CRFs /eCRFs) <br> CRFs /eCRFs for deaths, other SAEs and withdrawals due to <br> adverse events | 16.3 <br> Study Administrative Table |

## Protocol and Protocol Amendments

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## Clinical Study Protocol

Sponsor:
GlaxoSmithKline Biologicals
Rue de l'Institut 89, 1330 Rixensart, Belgium

Primary Study vaccine and number Other Study product

GlaxoSmithKline Biologicals' Lyophilised formulation of the Herpes Zoster subunit (HZ/su) vaccine (GSK 1437173A) Control: Placebo (Lyophilised sucrose reconstituted with saline ( NaCl ) solution)
eTrack study number and Abbreviated Title Investigational New Drug (IND) number EudraCT number Date of protocol Date of protocol amendments Title

Detailed Title
116427 (ZOSTER-028)

BB-IND 13879

2012-002966-11
Final: 16 August 2012
Amendment 1 Final: 19 November 2012
Amendment 2 Final: 11 August 2014
An observer-blind study to evaluate immunogenicity and safety of GSK Biologicals' Herpes Zoster vaccine GSK1437173A in adults $\geq 18$ years of age with solid tumours receiving chemotherapy.
A phase II/III, randomised, observer-blind, placebo- controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy.
Co-ordinating author

PPD
Business Solutions for GSK Biologicals

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Protocol Amendment 2 Final

| eTrack study number and Abbreviated Title | 116427 (ZOSTER-028) |
| :---: | :---: |
| Investigational New | BB-IND 13879 |
| Drug (IND) number |  |
| EudraCT number | 2012-002966-11 |
| Date of protocol | Final: 16 August 2012 |
| Date of protocol | Amendment 1 Final: 19 November 2012 |
| amendments | Amendment 2 Final: 11 August 2014 |
| Detailed Title | A phase II/III, randomised, observer-blind, placebocontrolled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy. |
| Contributing authors | - PPD Clinical Research and Development Lead, Director, Vaccine Discovery and Development <br> - PPD Clinical Research and Development |
|  | Lead  <br> - PPD Study Delivery Lead <br> - PPD Study Delivery Manager |
|  | - PPD Project Statistician |
|  | - PPD Lead Statistician |
|  | - PPD Study Statistician |
|  | - PPD Clinical Operations Lead |
|  | - PPD Global Vaccine Clinical Laboratory |
|  | Study Manager |
|  | - PPD Global Vaccine Clinical |
|  | Laboratories Project Manager |
|  | - PPD Global Vaccines Clinical |
|  | Laboratories Project Manager |
|  | - PPD Safety representative |
|  | - PPD Safety representative |
|  | - PPD Clinical Safety representative |
|  | - PPD Study Data Manager, 4Clinics for |
|  | GSK Biologicals |
|  | - PPD Global Regulatory Affairs |
|  | - PPD US Regulatory Affairs |
|  | - PPD Director, US Regulatory Affairs |
|  | - PPD Project Level Clinical Research and |
|  | Development Lead, Director, Vaccine Discovery and |
|  | Development |

(Amended: 11 August 2014)
GSK Biologicals' Protocol DS v 14.0
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## Protocol Amendment 2 Sponsor Signatory Approval

| eTrack study number and <br> Abbreviated Title | 116427 (ZOSTER-028) |
| :--- | :--- |
| IND number | BB-IND 13879 |
| EudraCT number | $2012-002966-11$ |
| Date of protocol amendment | Amendment 2 Final: 11 August 2014 |
| Detailed Title | A phase II/III, randomised, observer-blind, placebo- <br> controlled, multicentre, clinical trial to assess the <br> immunogenicity and safety of GSK Biologicals’ <br> herpes zoster HZ/su candidate vaccine when <br> administered intramuscularly on a 0 and 1 to 2 <br> months schedule to adults $\geq 18$ years of age with solid <br> tumours receiving chemotherapy. |
| Sponsor signatory | Lidia Oostvogels, Project Level Clinical Research <br> and Development Lead, Director, Vaccine Discovery |
| and Development |  |

## Signature

## Date

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## Protocol Amendment 2 Rationale

## Amendment number: Amendment 2

- The cut-off of the gE-specific ELISA assay has been changed from 18 to 97 $\mathrm{mIU} / \mathrm{mL}$. Background signal has been measured with the anti-gE ELISA on samples from Varicella Zoster Virus (VZV) naïve paediatric subjects. This observation of background signal on VZV naïve samples was not part of the original validation of the assay and establishment of the assay cut-off. Background signal measured with the anti-gE ELISA has no impact on Zoster project clinical conclusions as the vast majority of the samples (at all timepoints) have high titres well above the unspecific response level measured on VZV naïve samples from Measles, Mumps, Rubella and Varicella (MMRV) studies and Zoster vaccine responses are very robust. However this finding triggered re-evaluation of the assay cut-off. Based on complementary validation experiments performed in line with Clinical and Laboratory Standards Institute (CLSI) guidelines and taking into account internal company guidelines the technical and seropositivity cut-off has been set at $97 \mathrm{mIU} / \mathrm{mL}$. (Section 5.7.3, Table 9, and Appendix A).
- Within the immunocompromised populations undergoing clinical trials with $\mathrm{HZ} / \mathrm{su}$, GlaxoSmithKline (GSK) has observed that the clinical condition of the subjects impacts their ability to meet the targeted allowed clinical intervals between study visits. For example, a subject may not be able to attend a visit within the clinically allowed interval due to being hospitalised for his/ her underlying immunocompromising (IC) disease or its treatment. Or the second vaccination visit may be delayed due to complications from the underlying IC disease or its treatment, making intramuscular injection unsafe within clinically allowed interval. Considering this, GSK has revised the allowed intervals for the ATP cohort for analysis of immunogenicity. The intervals between vaccinations (dose 1 to dose 2) and between dose 2 and blood sampling at Visit 3 (i.e. the 1 month post dose 2 visit) for inclusion in the According to Protocol cohort (ATP) cohort for immunogenicity/persistence phase are being enlarged to respectively 30-84 days and 21-63 days. The observation and interpretation of the immunogenicity/persistence data are not anticipated to be compromised by this modification. The increased flexibility will allow meaningful analysis of the data collected in this immunocompromised populations, where the underlying disease and implications of its treatment (such as cancer treatment schedule, side effects of the concomitant treatment) lead to a higher number of out of window visits compared to what is observed in a healthy population. In addition, Visit 4 has been removed from the ATP cohort (ATPc) for analysis of immunogenicity as this visit does not occur for all subjects. The ATPc for analysis of immunogenicity will be now defined by Visit $1 \rightarrow$ Visit 2, Visit $2 \rightarrow$ Visit 3, and Visit $2 \rightarrow$ Visit 5 (Section 9.4.3, Section 9.8)
- Secondary to the clinical course of IC populations, the projected subject loss as cancer deaths, consent withdrawals, and non-evaluable subjects at Month 2 in Zoster-028 has been revised from $20 \%$ to $27 \%$. Therefore, the target enrolment has been changed from 210 to 232 adults diagnosed with solid tumours receiving chemotherapy. Similarly, the targeted enrolment numbers increased for the


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PreChemo group from 168 (84 per treatment group) to 186 (93 per treatment group) and for the OnChemo group from 42 (21 per treatment group) to 46 ( 23 per treatment group), based on the projected $27 \%$ drop-out and non-evaluable subjects at Month 2. (Synopsis rationale for study design, Synopsis Table 1, Synopsis Number of subjects, Section 1.2, Table 1, Section 4.1, Table 5, Section 5.2.2.2.1, Section 9.3.1).

- Intercurrent medical conditions were clarified with examples. (Section 6.7).
- The list of potential immune-mediated diseases has been updated. (Section 7.1.5.1, Table 16)
- Temperature measurement grading scale has been removed, since all temperature measurements will be recorded. The description of the temperature analyses will be described in details in the Statistical Analysis Plan. (Section 7.3.3.2.1)
- The definition of the according-to-protocol (ATP) cohort for safety was updated. (Section 9.4.2)
- Statistical section was updated to describe the descriptive cell-mediated immune (CMI) response analysis, to clarify other descriptive analysis for immunogenicity and safety. (Section 9.5.3)
- The requirement for reporting an abnormal laboratory findings as an AE or SAE has been modified. Now, if the abnormal assessments are judged by the investigator to be clinically significant and unexpected, considering the specific underlying disease and chemotherapy, they are to be recorded as an AE or SAE. Abnormal laboratory results which are secondary to the clinical course of malignancies and their treatment (cytotoxic or immunosuppressive chemotherapy) are to be expected and frequently occurring for the subject population in this study. The laboratory abnormalities of interest for safety reporting in this study are those judged by the investigators to be clinically significant and unexpected, as this subset may have the possibility to be related to the study vaccine. (Section 7.1.4).
- Minor edits in other sections were made for clarification.


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## Protocol Amendment 2 Investigator Agreement

## I agree:

- To conduct the study in compliance with this protocol, any future protocol amendments or protocol administrative changes, with the terms of the clinical trial agreement and with any other study conduct procedures and/or study conduct documents provided by GlaxoSmithKline (GSK) Biologicals.
- To assume responsibility for the proper conduct of the study at this site.
- That I am aware of, and will comply with, 'Good Clinical Practice' (GCP) and all applicable regulatory requirements.
- To ensure that all persons assisting me with the study are adequately informed about the GSK Biologicals' investigational product(s) and other study-related duties and functions as described in the protocol.
- To acquire the reference ranges for laboratory tests performed locally and, if required by local regulations, obtain the laboratory's current certification or Quality Assurance procedure manual.
- To ensure that no clinical samples (including serum samples) are retained onsite or elsewhere without the approval of GSK Biologicals and the express written informed consent of the subject and/or the subject's legally acceptable representative.
- To perform no other biological assays on the clinical samples except those described in the protocol or its amendment(s).
- To co-operate with a representative of GSK Biologicals in the monitoring process of the study and in resolution of queries about the data.
- That I have been informed that certain regulatory authorities require the sponsor to obtain and supply, as necessary, details about the investigator's ownership interest in the sponsor or the investigational product(s), and more generally about his/her financial ties with the sponsor. GSK Biologicals will use and disclose the information solely for the purpose of complying with regulatory requirements.


## Hence I:

- Agree to supply GSK Biologicals with any necessary information regarding ownership interest and financial ties (including those of my spouse and dependent children).
- Agree to promptly update this information if any relevant changes occur during the course of the study and for one year following completion of the study.
- Agree that GSK Biologicals may disclose any information it has about such ownership interests and financial ties to regulatory authorities.
- Agree to provide GSK Biologicals with an updated Curriculum Vitae and other documents required by regulatory agencies for this study.


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eTrack study number and Abbreviated Title

EudraCT number
Date of protocol amendment
Detailed Title

## Investigator name

## Signature

## Date

116427 (ZOSTER-028)

BB-IND 13879
2012-002966-11
Amendment 2 Final: 11 August 2014
A phase II/III, randomised, observer-blind, placebocontrolled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy.
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## Sponsor Information

## 1. Sponsor

GlaxoSmithKline Biologicals, Rue de 1'Institut 89, 1330 Rixensart, Belgium

## 2. Sponsor Medical Expert for the Study

Refer to the local study contact information document.

## 3. Sponsor Study Monitor

Refer to the local study contact information document.

## 4. Sponsor Study Contact for Reporting of a Serious Adverse Event

GSK Biologicals Central Back-up Study Contact for Reporting SAEs: refer to protocol Section 7.4.2.
5. GSK Biologicals Central Safety Physician On-Call Contact information for Emergency Unblinding

GSK Biologicals Central Safety Physician and Back-up Phone contact: refer to protocol Section 7.8.

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## SYNOPSIS

Detailed Title<br>Indication<br>Rationale for the study and study design

A phase II/III, randomised, observer-blind, placebocontrolled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster $\mathrm{HZ} /$ su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy.

Prevention of Herpes Zoster (HZ) and related complications in adults $\geq 50$ years of age and immunocompromised adults $\geq$ 18 years of age.

- Rationale for the study

Varicella-Zoster Virus (VZV) causes two distinct diseases. Varicella (chickenpox) occurs shortly after primary VZV infection and is characterized by systemic illness and a widely disseminated rash. Herpes Zoster (shingles) occurs when VZV reactivates from latency and typically manifests as a localized, dermatomal rash.

The typical HZ rash usually lasts 2 to 4 weeks and is usually accompanied by pain that is often described as burning, shooting, or stabbing. In some patients, even touching the affected area lightly may cause pain, a phenomenon known as allodynia. This HZ-associated pain may be severe, and pruritus, which can also be severe, may be as common as pain.

The increase in HZ within patients with solid tumours receiving chemotherapy is likely due to their immunocompromised state and indicates that there is a medical need to vaccinate these patients to reduce the morbidity associated with HZ. The increased cumulative incidence rate of HZ following diagnosis of malignant neoplasm, relative to the general population, is in part attributed to impaired immunity due to chemotherapy and radiotherapy. Although a live attenuated VZV vaccine, called Zostavax ${ }^{\circledR}$ (Merck \& Co), is licensed in the United States (US), the European Union (EU) and elsewhere to prevent HZ in persons $\geq 50$ years of age (YOA) this vaccine is contraindicated in immunosuppressed or immunodeficient individuals. Thus, there is currently no licensed vaccine for the prevention of HZ in immunocompromised populations.

GlaxoSmithKline (GSK) Biologicals' candidate vaccine for the prevention of HZ is a recombinant subunit (su) vaccine consisting of the VZV glycoprotein E (gE) antigen and an

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Adjuvant System (AS01B). In the studies currently analysed it was shown to elicit strong cellular and humoral immune responses. Furthermore, the safety and reactogenicity profile of this candidate vaccine was acceptable. Based on phase II data from the antigen dose-ranging study, ZOSTER-003, and the adjuvant dose comparison study, ZOSTER-010, a gE antigen dose of $50 \mu \mathrm{~g}$ and the Adjuvant System AS $01_{\mathrm{B}}$ were selected as the final vaccine formulation (henceforth, the final vaccine formulation of GSK Biologicals' candidate HZ vaccine will be referred to as $\mathrm{HZ} / \mathrm{su}$ ).

A phase I/IIa study, ZOSTER-001, is currently being conducted to evaluate the safety and immunogenicity of $\mathrm{HZ} / \mathrm{su}$ in autologous HCT recipients 18 YOA and older. The primary endpoint data from this study showed that gE-specific cell-mediated immune (CMI) responses to HZ/su administered on schedules of 0,1 and 3 months, 0 and 1 months (as part of the 3 -dose schedule), or 1 and 3 months (with month 0 defined as 50-70 days following autologous HCT ), were significantly higher than in placebo recipients. Also, the safety profile of $\mathrm{HZ} / \mathrm{su}$ through 1-month following the final vaccine dose was acceptable in this study. Therefore, the results of study ZOSTER-001 support the further evaluation of $\mathrm{HZ} /$ su in phase II/III studies for the prevention of HZ in other immunocompromised populations such as patients with solid tumours receiving chemotherapy. An extension of the ZOSTER-001 study remains ongoing for assessment of long-term safety and immunogenicity observations.

- Rationale for the study design

Study ZOSTER-028 will be conducted to evaluate the immunogenicity and safety of HZ/su in patients 18 YOA and older diagnosed with one or more solid tumours and receiving chemotherapy. The results of studies in healthy adults and from the active phase of ZOSTER-001 (in autologous HCT patients) support the selection of a 2-dose vaccine schedule. Studies in healthy adults demonstrated strong vaccine-induced immune responses following vaccine administration at 0 and 2 months. In addition, the results of ZOSTER-001 demonstrate comparably strong immune responses following vaccine administration at Months 0 and 1 . Therefore, in the present study, the window for administration of the second vaccine dose will be 30-60 days after the first dose. giving some flexibility to the patient and the investigator while dealing with chemotherapy cycles.

This study is part of a clinical development plan (CDP)

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designed to evaluate $\mathrm{HZ} /$ su for the prevention of HZ and related complications in adults with immunocompromising conditions. The present study will evaluate the immunogenicity and safety of $\mathrm{HZ} / \mathrm{su}$ vaccination in adults 18 YOA and above with solid tumours receiving chemotherapy.

Subjects in the ZOSTER-028 study will initially be randomised into two groups based on the vaccination schedule in relation to the start of $\boldsymbol{a}$ chemotherapy cycle. The OnChemo group receives their first HZ/su vaccination at the start of $\boldsymbol{a}$ chemotherapy cycle, while the PreChemo group receives their first $\mathrm{HZ} / \mathrm{su}$ vaccination at least 10 days before the start of $\boldsymbol{a}$ chemotherapy cycle. Unpublished data with other GSK candidate vaccines indicates that vaccination at the start of $\boldsymbol{a}$ chemotherapy cycle can lead to a decreased/suppressed immune response, possibly due to steroids used concomitantly in high doses to prevent nausea and vomiting. Therefore, the primary objective linked to immunogenicity will be assessed in the PreChemo groups only. For this reason, the study groups will be allocated 4:1 (186/46) PreChemo:OnChemo.
(Amended: 11 August 2014)

- Rationale for the use of placebo

A lyophilised sucrose cake reconstituted with saline ( NaCl ) solution is included as a negative control (placebo) in the study evaluating the immunogenicity and safety profile of the candidate $\mathrm{HZ} / \mathrm{su}$ vaccine in this study population. Use of the placebo control and the observer-blind, randomised study design, will allow to control for potential biases in the conduct of the study.

## Objectives

## Co-Primary

- To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).


## Criteria to be used:

The objective is met if the lower limit of the $95 \%$ confidence interval (CI) of the Geometric Mean (GM) ratio (HZ/su PreChemo group over placebo PreChemo group) in anti-gE ELISA antibody concentrations is greater than 3 .

- To evaluate the safety and reactogenicity following


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administration of the $\mathrm{HZ} /$ su vaccine as compared to placebo up to 30 days post last vaccination in subjects with solid tumours receiving chemotherapy.
Criteria to be used:
This analysis is descriptive, no criterion has been defined.

## Secondary

- To evaluate vaccine response rate in anti-gE humoral immunogenicity responses at Month 2, following a twodose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).


## Criteria to be used:

The objective is met if the lower limit of the $95 \%$ CI of the vaccine response rate for anti-gE ELISA antibody concentrations at Month 2 in the HZ/su PreChemo group is at least $60 \%$.

- To evaluate gE-specific CD4+ T-cell immunogenicity responses at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only) (in the CMI subcohort).

Criteria to be used:
The objective is met if the lower limit of the $95 \%$ CI of the GM ratio (HZ/su PreChemo group over placebo PreChemo group) in gE-specific CD4+ T-cell frequencies at Month 2 is greater than 1.

- To evaluate vaccine response rate in gE-specific CD4+ Tcell mediated immunogenicity at Month 2 , following a two-dose administration of the HZ/su vaccine in subjects with solid tumours receiving chemotherapy (PreChemo Groups only) (in the CMI sub-cohort).
Criteria to be used:
The objective is met if the lower limit of the $95 \%$ CI of the vaccine response rate for gE-specific CD4+ T-cell frequencies at Month 2 in the HZ/su PreChemo group is at least $50 \%$.
- To evaluate the anti-gE humoral immunogenicity response at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo, in subjects


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with solid tumours receiving chemotherapy (all subjects).
Criteria to be used:
The objective is met if the lower limit of the $95 \%$ confidence interval (CI) of the Geometric Mean (GM) ratio (HZ/su group over placebo group) in anti-gE ELISA antibody concentrations is greater than 3 .

- To evaluate vaccine response rate in anti-gE humoral immunogenicity responses at Month 2, following a twodose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (all subjects receiving the HZ/su vaccine).


## Criteria to be used:

The objective is met if the lower limit of the $95 \%$ CI of the vaccine response rate for anti-gE ELISA antibody concentrations at Month 2 in the HZ/su group is at least $60 \%$.

- To evaluate safety following administration of the HZ/su vaccine, as compared to placebo, from 30 days post last vaccination until study end in subjects with solid tumours receiving chemotherapy.
- To characterize anti-gE humoral immunogenicity responses at Month 0, Month 1, Month 2, Month 6 (Visit 4 , at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13 within the HZ/su and placebo groups.
- To characterize gE-specific CD4+ T-cell mediated immunogenicity responses at Month 0 , Month 1, Month 2, and Month 13 within the $\mathrm{HZ} / \mathrm{su}$ and placebo groups (PreChemo Groups only) (in the CMI sub-cohort).


## Study design

- Experimental design:

Phase II/III, observer-blind randomised, placebo controlled, multi-centric, multi-country study with two parallel groups.

- Duration of the study:

Epoch 001: Primary starting from the Pre-vaccination visit (up to -30 days) and ending at Visit 5 (Month 13). The study end will take place when all subjects have completed their 12 month post-dose 2 follow-up visit (at Month 13, Visit 5). The total duration of the study for each subject is expected to be approximately 14 months including the Pre-vaccination visit.

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- Study groups:


## Synopsis Table 1 Study groups and epochs foreseen in the study

(Amended: 11 August 2014)

| Study groups | Number of subjects | Age (Min.) | Epoch |
| :---: | :---: | :---: | :---: |
|  |  | Epoch 001 |  |
| HZ/su-PreChemo | 93 | 18 years | $\bullet$ |
| Placeb-PreChemo | 93 | 18 years | $\bullet$ |
| HZ/su-OnChemo | 23 | 18 years | $\bullet$ |
| Placeb-OnChemo | 23 | 18 years | $\bullet$ |

HZ/su = Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb =
Placebo; Min. = Minimum

* And above the legal age of consent (see Table 28)

Synopsis Table 2 Study groups and treatment foreseen in the study

| Treatment name | Vaccinel Product name | Study Groups |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | HZ/suPreChemo | PlacebPreChemo | $\begin{aligned} & \text { HZ/su- } \\ & \text { OnChemo } \end{aligned}$ | PlacebOnChemo |
| HZ/su | VZV gE | - |  | $\bullet$ |  |
|  | AS01 ${ }_{\text {b }}$ | - |  | $\bullet$ |  |
| Placebo | Lyophilised sucrose cake |  | $\bullet$ |  | - |
|  | Saline ( NaCl ) solution for reconstitution |  | - |  | $\bullet$ |

HZ/su = Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb = Placebo; VZV = Varicella Zoster Virus; gE = recombinant purified Glycoprotein E; AS01B = Adjuvant System AS01B; $\mathrm{NaCl}=$ sodium chloride

- Control: placebo control [Lyophilised sucrose reconstituted with saline $(\mathrm{NaCl})$ solution].
- Vaccination schedule: 0, 1-2 Month
- Treatment allocation:

Eligible subjects will be randomised to the investigational $\mathrm{HZ} / \mathrm{su}$ vaccine or placebo (1:1 ratio) and to the PreChemo Group, first vaccination at least 10 days (up to 1 month) before the start of a chemotherapy cycle, or OnChemo Group, first vaccination at the start of $a$ chemotherapy cycle (4:1 ratio). (Amended: 11 August 2014)

- Blinding:

Observer-blind for study vaccine but not for time of

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vaccination relative to chemotherapy.

## Synopsis Table 3 Blinding of study epochs

| Study Epoch | Blinding |
| :--- | :--- |
| Epoch 001 | observer-blind* |

* Beyond Visit 3 (Month 2), the investigator may be unblinded with respect to individual subject data summarised in the clinical study report.
- Biological samples to be collected:
- A urine specimen will be collected from all female subjects of childbearing potential at the Pre-vaccination Visit, Visit 1 and Visit 2. If a serum pregnancy test instead of a urine pregnancy test is required by country, local or ethics committee regulations, a blood sample will be collected from women of childbearing potential at Visit 1 and Visit 2 and used for the test as per local guidance.
- Blood samples (approximately 8 mL ) will be collected from all subjects at Visits 1, 2, 3, 4 and 5. Blood samples will be used to assess humoral immune responses with respect to the study/investigational vaccine in all subjects.
- Blood samples (approximately 30 mL ) will be collected from a sub-cohort of subjects at Visits 1, 2, 3 and 5 to assess CMI responses (CMI sub-cohort).
- Type of study: self-contained.
- Data collection: Standardised electronic Case Report Form (eCRF).
- Safety monitoring:

Unblinded evaluation of safety for the subjects (with coded group names) will be performed by an internal Safety Review Committee (iSRC) on a regular basis.

Number of Target enrolment is approximately 232 eligible adults diagnosed subjects with solid tumours receiving chemotherapy. (Amended 11
August 2014)

## Endpoints Primary

- Anti-gE humoral immunogenicity with respect to components of the study/investigational vaccine.
- Anti-gE Ab concentrations as determined by ELISA at


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Month 2.

- Occurrence of solicited local and general symptoms.
- Occurrence, intensity and duration of each solicited local symptom within 7 days (Days 0-6) after each vaccination.
- Occurrence, intensity, duration and relationship to vaccination of each solicited general symptom within 7 days (Days 0-6) after each vaccination.
- Occurrence of unsolicited adverse events (AEs).
- Occurrence, intensity and relationship to vaccination of unsolicited AEs during 30 days (Days 0-29) after each vaccination, according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence of serious Adverse Events (SAEs).
- Occurrence and relationship to vaccination of SAEs up to 30 days post last vaccination.
- Occurrence of AEs of specific interest.
- Occurrence and relationship to vaccination of any potential Immune Mediated Diseases (pIMDs) up to 30 days post last vaccination.


## Secondary

- For immunogenicity with respect to components of the study/investigational vaccine.
- Anti-gE Ab concentrations as determined by ELISA at Month 0, Month 1, Month 2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13.
- Vaccine response for anti-gE Abs at Month 1, Month 2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13.
- Frequencies of gE-specific CD4+ T-cells, expressing at least 2 activation markers (from among IFN- $\gamma$, IL-2, TNF- $\alpha$ and CD40 L), as determined by in vitro intracellular cytokine staining (ICS), at Month 0, Month 1, Month 2, and Month 13.
- Vaccine response for gE-specific CD4+ T-cells expressing at least 2 activation markers (from among IFN- $\gamma$, IL- 2 , TNF- $\alpha$ and CD40L), as determined by in vitro ICS, at Month 1, Month 2 and Month 13.


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- Occurrence of Serious Adverse Events (SAEs).
- Occurrence and relationship to vaccination of SAEs during the period starting after 30 days post last vaccination until study end.
- Occurrence of AEs of specific interest.
- Occurrence of any pIMDs during the period starting after 30 days post last vaccination until study end.


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LIST OF ABBREVIATIONS

| Ab: | Antibody |
| :---: | :---: |
| AE: | Adverse Event |
| AS01 ${ }_{\text {B }}$ : | MPL, QS21, liposome based Adjuvant System [50 $\mathrm{\mu g}$ MPL and $50 \mu \mathrm{~g}$ QS21] |
| ATP: | According-To-Protocol |
| CD40 L: | CD40 Ligand |
| CDC: | Centres for Disease Control |
| CDM: | Clinical Development Manager |
| CDP: | Clinical Development Plan |
| CI: | Confidence Interval |
| CMI: | Cell-Mediated Immunity |
| D: | Deltoid |
| DNA: | Deoxyribonucleic Acid |
| ECOG: | Eastern Cooperative Oncology Group |
| eCRF: | electronic Case Report Form |
| EDD: | Estimated Date of Delivery |
| EGA: | Estimated Gestational Age |
| ELISA: | Enzyme-Linked Immunosorbent Assay |
| EMA: | European Medicines Agency |
| eTDF: | Electronic Temperature excursion Decision Form |
| EU: | European Union |
| FDA: | Food and Drug Administration, United States of America |
| GCP: | Good Clinical Practice |
| gE: | Glycoprotein E |
| GM: | Geometric Mean |

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| GMC: | Geometric Mean Concentration |
| :--- | :--- |
| GSK: | GlaxoSmithKline |
| GVCL: | Global Vaccines Clinical Laboratories |
| HCG: | Human Chorionic Gonadotropin |
| HCT: | Haematopoietic stem Cell Transplant |
| HIV: | Human Immunodeficiency Virus |
| HZ: | Herpes Zoster |
| HZ/su: | Herpes Zoster subunit vaccine [gE[50 ug]/AS01 $\left.{ }_{\mathrm{B}}\right]$ |
| IB: | Investigator Brochure |
| ICF: | Informed Consent Form |
| ICH: | International Conference on Harmonization |
| ICS: | Intracellular Cytokine Staining |
| IFN- $\boldsymbol{\gamma}:$ | Interferon Gamma |
| IgG: | Interleukin-2 |
| IL 2: | Intramuscular |
| IM: | Investigational Medicinal Product |
| IMP: | Investigational New Drug |
| IND: | Institutional Review Board |
| IRB: | internal Safety Review Committee |
| iSRC: | Last Menstrual Period |
| LMP: | Natural Logarithm |
| In: | Decimal Logarithm |
| log $\mathbf{1 0}:$ | Missing Completely at Random |
| MAR: | MCAR: |

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| MedDRA: | Medical Dictionary for Regulatory Activities |
| :--- | :--- |
| Mg: | Milligram |
| mIU: | Milli-International Unit |
| mL: | Millilitre |
| mM: | Millimolar |
| MPL: | 3-O-desacyl-4'-Monophosphoryl Lipid A |
| Mg: | Microgram |
| NA: | Not applicable |
| NaCl: | Sodium Chloride |
| N-D: | Non-Dominant |
| PBMC: | Poripheral Blood Mononuclear Cells |
| PCR: | Postherpetic Neuralgia Chain Reaction |
| PHN: | Potential Immune-Mediated Disease |
| pIMD: | Quillaja saponaria Molina, fraction 21 (purified saponin |
| QS21: | extract from the South American tree) |
| RDE: | Remote Data Entry |
| SAE: | Serious Adverse Event |
| SAP: | Stuatistical Analysis Plan Procedures Manual |
| SBIR: | Randomisation System on Internet |
| SD: | Standard Deviation |
| SDV: | Source Document Verification |
| SOT: | Solid Organ Transplant |
| SPM: | TNF-a: |

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| US: | United States (of America) |
| :--- | :--- |
| Vacc: | Vaccination |
| VRR: | Vaccine Response Rates |
| VZV: | Varicella Zoster Virus |
| YOA: | Years of Age |

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## GLOSSARY OF TERMS

## Adequate contraception:

Adequate contraception is defined as a contraceptive method with failure rate of less than $1 \%$ per year when used consistently and correctly and when applicable, in accordance with the product label for example:

- abstinence from penile-vaginal intercourse, when this is their preferred and usual lifestyle,
- oral contraceptives, either combined or progestogen alone,
- injectable progestogen,
- implants of etenogestrel or levonorgestrel,
- estrogenic vaginal ring,
- percutaneous contraceptive patches,
- intrauterine device or intrauterine system,
- male partner sterilisation prior to the female subject's entry into the study, and this male is the sole partner for that subject,
The information on the male sterility can come from the site personnel's review of the subject's medical records; or interview with the subject on her medical history.
- male condom combined with a vaginal spermicide (foam, gel, film, cream or suppository),
- male condom combined with a female diaphragm, either with or without a vaginal spermicide (foam, gel, film, cream, or suppository).
Adequate contraception does not apply to subjects of child bearing potential with same sex partners, when this is their preferred and usual lifestyle.


## Adverse event:

Any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected benefits (i.e., lack of efficacy), abuse or

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misuse.

| Blinding: | A procedure in which one or more parties to the trial are kept <br> unaware of the treatment assignment in order to reduce the <br> risk of biased study outcomes. The level of blinding is <br> maintained throughout the conduct of the trial, and only <br> when the data are cleaned to an acceptable level of quality <br> will appropriate personnel be unblinded or when required in <br> case of a serious adverse event. In an observer-blind study, <br> the subject and the site and sponsor personnel involved in the <br> clinical evaluation of the subjects are blinded while other <br> study personnel may be aware of the treatment assignment <br> (see Section 5.3 for details on observer-blinded studies). |
| :--- | :--- |
| Chemotherapeutic | As used in this document refers to an entire series of <br> chemotherapeutic cycles (repeated treatments) often lasting |
| several months. |  |

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agent.
Investigational
vaccine/product:
(Synonym of
Investigational
Medicinal Product)

Menarche:

Menopause: $\quad$ Menopause is the age associated with complete cessation of menstrual cycles, menses, and implies the loss of reproductive potential by ovarian failure. A practical definition accepts menopause after 1 year without menses
with an appropriate clinical profile at the appropriate age e.g. definition accepts menopause after 1 year without menses
with an appropriate clinical profile at the appropriate age e.g. $>45$ years.

OnChemo OnChemo refers to the administration of first dose of $H Z / s u$ vaccine simultaneous with the administration of a chemotherapeutic cycle (+/-1day), i.e. vaccination is "on" top of the next chemotherapeutic cycle.
A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

Menarche is the onset of menses for the first time in a young female and is preceded by several changes associated with puberty including breast development and pubic hair growth. Menarche usually occurs within 1-2 years of breast development, thelarche. However, a young female can become pregnant before her first menses. Thus, a conservative definition of non-childbearing potential in a pre-menarcheal female is a young female who has not yet entered puberty as evidenced by lack of breast development (palpable glandular breast tissue).

## Potential ImmuneMediated Disease:

PreChemo
PreChemo

Primary completion date:

Potential immune-mediated diseases (pIMDs) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology.

PreChemo refers to the administration of first dose of HZ/su vaccine at least 10 days prior to a chemotherapeutic cycle, i.e. vaccination is "pre" the next chemotherapeutic cycle.

The date that the final subject was examined or received an intervention for the purpose of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated.

Protocol amendment: The International Conference on Harmonisation (ICH) defines a protocol amendment as: 'A written description of a

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change(s) to or formal clarification of a protocol.' GSK Biologicals further details this to include a change to an approved protocol that affects the safety of subjects, scope of the investigation, study design, or scientific integrity of the study.
Protocol
administrative
change:

Randomisation:

Self-contained study:
Site Monitor:
Solicited adverse
event:

Sub-cohort: A group of subjects for whom specific study procedures are planned as compared to other subjects.

Term used throughout the protocol to denote an individual who has been contacted in order to participate or participates in the clinical study, either as a recipient of the vaccine(s)/product(s) or as a control.

Subject number: A unique number identifying a subject, assigned to each subject consenting to participate in the study.

Term used throughout the clinical study to denote a set of investigational product(s) or marketed product(s) or placebo intended to be administered to a subject, identified by a unique number, according to the study randomisation or treatment allocation.

Treatment number: A number identifying a treatment to a subject, according to the study randomisation or treatment allocation.

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| Unsolicited adverse | Any AE reported in addition to those solicited during the <br> event: |
| :--- | :--- |
| clinical study. Also any 'solicited' symptom with onset <br> outside the specified period of follow-up for solicited <br> symptoms will be reported as an unsolicited adverse event. |  |

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TRADEMARKS
The following trademarks are used in the present protocol.
Note: In the body of the protocol (including the synopsis), the names of the vaccines/products and/or medications will be written without the superscript symbol ${ }^{\text {TM }}$ or ${ }^{\circledR}$.

| Trademarks not owned by the <br> GlaxoSmithKline group of companies <br> (Amended: 11 August 2014) |
| :---: |
| Zostavax ${ }^{\circledR}$ (Merck \& Co., Inc.) |


| Generic description |
| :--- |
| Herpes zoster vaccine consisting of high- <br> titre live attenuated varicella-zoster virus <br> (Oka strain) |

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## 1. INTRODUCTION

### 1.1. Background

Varicella-Zoster Virus (VZV) causes two distinct diseases. Varicella (chickenpox) occurs shortly after primary VZV infection and is characterized by systemic illness and a widely disseminated rash. Herpes Zoster (shingles) occurs when VZV reactivates from latency and typically manifests as a localized, dermatomal rash.

The typical HZ rash usually lasts 2 to 4 weeks and is usually accompanied by pain that is often described as burning, shooting, or stabbing. In some patients, even touching the affected area lightly may cause pain, a phenomenon known as allodynia. This HZassociated pain may be severe, and pruritus, which can also be severe, may be as common as pain.

Although age is the most common risk factor for developing HZ, an increased incidence of HZ is also associated with immune suppression caused by haematologic malignancies (such as lymphoma), certain solid tumours, iatrogenic immunosuppression, human immunodeficiency virus (HIV) infection and some autoimmune diseases [Rusthoven, 1988; Feller, 2007; Kim, 2008; Rogers, 2011; Hata, 2011]. In a recent retrospective cohort study of over 55,000 hospital patients using Cox proportional hazards models, it was found that patients with diseases such as brain, breast, esophageal, gastric, colorectal or gynecologic cancers, and malignant lymphoma displayed a 1.8-8.4-fold increased risk of HZ events, compared to patients in this cohort with none of these diseases [Hata, 2011]. Notable in this study is that these patients at increased risk of HZ were not compared to healthy individuals but instead emerged through the analysis of patients with other underlying diseases within this hospitalized cohort. The increase in HZ within these populations is likely due to their immunocompromised state and indicates that there is a medical need to vaccinate these patients to reduce the morbidity associated with HZ. The increased cumulative incidence rate of HZ following diagnosis of malignant neoplasm, relative to the general population, is in part attributed to impaired immunity due to chemotherapy and radiotherapy [Rusthoven, 1988]. Patients with hematologic malignancies tend to be even more immunocompromised than those with solid tumours receiving chemotherapy. Nevertheless, patients with solid tumours receiving chemotherapy are also at increased risk of HZ on the basis of debility and malnutrition and may also be at high HZ risk due to immunosuppressive therapy for their underlying disease [Tong, 2007; Gopalan, 2012].

A live attenuated VZV vaccine, Zostavax ${ }^{\circledR}$ (Merck \& Co), is licensed in the United States (US), the European Union (EU) and elsewhere to prevent HZ in persons $\geq 50$ years of age (YOA) [Zostavax Prescribing Information, 2011; Zostavax, Summary of Product Characteristics, 2006]. This vaccine, however, is contraindicated in immunosuppressed or immunodeficient individuals [Kroger, 2011]. There is currently no licensed vaccine for the prevention of HZ in immunocompromised populations.

GlaxoSmithKline (GSK) Biologicals' candidate vaccine for the prevention of HZ is a recombinant subunit (su) vaccine consisting of the VZV glycoprotein E (gE) antigen and an Adjuvant System (AS01B). Different gE antigen doses (25,50 or $100 \mu \mathrm{~g}$ ) combined

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with the Adjuvant System AS01 ${ }_{B}$ have been evaluated in previous studies in over a thousand adults and administered to approximately 15,000 subjects in ongoing trials not yet analyzed. In the analyzed studies it was shown to elicit strong cellular and humoral immune responses. Furthermore, the safety and reactogenicity profile of this candidate vaccine was acceptable. Based on phase II data from the antigen dose-ranging study, ZOSTER-003, and the adjuvant dose comparison study, ZOSTER-010, a gE antigen dose of $50 \mu \mathrm{~g}$ and the Adjuvant System $\mathrm{AS} 01_{\mathrm{B}}$ were selected as the final vaccine formulation (henceforth, the final vaccine formulation of GSK Biologicals' candidate HZ vaccine will be referred to as HZ/su).

In addition to older adults, the present study seeks to confirm that $\mathrm{HZ} /$ su provides protection for persons of all ages with compromised immune systems, such as Haematopoietic stem Cell Transplant (HCT) recipients, HIV-infected individuals, Solid Organ Transplants (SOT) recipients and patients with malignant haematologic or solid tumours. Since $\mathrm{HZ} / \mathrm{su}$ is a subunit vaccine, there is no risk that the vaccine itself will cause varicella, a potential concern following vaccination with a live VZV vaccine [Zostavax Prescribing Information, 2011; Loparev, 2007]. The increased incidence of HZ in patients with solid tumours receiving chemotherapy establishes the basis for evaluating $\mathrm{HZ} / \mathrm{su}$ for the prevention of HZ in this population.

A phase I/IIa study, ZOSTER-001, was conducted to evaluate the safety and immunogenicity of HZ/su in autologous HCT recipients 18 YOA and older. The primary endpoint data from this study showed that gE-specific cell-mediated immune (CMI) responses to HZ/su administered on schedules of 0,1 and 3 months, 0 and 1 months (as part of the 3 dose schedule), or 1 and 3 months (with month 0 defined as 50-70 days following autologous HCT), were significantly higher than in placebo recipients. Also, the safety profile of HZ/su through 1-month following the final vaccine dose was acceptable in this study. Therefore, the results of study ZOSTER-001 support the further evaluation of $\mathrm{HZ} / \mathrm{su}$ in phase II/III studies for the prevention of HZ in other immunocompromised populations such as patients with solid tumours receiving chemotherapy. An extension of the ZOSTER-001 study remains ongoing for assessment of long-term safety and immunogenicity observations.

Although immunization is the optimal way to prevent infection, immunocompromised patients may be unable to mount a protective immune response to active vaccination. Data in the literature on their immune responses to vaccination are sparse and sometimes contradictory. It is also unclear what the optimal vaccine dosing schedule is for patients receiving chemotherapy. However recent publications on vaccination against the H1N1 influenza virus show that cancer patients, even if under chemotherapy, are able to mount a reasonably robust immune response [Mackay, 2011; Hottinger, 2012; Kotton, 2012; Rousseau, 2012; Xu, 2012]. Furthermore, immunization of highly immunocompromised persons with live virus vaccines may result in uncontrolled proliferation of attenuated strains [Loparev, 2007]. Thus, patients with solid tumours receiving chemotherapy comprise an immunocompromised population that may benefit from vaccination with a non-replicating vaccine such as HZ/su.

Please refer to the current Investigator Brochure for information regarding the preclinical and clinical studies and the potential risks and benefits of GSK Biologicals'

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candidate HZ/su vaccine and related GSK Biologicals' candidate vaccines (collectively referred to as $\mathrm{gE} / \mathrm{AS} 01$ in that document).

### 1.2. Rationale for the study and study design

Study ZOSTER-028 will be conducted to evaluate the immunogenicity and safety of $\mathrm{HZ} / \mathrm{su}$ in patients 18 YOA and older diagnosed with one or more solid tumours and receiving chemotherapy. The results of studies in healthy adults and from the active phase of ZOSTER-001 (in autologous HCT patients) support the selection of a 2-dose vaccine schedule. Studies in healthy adults demonstrated strong vaccine-induced immune responses following vaccine administration at 0 and 2 months. In addition, the results of ZOSTER-001 demonstrate comparably strong immune responses following vaccine administration at months 0 and 1. Therefore, in the present study, the window for administration of the second vaccine dose will be 30-60 days after the first dose giving some flexibility to the patient and the investigator while dealing with chemotherapy cycles.

Subjects in the ZOSTER-028 study will initially be randomised into two groups based on the vaccination schedule in relation to the start of $\boldsymbol{a}$ chemotherapy $\boldsymbol{c y c l e}$. The OnChemo group receives their first $\mathrm{HZ} / \mathrm{su}$ vaccination at the start of $\boldsymbol{a}$ chemotherapy cycle, while the PreChemo group receives their first HZ/su vaccination at least 10 days before the start of $\boldsymbol{a}$ chemotherapy cycle. Unpublished data with other GSK candidate vaccines indicates that vaccination at the start of $\boldsymbol{a}$ chemotherapy cycle can lead to a decreased/suppressed immune response, possibly due to steroids used concomitantly in high doses to prevent nausea and vomiting. Therefore, the primary objective linked to immunogenicity will be assessed in the PreChemo groups only. For this reason, the study groups will be allocated 4:1 (186/46) PreChemo:OnChemo. (Amended: 11 August 2014)

This study is part of a clinical development plan (CDP) designed to evaluate HZ/su for the prevention of HZ and related complications in adults with immunocompromising conditions. In a second arm of the CDP, the vaccine is being studied in older subjects, $\geq 50 \mathrm{YOA}$. The present study will evaluate the immunogenicity and safety of $\mathrm{HZ} / \mathrm{su}$ vaccination in subjects 18 YOA and above with solid tumours receiving chemotherapy.

### 1.2.1. Rationale for the use of placebo

A lyophilised sucrose cake reconstituted with saline $(\mathrm{NaCl})$ solution is included as a negative control (placebo) in the study evaluating the immunogenicity and safety profile of the candidate $\mathrm{HZ} / \mathrm{su}$ vaccine in this study population. Use of the placebo control and the observer-blind, randomised study design, will allow to control for potential biases in the conduct of the study.

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## 2. OBJECTIVES

### 2.1. Co-Primary objectives

- To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).

Criteria to be used:
The objective is met if the lower limit of the $95 \%$ confidence interval (CI) of the Geometric Mean (GM) ratio (HZ/su PreChemo group over placebo PreChemo group) in anti-gE ELISA antibody concentrations is greater than 3.

- To evaluate the safety and reactogenicity following administration of the HZ/su vaccine as compared to placebo up to 30 days post last vaccination in subjects with solid tumours receiving chemotherapy.
Criteria to be used:
This analysis is descriptive, no criterion has been defined.
Refer to Section 9.1 for the definition of the primary endpoints.


### 2.2. Secondary objectives

- To evaluate vaccine response rate in anti-gE humoral immunogenicity responses at Month 2, following a two-dose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).
Criteria to be used:
The objective is met if the lower limit of the $95 \%$ CI of the vaccine response rate for anti-gE ELISA antibody concentrations at Month 2 in the HZ/su PreChemo group is at least $60 \%$.
- To evaluate gE-specific CD4+T-cell immunogenicity responses at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only) (in the CMI sub-cohort).
Criteria to be used:
The objective is met if the lower limit of the $95 \%$ CI of the GM ratio (HZ/su PreChemo group over placebo PreChemo group) in gE-specific CD4+ T-cell frequencies at Month 2 is greater than 1.
- To evaluate vaccine response rate in gE-specific CD4+ T-cell mediated immunogenicity at Month 2, following a two-dose administration of the HZ/su vaccine in subjects with solid tumours receiving chemotherapy (PreChemo Groups only) (in the CMI sub-cohort).


## Criteria to be used:

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The objective is met if the lower limit of the $95 \%$ CI of the vaccine response rate for gE-specific CD4+ T-cell frequencies at Month 2 in the HZ/su PreChemo group is at least $50 \%$.

- To evaluate the anti-gE humoral immunogenicity response at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (all subjects).


## Criteria to be used:

The objective is met if the lower limit of the $95 \%$ confidence interval (CI) of the Geometric Mean (GM) ratio (HZ/su group over placebo group) in anti-gE ELISA antibody concentrations is greater than 3.

- To evaluate vaccine response rate in anti-gE humoral immunogenicity responses at Month 2, following a two-dose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (all subjects receiving the HZ/su vaccine).
Criteria to be used:
The objective is met if the lower limit of the $95 \%$ CI of the vaccine response rate for anti-gE ELISA antibody concentrations at Month 2 in the HZ/su group is at least $60 \%$.
- To evaluate safety following administration of the HZ/su vaccine, as compared to placebo, from 30 days post last vaccination until study end in subjects with solid tumours receiving chemotherapy.
- To characterize anti-gE humoral immunogenicity responses at Month 0, Month 1, Month 2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13 within the HZ/su and placebo groups.
- To characterize gE-specific CD4+ T-cell mediated immunogenicity responses at Month 0, Month 1, Month 2, and Month 13 within the HZ/su and placebo groups (PreChemo Groups only) (in the CMI sub-cohort). (Amended: 11 August 2014)
Refer to Section 9.2 for the definition of the secondary endpoints.


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## 3. STUDY DESIGN OVERVIEW



## (Amended: 11 August 2014)

[^13]Protocol waivers or exemptions are not allowed with the exception of immediate safety concerns. Therefore, adherence to the study design requirements, including those specified in the outline of study procedures (Section 5.5), are essential and required for study conduct.

- Experimental design:

Phase II/III, observer-blind randomised, placebo controlled, multi-centric, multicountry study with two parallel groups.

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- Duration of the study:

Each subject will be followed at least until he/she completes Visit 5 (i.e., until Month 13 , approximately 12 months after the second dose of study vaccine/ placebo). The first vaccination visit at Month 0 (Visit 1) will be preceded by a mandatory Prevaccination visit that will take place from 30 days prior to Visit 1 up to the day of Visit 1 (the Pre-vaccination visit can occur on the same day as Visit 1).

- Epoch 001: Primary starting from the Pre-vaccination visit (up to -30 days) and ending at Visit 5 (Month 13). The study end will take place when all subjects have completed their 12 month post-dose 2 follow-up visit (at Month 13, Visit 5). The total duration of the study for each subject is expected to be approximately 14 months including the Pre-vaccination visit.
- Study groups:

Table $1 \quad$ Study groups and epochs foreseen in the study (Amended: 11 August 2014)

| Study groups | Number of subjects | Age (Min.) $^{*}$ | Epoch |
| :---: | :---: | :---: | :---: |
|  |  | Epoch 001 |  |
| HZ/su-PreChemo | 93 | 18 years | $\bullet$ |
| Placeb-PreChemo | 93 | 18 years | $\bullet$ |
| HZ/su-OnChemo | 23 | 18 years | $\bullet$ |
| Placeb-OnChemo | 23 | 18 years | $\bullet$ |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb $=$ Placebo; Min. $=$ Minimum

* And above the legal age of consent (see Table 28)

Table 2 Study groups and treatment foreseen in the study

| Treatment <br> name | Vaccine/ <br> Product name | Study Groups |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | HZ/su- <br> PreChemo | Placeb- <br> PreChemo | HZ/su- <br> OnChemo | Placeb- <br> OnChemo |  |
| HZ/su | VZV gE | $\bullet$ |  | $\bullet$ |  |
|  | AS01B | $\bullet$ |  | $\bullet$ |  |
|  | Lyophilised sucrose cake |  | $\bullet$ |  | $\bullet$ |
|  | Saline (NaCl) solution for <br> reconstitution |  | $\bullet$ |  | $\bullet$ |

HZ/su = Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb = Placebo; VZV = Varicella Zoster Virus; gE $=$ recombinant purified Glycoprotein E; ASO1B $=$ Adjuvant System $\mathrm{ASO1} \mathrm{~B} ; \mathrm{NaCl}=$ sodium chloride

- Control: placebo control [Lyophilised sucrose reconstituted with saline $(\mathrm{NaCl})$ solution].
- Vaccination schedule: 0, 1-2 Month
- Treatment allocation:

Eligible subjects will be randomised to two treatment groups: investigational HZ/su vaccine or placebo (1:1); and to two vaccination strata: PreChemo Group, first

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vaccination at least 10 days before the start of $\boldsymbol{a}$ chemotherapy cycle, or OnChemo
Group, first vaccination at the start of $\boldsymbol{a}$ chemotherapy cycle (4:1). The overall ratio of these 4 study groups will be 4:4:1:1 (see Table 5). (Amended: 11 August 2014)

- Blinding:

Observer-blind for study vaccine but not for time of vaccination relative to chemotherapy.

## Table 3 Blinding of study epochs

| Study Epoch | Blinding |
| :--- | :--- |
| Epoch 001 | observer-blind |
| *Beyond Visit 3 (Month 2), the investigator may be unblinded with respect to individual subject data summarised in the |  |
| clinical study report. For details, please refer to Section 9.11.1. |  |

Refer to Section 5.3 for details of the blinding procedure.

- Biological samples to be collected:
- A urine specimen will be collected from all female subjects of childbearing potential at the Pre-vaccination Visit, Visit 1 and Visit 2. If a serum pregnancy test instead of a urine pregnancy test is required by country, local or ethics committee regulations, a blood sample will be collected from women of childbearing potential at Visit 1 and Visit 2 and used for the test as per local guidance.
- Blood samples (approximately 8 mL ) will be collected from all subjects at Visits $1,2,3,4$ and 5 . Blood samples will be used to assess humoral immune responses by with respect to the study/investigational vaccine in all subjects.
- Blood samples (approximately 30 mL ) will be collected from a sub-cohort of subjects at Visits 1, 2, 3 and 5 to assess CMI responses (CMI sub-cohort).
- Type of study: self-contained.
- Data collection: Standardised electronic Case Report Form (eCRF).
- Safety monitoring:

Unblinded evaluation of safety for the subjects (with coded group names) will be performed by an iSRC on an ongoing basis. Operational details for the iSRC will be provided in the iSRC Charter.

## 4. STUDY COHORT

### 4.1. Number of subjects

Target enrolment is approximately 232 eligible adults diagnosed with solid tumours receiving chemotherapy. Taking into account a projected $\mathbf{\sim 2 7 \%}$ rate from drop-out and non-evaluable subjects at Month 2 (Visit 3), the number of evaluable subjects is estimated to be 168 ( 84 per treatment group). See Section 9.3 for a description of the criteria used

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in the determination of sample size. Refer to Sections 4.2 and 4.3 for eligibility criteria.

## (Amended 11 August 2014)

The sub-cohort foreseen for CMI analyses is described in Table 4. Refer to Section 9.3 for details regarding the estimation of its sample size.

Table 4 Sub-cohorts

| Sub-cohort name | Description | Estimated number of <br> enrolled subjects |
| :--- | :--- | :---: |
| CMI sub-cohort* | Blood samples (approximately 30 mL ) collected at Visits <br> $1,2,3$ and 5 will be analysed to assess CMI response | 76 |

* This CMI sub-cohort will be comprised exclusively of subjects from the PreChemo Groups. $\mathrm{mL}=$ Millilitre; CMI = Cell-mediated Immunity
- Overview of the recruitment plan:

Study ZOSTER-028 is planned to be conducted at sites in different countries worldwide. The number of subjects required for enrolment for the study groups and within the CMI Sub-cohort is indicated in Table 5.

Table 5 Number of subjects required for enrolment (Amended: 11 August 2014)

| Vaccination Start stratum |  | Study groups |  |
| :--- | :--- | :---: | :---: |
|  |  | Overated number of subjects <br> $\mathbf{N}$ | CMI sub-cohort <br> $\mathbf{N}$ |
| First Vaccination <br> at least 10 days before the start of a chemotherapy <br> cycle | HZ/su-PreChemo | 93 | 38 |
|  | Placeb-PreChemo | 93 | 38 |
| First Vaccination <br> at the start of $a$ chemotherapy cycle | HZ/su-OnChemo | 23 | 0 |
|  | Placeb-OnChemo | 23 | 0 |
|  | Total | 232 | 76 |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb = Placebo
The enrolment period is estimated to be approximately 6 months after the first subject has been enrolled depending on the enrolment rate. Refer to Section 9.3 for a description of the assumptions used in the estimation of sample size. Enrolment target numbers per region, country and sub-cohort will be assigned at the study start and may be adjusted during the study. The recruitment rate will be monitored using a study-specific central randomisation system on the Internet (SBIR).

Transfer of supplies will be tracked by the central randomisation system. Monitoring visit frequency will be adapted to the pace of enrolment. Vaccine doses will be distributed to each study site respecting the randomisation block size.

### 4.2. Inclusion criteria for enrolment

Deviations from inclusion criteria are not allowed because they can potentially jeopardize the scientific integrity of the study, regulatory acceptability or subject safety. Therefore, adherence to the criteria as specified in the protocol is essential.

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All subjects must satisfy ALL the following criteria at study entry:
Study entry occurs at the Pre-vaccination visit. Inclusion criteria are checked at the Prevaccination visit, and a check for any changes compared to the Pre-vaccination visit will be performed at Visit 1 and recorded in the Pre-vaccination Section of the eCRF.

- Subjects who, in the opinion of the investigator, can and will comply with the requirements of the protocol (e.g., completion of the diary cards, return for follow-up visits, ability to have scheduled contacts to allow evaluation during the study);
- Written informed consent obtained from the subject;
- A male or female aged 18 years or older (and has reached the age of legal consent) at the time of study entry (i.e., when informed consent is signed). Refer to Section 11.1 for country-specific age of legal consent;
- Subject who has been diagnosed with one or more solid tumours (defined as a solid malignancy, i.e., not a blood element malignancy);
- Subject who is receiving or will receive a cytotoxic or immunosuppressive chemotherapy (such that the study vaccine can be administered at the latest at the start of the second cycle of chemotherapy).
- Life expectancy of greater than one year;
- Female subjects of non-childbearing potential may be enrolled in the study;
- Non-childbearing potential is defined as pre-menarche, current tubal ligation, hysterectomy, ovariectomy or post-menopause;
Please refer to the GLOSSARY OF TERMS for the definition of menopause.
- Female subjects of childbearing potential may be enrolled in the study, if the subject:
- has practiced adequate contraception for 30 days prior to vaccination, and
- has a negative pregnancy test on the day of vaccination, and
- has agreed to continue adequate contraception during the entire treatment period and for 2 months after completion of the vaccination series.

Please refer to the GLOSSARY OF TERMS for the definition of adequate contraception.

### 4.3. Exclusion criteria for enrolment

Deviations from exclusion criteria are not allowed because they can potentially jeopardize the scientific integrity of the study, regulatory acceptability or subject safety. Therefore, adherence to the criteria as specified in the protocol is essential.

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The following criteria should be checked at the time of study entry. If ANY exclusion criterion applies, the subject must not be included in the study:

Study entry occurs at the Pre-vaccination visit. Exclusion criteria are checked at the Prevaccination visit, and a check for any changes compared to the Pre-vaccination visit will be performed at Visit 1 and recorded in the Pre-vaccination Section of the eCRF.

- Subjects receiving only newer, more targeted therapies (e.g., trastuzumab) if not taken together with a classical chemotherapy (since these new more targeted therapies are not considered immunosuppressant);
- Chronic administration and/or planned administration of systemic glucocorticoids (defined as prednisone $\geq 20 \mathrm{mg} /$ day, or equivalent, for more than 14 consecutive days in total) within one month prior to the first vaccine dose and up to Visit 3 (Month 2). Inhaled, intra-articularly injected, and topical steroids are allowed; (Amended: 11 August 2014)
- Previous vaccination against HZ or varicella within 12 months preceding the first dose of study vaccine/ placebo;
- Planned administration during the study of a HZ vaccine (including an investigational or non-registered vaccine) other than the study vaccine;
- Previous chemotherapy course less than one month before first study vaccination;
- Occurrence of a varicella or HZ episode by clinical history within the 12 months preceding the first dose of study vaccine/ placebo;
- History of allergic disease or reactions likely to be exacerbated by any component of the vaccine or study material and equipment;
- Administration or planned administration of a live vaccine in the period starting 30 days before the first dose of study vaccine and ending 30 days after the last dose of study vaccine, or, administration or planned administration of a non-replicating vaccine* within 8 days prior to or within 14 days after either dose of study vaccine.
* E.g., inactivated and subunit vaccines, including inactivated and subunit influenza vaccines and pneumococcal conjugate vaccines;
- HIV infection by clinical history;
- Acute disease and/or fever at the time of vaccination. Acute disease is defined as the presence of a moderate or severe illness with or without fever, but excludes the underlying malignancy, as well as the expected symptoms/signs associated with that disease or its treatment;

Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ on oral, axillary or tympanic setting, or $\geq 38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$ on rectal setting. The preferred route for recording temperature in this study will be oral.
Subjects with a minor illness (such as mild diarrhoea, mild upper respiratory infection) without fever, may receive the first dose of study vaccine/ placebo at the discretion of the investigator.

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- Any condition which, in the judgment of the investigator would make intramuscular injection unsafe;
- Pregnant or lactating female;
- Female planning to become pregnant or planning to discontinue contraceptive precautions (if of childbearing potential) before Month 3 (i.e., 2 months after the last dose of study vaccine/ placebo).


## 5. CONDUCT OF THE STUDY

### 5.1. Regulatory and ethical considerations, including the informed consent process

The study will be conducted in accordance with all applicable regulatory requirements.
The study will be conducted in accordance with the ICH Guideline for Good Clinical Practice (GCP), all applicable subject privacy requirements and the guiding principles of the Declaration of Helsinki.

The study has been designed and will be conducted in accordance with the ICH Harmonised Tripartite Guideline for clinical investigation of medicinal products in the paediatric population (ICH E11) and all other applicable ethical guidelines.

GSK will obtain favourable opinion/approval to conduct the study from the appropriate regulatory agency, in accordance with applicable regulatory requirements, prior to a site initiating the study in that country.

Conduct of the study includes, but is not limited to, the following:

- Institutional Review Board (IRB)/Independent Ethics Committee (IEC) review and favourable opinion/approval of study protocol and any subsequent amendments.
- Subject informed consent.
- Investigator reporting requirements as stated in the protocol.

GSK will provide full details of the above procedures to the investigator, either verbally, in writing, or both.

Freely given and written (or witnessed thumb printed consent in case of an illiterate subject) informed consent must be obtained from each subject prior to participation in the study.

GSK Biologicals will prepare a model Informed Consent Form (ICF) which will embody the ICH GCP and GSK Biologicals required elements. While it is strongly recommended that this model ICF is to be followed as closely as possible, the informed consent requirements given in this document are not intended to pre-empt any local regulations which require additional information to be disclosed for informed consent to be legally effective. Clinical judgement, local regulations and requirements should guide the final structure and content of the local version of the ICF.

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The investigator has the final responsibility for the final presentation of the ICF, respecting the mandatory requirements of local regulations. The ICF generated by the investigator with the assistance of the sponsor's representative must be acceptable to GSK Biologicals and be approved (along with the protocol, and any other necessary documentation) by the IRB/IEC.

### 5.2. Subject identification and randomisation of treatment

### 5.2.1. Subject identification

Subject numbers will be assigned sequentially to subjects consenting to participate in the study, according to the range of subject numbers allocated to each study centre.

### 5.2.2. Randomisation of treatment

### 5.2.2.1. Randomisation of supplies

The randomisation will be performed at GSK Biologicals, Belgium, using MATEX, a program developed for use in SAS $^{\circledR}$ (Cary, NC, USA) by GSK Biologicals.

To allow GSK Biologicals to take advantage of greater rates of recruitment than anticipated at individual centres in this multicentre study, and to thus reduce the overall study recruitment period, an over-randomization of supplies will be prepared.

The vaccine/placebo doses will be distributed to each study centre, respecting the randomization block size.

### 5.2.2.2. Treatment allocation to the subject

The treatment allocation at the investigator site will be performed using a central randomisation system on internet (SBIR). The treatment numbers will be allocated by dose. Eligible subjects will be randomised to the investigational $\mathrm{HZ} / \mathrm{su}$ vaccine or placebo (1:1).

When SBIR is not available, please refer to the SBIR user guide or the Study Procedures Manual (SPM) for specific instructions.

After having checked the eligibility of the subject and obtaining the ICF, the site staff in charge of the vaccination will access SBIR. Upon providing the subject identification number, the randomisation system will use the minimisation algorithm to determine the treatment number to be used for the subject. Each treatment number must be recorded in the eCRF on the Vaccine Administration screen.

### 5.2.2.2.1. Study group and treatment number allocation

Target enrolment is approximately 232 eligible adults diagnosed with solid tumours receiving chemotherapy. During the Pre-vaccination visit eligible subjects will be randomised to the investigational $\mathrm{HZ} / \mathrm{su}$ vaccine or placebo according to a $1: 1$ ratio (vaccine:placebo), and stratified to PreChemo Group, first vaccination at least 10 days before the start of a chemotherapy cycle or OnChemo Group, first vaccination at the

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start of $\boldsymbol{a}$ chemotherapy cycle (4:1). The overall ratio of these 4 study groups ( $\mathbf{H Z} / \mathbf{s} \boldsymbol{u}$ PreChemo, Placeb-PreChemo, HZ/su-OnChemo, and Placeb-OnChemo) will be 4:4:1:1. (Amended: 11 August 2014)

Allocation of the subject to a study group at the investigator site will be performed using a randomisation system on internet (SBIR). The randomisation algorithm will use a minimisation procedure accounting for age ( $18-49 \mathrm{YOA}$ and $\geq 50 \mathrm{YOA}$ ), centre, country and gender (Male and Female). (Amended: 11 August 2014)

After obtaining the signed and dated ICF from the subject and having checked the eligibility of the subject, the site staff in charge of the vaccine administration will access SBIR. Upon providing the subject identification number, the randomisation system will determine the study group and will provide the treatment number to be used for each dose.

The number of each administered treatment must be recorded in the eCRF on the Vaccine Administration screen.

When SBIR is not available, please refer to the SBIR user guide or the SPM for specific instructions.

### 5.2.2.2.2. Treatment number allocation for subsequent doses

For each dose subsequent to the first dose, the study staff in charge of the vaccine administration will access SBIR, provide the subject identification number, and the system will provide a treatment number consistent with the allocated group.

The number of each administered treatment must be recorded in the eCRF on the Vaccine Administration screen.

### 5.2.3. Allocation of subjects to assay subsets (CMI sub-cohort)

The CMI analyses will be performed at specified timepoints for subjects included in the CMI sub-cohort (Refer to Table 4). This CMI sub-cohort will be comprised exclusively of subjects from the PreChemo Groups. This is a subgroup of the subjects in the study in selected countries at designated sites that have access to a peripheral blood mononuclear cells (PBMC) processing facility within the acceptable time window from sample collection to PBMC processing.

The target number for the CMI sub-cohort is 76 subjects (30 evaluable subjects per treatment group). A randomization algorithm will be used to attribute the subjects to the sub-cohorts at the designated sites (see Table 5). (Amended: 11 August 2014)

### 5.3. Method of blinding

Data will be collected in an observer-blind manner. By observer-blind, it is meant that during the course of the study, the vaccine recipient and those responsible for the evaluation of any study endpoint (e.g., safety and reactogenicity) will all be unaware of which vaccine was administered. To do so, vaccine preparation and administration will

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be done by authorised medical personnel who will not participate in any of the study clinical evaluation assays.

From study start until Month 2 (when the study report of the main analysis will be written see Section 9.11.1), the study is observer-blind. From Month 2 (Visit 3) until Month 13 (Visit 5, study end), the study remains blinded for the subjects and for the study staff to ensure that study-related procedures and observations performed at the study sites will continue to be conducted in a single-blind manner.

Beyond Month 2, the subjects will continue to be blinded and access to unblinded individual subject treatment assignments will be restricted to GSK personnel only on an as-needed basis. The investigators will receive a copy of the study report of the final analysis for immunogenicity and safety data up to Month 2, and may thus be unblinded only with respect to any individual subject data summarised in the study report. However, the individual data listings and subject treatment assignments will not be provided to the investigators until after the conclusion of the study, following the completion of Month 13 (Visit 5, study end).

The laboratory in charge of the laboratory testing will be blinded to the treatment, and codes will be used to link the subject and study (without any link to the treatment attributed to the subject) to each sample.

### 5.4. General study aspects

Supplementary study conduct information not mandated to be present in this protocol is provided in the accompanying SPM. The SPM provides the investigator and the site personnel with administrative and detailed technical information that does not impact the safety of the subjects.

Refer to the Section 7.10 for information about safety evaluation by the iSRC.

### 5.4.1. Suspected HZ cases

Suspected HZ is defined as a new rash characteristic of HZ (i.e., unilateral, dermatomal and accompanied by pain broadly defined to include allodynia, pruritus or other sensations), or a vesicular rash suggestive of VZV infection regardless of the dermatomal distribution, and without alternative diagnosis. Additionally, sometimes HZ cases do not present with the characteristic HZ or VZV rash, but have a clinical presentation and specific laboratory findings* suggestive of VZV infection. These cases should also be considered as occurrences of HZ. Complications of HZ include, but are not limited to, postherpetic neuralgia (PHN), HZ vasculitis, disseminated disease, ophthalmic disease, neurologic disease, and visceral disease.

* Specific laboratory findings include VZV-positive polymerase chain reaction (PCR), culture, immunohistochemical staining, or other tests that strongly suggest VZVinfection, which have been performed in the course of a medical evaluation.

The occurrence of HZ and/or HZ complications will constitute an AE/SAE as appropriate. The occurrence of HZ is an intercurrent medical condition (see Section 6.7).

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The reporting period for cases of HZ will be from Month 0 to study end. The standard reporting period as specified in Section 7.3.1 for AE/SAE should be used for HZ complications.

At Visit 1, all subjects will be informed of the signs and symptoms of typical HZ.

### 5.5. Outline of study procedures

Table 6 summarises the list of study procedures to be followed during the study visits and contact(s).

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## Table 6 List of study procedures

| Epoch | Epoch 001 |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of contact | Prevaccination Visit ${ }^{\dagger}$ | Visit ${ }^{*}$ | Visit 2** | Visit 3 | Visit 4*** | Month 5 Phone Contact | Month 9 Phone Contact | Visit $5^{\boldsymbol{\Delta}}$ |
| Timepoints | $\begin{array}{\|c\|} \hline \text { Up to }-30 \\ \text { to }-10 \text { days } \\ \hline \end{array}$ | Month 0 | Month 1 | Month 2 | Month 6 (Months 4 to 13) | Month 5 | Month 9 | Month 13 |
| Sampling timepoints |  | Pre-Vacc | Post-Vacc 1 | Post-Vacc 2 | Post-Vacc 2 |  |  | Post-Vacc 2 |
| Informed consent | - | $0{ }^{\text {a }}$ |  |  |  |  |  |  |
| Check inclusion criteria ${ }^{\text {b }}$ | - | $\bullet$ |  |  |  |  |  |  |
| Check exclusion criteria ${ }^{\text {b }}$ | $\bullet$ | $\bullet$ |  |  |  |  |  |  |
| Record demographic data | - |  |  |  |  |  |  |  |
| Randomisation | - |  |  |  |  |  |  |  |
| Pre-vaccination visit conclusion | $\bullet$ |  |  |  |  |  |  |  |
| Medical history |  | $\bullet$ |  |  |  |  |  |  |
| Specific subject characteristics ${ }^{\text {c }}$ |  | $\bullet$ |  |  |  |  |  |  |
| Check contraindications |  | - | - |  |  |  |  |  |
| History directed physical examination |  | 0 |  |  |  |  |  |  |
| Training on self-reporting by subjects ${ }^{\text {d }}$ | 0 | 0 | 0 | 0 | 0 |  |  |  |
| HCG pregnancy test if applicable ${ }^{\text {e }}$ | - ${ }^{\text {e }}$ | $\bullet$ | $\bullet$ |  |  |  |  |  |
| Pre-vaccination body temperature |  | $\bullet$ | $\bullet$ |  |  |  |  |  |
| Blood sampling (approximately 8 mL ) for humoral immune response from all subjects |  | - | - | - | - |  |  | - |
| Blood sampling (approximately 30 mL ) for CMI response in CMI sub-cohort subjects only |  | $\bullet$ | $\bullet$ | - |  |  |  | $\bullet$ |
| Assignment/recording of treatment number |  | $\bullet$ | $\bullet$ |  |  |  |  |  |
| Vaccination |  | - | - ${ }^{\text {f }}$ |  |  |  |  |  |
| Training on completion of diary cards |  | 0 | 0 |  |  |  |  |  |
| Dispensing of a diary card for solicited AEs and for unsolicited AEs and concomitant medication/vaccination to the subjects |  | 0 | 0 |  |  |  |  |  |
| Daily post-vaccination recording of solicited adverse events (Days 0-6) by subjects on diary card 9 |  | 0 | 0 | 0 |  |  |  |  |
| Return of diary cards (for solicited and unsolicited symptoms) |  |  | 0 | 0 |  |  |  |  |

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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Epoch | Epoch 001 |  |  |  |  |  |  |  |
| Type of contact | Prevaccination Visit ${ }^{\dagger}$ | Visit ${ }^{*}$ | Visit 2** | Visit 3 | Visit 4*** | Month 5 Phone Contact | Month 9 Phone Contact | Visit 5 ${ }^{\text {a }}$ |
| Timepoints | $\begin{array}{\|c\|} \hline \text { Up to }-30 \\ \text { to }-10 \text { days } \\ \hline \end{array}$ | Month 0 | Month 1 | Month 2 | Month 6 (Months 4 to 13) | Month 5 | Month 9 | Month 13 |
| Sampling timepoints |  | Pre-Vacc | Post-Vacc 1 | Post-Vacc 2 | Post-Vacc 2 |  |  | Post-Vacc 2 |
| Transcription of the diary card for solicited symptoms, unsolicited AE and concomitant medication and vaccination by study staff/investigator 9 |  |  | $\bullet$ | $\bullet$ |  |  |  |  |
| Recording of any concomitant medication//product/vaccine/treatment which could impact the immune response or is part of a chemotherapy |  | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Recording of non-serious adverse events within 30 days (Days 0-29) post-vaccination, by investigator |  | - | - | - |  |  |  |  |
| Reporting of intercurrent medical conditions including HZ h |  | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Reporting of serious adverse events (SAEs) ${ }^{\text {g }}$ |  | $\bullet$ - | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | - |
| Reporting of SAEs related to study participation or to a concurrent GSK medication/vaccine $g$ | $\bullet$ | $\bullet$ | - | - | $\bullet$ | - | - | - |
| Reporting of pregnancies |  | - ${ }^{i}$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Reporting of potential immune-mediated diseases (pIMDs) ${ }^{\text {g }}$ |  | - ${ }^{\text {i }}$ | $\bullet$ | $\bullet$ | $\bullet$ | - | $\bullet$ | $\bullet$ |
| Study analysis |  |  |  | 0 |  |  |  | 0 |
| Study conclusion |  |  |  |  |  |  |  | $\bullet$ |

Note: The double-line border following Month 2 indicates the analyses which will be performed on all data (i.e., data that are as clean as possible) obtained after completion of Visit Note
3.

Vacc = vaccination; HCG = Human Chorionic Gonadotropin; pIMDs = potential Immune-Mediated Diseases; GSK = GlaxoSmithKline; CMI = Cell-Mediated Immunity; HZ $=$ Herpes Zoster.

- is used to indicate a study procedure that requires documentation in the individual eCRF
- is used to indicate a study procedure that does not require documentation in the individual eCRF.
$\dagger$ The Pre-vaccination visit is mandatory and can occur on the same day as Visit 1 . If the Pre-vaccination visit occurs on the same day as Visit 1 , all procedures indicated under the Pre-vaccination visit will be performed and recorded in the eCRF at Visit 1.
Visit 1 will be the day of first vaccination.
** Visit 2 (the second dose of study vaccine/ placebo administration) will be 1 to 2 months after the first vaccination AND should be at the first day (allowing a window of $+/-1$ day) of a subsequent cycle of chemotherapy. (Amended: 11 August 2014)


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*** Visit 4 will occur within Months 4 to 13 for a Blood Sampling at the start of the last cycle of chemotherapy (if at least two months after the previous Blood Sampling (V3/M2)). Thus, the timing of this particular visit will be variable depending on the subject's chemotherapy schedule and also on when they started vaccination in relation to their chemotherapeutic regimen (see Table 7). This visit will coincide with the subject's lowest immune status.
${ }^{\Delta}$ Should Visit 4 coincide with Month 13, it will be recorded as Visit 5 in the eCRF, i.e., the Visit 5 procedures will be conducted (including a Blood Sampling for CMI) and Visit 5 will be the visit recorded using the special Visit 5 tick-box in the eCRF indicating that Visit 5 has superseded Visit 4.
If a Pre-vaccination visit occurs, informed consent will be reconfirmed at Visit 1 , if needed per local requirements.
${ }^{\text {b }}$ If study entry occurs at the Pre-vaccination visit, eligibility criteria, medical history and demographic characteristics will be checked at this visit (otherwise these will be checked at Visit 1). A check for any changes compared to the Pre-vaccination Visit will be performed at Visit 1 and recorded in the Pre-vaccination section of the eCRF. In case the subject is no longer eligible at Visit 1, the subject will be withdrawn from the study. The reason for this will be recorded in the Pre-vaccination section of the eCRF.
© The following subject characteristics will be recorded in the eCRF for each subject at the time of enrolment:

1. Diagnosis for solid tumour malignancy;
2.Previous varicella and HZ vaccination status;
2. Evidence of prior VZV infection: when readily available, serological evidence of prior VZV infection, or else by medical history;
3. History of current and previous hospitalizations/surgery(s)/chemotherapy (based on readily available admissions and discharge for the solid tumour for which the subject is included in the study). Notes:
a. Number and dates of chemotherapy courses and cycles, and chemotherapeutic regimens;
b. Number and dates of radiotherapy courses and treatments;
c. Number and dates of surgeries.

Subjects will be instructed to contact their study site immediately if the subject develops any symptoms suggestive of HZ if the subject manifests any symptoms he/she perceive as serious and, in case of pregnancy for women of childbearing potential.
Only for women of childbearing potential. Pregnancy testing must be performed with a urine or serum sample. Serum test should only be considered, instead of a urine pregnancy test, if required by country, local or ethics committee requlations. In case, a serum pregnancy test is required, a blood sample will be collected and testing performed per local guidance. The results of the applicable test will be recorded in the eCRF. Pregnancy testing at the Pre-vaccination visit will be done only using urine samples.
Any subject with a HZ episode between Visit 1 and Visit 2 should not receive the second dose. (Amended: 11 August 2014)
${ }^{9}$ For each solicited and unsolicited symptom the subject experiences, the subject will be asked if he/she received medical attention defined as hospitalisation, an emergency room visit or a visit to or from medical personnel (medical doctor) for any reason and this information will be recorded in the eCRF. Any concomitant medication/product/vaccine/treatment which could interfere with the immune response or is part of a chemotherapy should be recorded throughout the entire stud (see Section 6.6.1).
${ }^{h}$ Refer to Section 6.7 for details regarding intercurrent medical conditions. The occurrence of HZ is an intercurrent medical condition. At Visit 1 , all subjects will be informed of the signs and symptoms of typical HZ .
Study procedure to be assessed only after administration of vaccine at Visit 1.

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Time intervals between study visits/contacts related to study procedures performed in subjects participating in the study are presented in Table 7.

## Table $7 \quad$ Intervals between study visits (Amended: 11 August 2014)

| Interval between visits ${ }^{1}$ | Optimal length of interval ${ }^{2}$ | Allowed interval ${ }^{3}$ (range in days) |
| :---: | :---: | :---: |
| Pre-vaccination visit ${ }^{4} \rightarrow$ Visit 1 | Up to 30 to 10 days | Maximally 30 days and minimally 10 days before Visit 1 |
| Visit $1 \rightarrow$ Visit 2 (1 month) | 1-2 months ${ }^{5}$ | 30-60 |
| Visit $2 \rightarrow$ Visit 3 (1 month) | 1 month | 30-48 |
| Visit $1 \rightarrow$ Visit 4 (between Month 4, and Month 13) ${ }^{7}$ | 4-13 months, Variable ${ }^{6}$ | Minimally ~120 days after Visit 1 <br> Maximally $\sim 335$ days after Visit 1 |
| Visit $3 \rightarrow$ Month 5 Phone Contact ${ }^{7}$ | 3 months ${ }^{8}$ | 80-110 |
| Month 5 Phone Contact $\rightarrow$ Month 9 Phone Contact ${ }^{7}$ (Visit $3 \rightarrow$ Month 9 Phone Contact) | 4 months ${ }^{9}$ (7 months) | $\begin{gathered} 110-150 \\ (190-260) \\ \hline \end{gathered}$ |
| Visit $2 \rightarrow$ Visit 5 (12 months) | 12 months ${ }^{10}$ | 335-425 |

1 Unless otherwise specified, Visit 1 is taken as a reference to determine the applicable allowed interval between Visits 2 and 4 ; and Visit 2 is taken as a reference to determine the applicable allowed interval between Visits 3 , and 5 .
${ }^{2}$ Whenever possible the investigator should arrange study visits within this interval.
${ }^{3}$ Whenever clinically possible the investigator should arrange study visits within this interval. Subjects may not be eligible for inclusion in the ATP cohort if they make the study visit or contact outside any of these intervals.

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${ }^{4}$ The Pre-vaccination visit can occur on the same day as Visit 1.
${ }^{5}$ The second dose of study vaccine/ placebo must be administered between 1 and 2 months after the first vaccination AND should be at the first day (allowing a window of $+/-1$ day) of a subsequent cycle of chemotherapy. (Amended: 11 August 2014)
${ }^{6}$ Visit 4 will occur within Months 4 to 13 for a Blood Sampling at the start of the last cycle of chemotherapy. (if at least two months after the previous Blood Sampling (V3/M2)). Thus, the timing of this particular visit will be variable depending on the subject's chemotherapy schedule and also on when they started vaccination in relation to their chemotherapeutic regimen (refer to Section 3). This visit will coincide with the subject's lowest immune status. ${ }^{7}$ Should Visit 4 coincide with Month 5 or Month 9 , it will replace the Month 5 or the Month 9 Phone Contact, respectively.
${ }^{8}$ Visit 3 is taken here as reference to determine the applicable allowed interval up to the Month 5 Phone Contact.
${ }^{9}$ The Month 5 Phone Contact is taken here as reference to determine the applicable allowed interval up to the Month 9 Phone Contact (If Visit 4 coincides with the Month 5 Phone Contact, the date of Visit 3 will be used as a reference instead of Month 5).
${ }^{10}$ Visit 5 occurs approximately 12 months after the second vaccination.

### 5.6. Detailed description of study procedures

### 5.6.1. Procedures during the Pre-vaccination visit

The mandatory Pre-vaccination visit should take place prior to the day of Visit 1. If the Pre-vaccination visit occurs, it should take place between 30 and 10 days prior to the day of Visit 1. Procedures occurring at the Pre-vaccination visit, will be recorded in the eCRF, with the exception of a positive Pre-vaccination pregnancy test (see Section 7.2.1). The Pre-vaccination visit can occur on the same day as Visit 1.

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### 5.6.1.1. Informed consent

The signed/witnessed/thumb printed informed consent of the subject must be obtained before study participation. Refer to Section 5.1 for the requirements on how to obtain informed consent.

Informed consent given at the Pre-vaccination visit, will be reconfirmed at Visit 1 if needed as per local requirements. Reference is made to the SPM for details regarding the process for reconfirmation, if applicable.

### 5.6.1.2. Check inclusion and exclusion criteria

Check all inclusion and exclusion criteria as described in Sections 4.2 and 4.3 before enrolment.

Enrolment may occur at the Pre-vaccination visit and therefore, inclusion and exclusion criteria are checked at the Pre-vaccination visit if that visit occurs.

### 5.6.1.3. Urine pregnancy test

Female subjects of childbearing potential are to have a urine pregnancy test prior to any study vaccine administration. Only a urine pregnancy test is sufficient for pregnancy testing at the Pre-vaccination visit. The results of the applicable test will be recorded in the eCRF (see Section 7.2.1).

### 5.6.1.4. Collect demographic data

Record demographic data such as date of birth, gender, geographic ancestry and ethnicity in the subject's eCRF.

### 5.6.1.5. Recording of AEs, SAEs related to study participation or GSK concomitant medication/vaccination

Refer to Section 7.3 for procedures for the investigator to record AEs, SAEs and pregnancies. Refer to Section 7.4 for guidelines on how to report AEs, SAEs, and pregnancies to GSK Biologicals. From the time of informed consent until the first vaccination at Visit 1, SAEs related to study participation or GSK concomitant medication/vaccination are to be reported.

### 5.6.2. Procedures prior to the first vaccination

### 5.6.2.1. Informed consent

If a Pre-vaccination visit occurs, note that informed consent will be reconfirmed at Visit 1 if needed per local standards. Refer to the SPM for detailed information.

If there is no Pre-vaccination visit, then informed consent of the subject is obtained at Visit 1(see Section 5.6.1.1).

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### 5.6.2.2. Check inclusion and exclusion criteria

Note that inclusion and exclusion criteria are initially checked at the Pre-vaccination visit (see Section 5.6.1.2). A check for any changes compared to the Pre-vaccination visit will be performed at Visit 1. In case the subject is no longer eligible at Visit 1, the reason for this will be recorded in the Pre-vaccination section of the eCRF.

### 5.6.3. Medical history

Obtain the subject's medical history by interview and/or review of the subject's medical records and record any pre-existing conditions or signs and/or symptoms present in a subject prior to the first study vaccination in the eCRF.

Refer to the SPM for details.

### 5.6.4. History directed physical examination

Perform a history-directed physical examination. If the investigator determines that the subject's health on the day of vaccination temporarily precludes vaccination, the visit will be rescheduled while respecting the allowed interval. Collected information needs to be recorded in the eCRF.

Treatment of any abnormality observed during this examination has to be performed according to local medical practice outside this study or by referral to an appropriate health care provider.

### 5.6.5. Collect subject characteristics

The following subject characteristics will be recorded in the eCRF:

- Diagnosis for which chemotherapy is performed, with approximate date and underlying diagnosis, i.e., types of solid tumours involved;
- Assess ECOG performance status (Eastern Cooperative Oncology Group, PPD
M.D., Group Chair [Oken, 1982];
- Previous varicella vaccination status;
- Evidence of prior VZV infection: when readily available, serological evidence of prior VZV infection or else by medical history;
- Type, number and dates of chemotherapy procedure(s) being performed, i.e., agent(s) administered and if there is/will be radiotherapy courses and/or surgery involved.


### 5.6.6. Pregnancy test

Female subjects of childbearing potential are to have a pregnancy test prior to any study vaccine administration. A urine pregnancy test is sufficient. A serum pregnancy test instead of a urine pregnancy test should only be considered if required by country, local or ethics committee regulations. The results of the applicable test will be recorded in the eCRF (see Section 7.2.1). The study vaccine/ placebo may only be administered if the

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pregnancy test is negative. Note: The pregnancy test must be performed even if the subject is menstruating at the time of the study visit.

### 5.6.7. Check contraindications to vaccination

Contraindications to vaccination are to be checked at the beginning of each vaccination visit. Refer to Sections 6.5.

See Section 5.6.11 for additional criteria to be checked prior to administration of the second vaccination dose.

### 5.6.8. Assess pre-vaccination body temperature

The axillary, rectal, oral or tympanic body temperature of all subjects needs to be measured prior to any administration of study vaccine/placebo. The preferred route for recording temperature in this study will be oral. If the subject has fever [fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ on oral, axillary or tympanic setting, or $\geq 38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$ on rectal setting] it will constitute a contraindication to administration of vaccine or placebo at that point in time (Section 6.5).

### 5.6.9. Study group and treatment number allocation

Study group and treatment number allocation will be performed as described in Section 5.2.2. The number of each administered treatment must be recorded in the eCRF.

### 5.6.10. Sampling

As specified in the List of Study Procedures in Section 5.5 (Table 6), blood samples are taken during certain study visits. Refer to the Module on Biospecimen Management in the SPM for general handling of blood samples.

- For female subjects of childbearing potential, in case a serum pregnancy test is required by country, local or ethics committee regulation, a blood sample will be collected at Visits 1 and 2 and used for the test as per local guidance.
- A volume of approximately 8 mL of whole blood will be collected from all subjects at Visits 1, 2, 3, 4 and 5. Blood samples will be used to assess humoral immune responses by with respect to the study/investigational vaccine in all subjects.
- An additional volume of approximately 30 mL of whole blood should be drawn from a sub-cohort of subjects at Visits 1, 2, 3 and 5 to asses CMI responses (CMI subcohort).


### 5.6.11. Study Vaccine administration

- After completing the prerequisite procedures prior to each vaccination, one dose of study vaccine/placebo will be administered as described in Section 6.3. If the Investigator or delegate determines that the subject's health on the day of vaccination temporarily precludes vaccination, the visit will be rescheduled within the interval for this visit.


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- The subjects will be observed closely for at least 30 minutes following the administration of the vaccine/placebo, with appropriate medical treatment readily available in case of anaphylaxis.
- Any subject with an event of HZ between Visit 1 and Visit 2 should not receive the second dose.
- Any subject with an SAE related to the first dose of study vaccine/placebo (as judged by the investigator) should not receive the second dose (Section 6.5).


### 5.6.12. Check and record concomitant medication/vaccination and intercurrent medical conditions

Concomitant medication/vaccination must be checked and recorded in the eCRF as described in Section 6.6. In addition, any medication/vaccination taken from Day 0 to Day 29 after each vaccination will be recorded by the subjects on a diary card (see Section 5.6.13).

Intercurrent medical conditions must be checked and recorded in the eCRF as described in Section 6.7. At each study visit subsequent to the first vaccination, it must be verified if the subject has experienced or is experiencing any intercurrent medical condition listed in Section 6.7. If it is the case, the condition(s) must be recorded in the eCRF.

### 5.6.13. Recording of AEs, SAEs, pregnancies and pIMDs

- Refer to Section 7.3 for procedures for the investigator to record AEs, SAEs, pregnancies and pIMDs. Refer to Section 7.4 for guidelines on how to submit SAE, pregnancy and pIMD reports to GSK Biologicals.
- The subjects will be instructed to contact the investigator immediately should they/the subjects manifest any signs or symptoms they perceive as serious.
- After each vaccination, a diary card will be provided to the subjects by study staff/investigator for daily recording of:
- solicited symptoms from Days 0 to 6 after each vaccination;
- unsolicited symptoms from Days 0 to 29 after each vaccination;
- any medication/vaccination taken from Days 0 to 29 after each vaccination.

The subjects will be trained on how to complete the diary cards.

- For subjects who are illiterate or who need assistance with completion of diary cards, refer to Section 5.8 of the SPM for guidelines on assistance in subject diary card completion.
- The subjects will be instructed to return the completed diary card to the investigator at Visit 2 and Visit 3.
- Collection and verification of the completed diary card will occur during discussion with the subject at Visit 2 and Visit 3. Any unreturned diary cards will be sought from the subject through telephone call(s) or any other convenient procedure. The


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investigator/designee will transcribe the collected information into the eCRF in English.

### 5.6.13.1. Follow up of events of HZ

The occurrence of HZ will constitute an $\mathrm{AE} / \mathrm{SAE}$ as appropriate. The occurrence of HZ is an intercurrent medical condition (see Section 6.7). The reporting period for cases of HZ will be from Month 0 to study end.

### 5.6.14. Study conclusion

Study end will take place when:

- Subjects complete Visit 5 (Month 13)

The investigator will:

- Review data collected to ensure accuracy and completeness;
- Complete the Study Conclusion screen in the eCRF.


### 5.7. Biological sample handling and analysis

Please refer to the SPM for details of biospecimen management (handling, storage and shipment).

Samples will not be labelled with information that directly identifies the subject but will be coded with the identification number for the subject (subject number).

Under the following circumstances, additional testing on the samples may be performed by GSK Biologicals outside the scope of this protocol:

- Collected samples may be used in other assays, for test improvement or development of analytical methods related to the study vaccine and its constituents or the disease under study to allow to achieve a more reliable measurement of the vaccine response. Under these circumstances, additional testing on the samples may be performed by GSK Biologicals outside the scope of this protocol.
- Collected samples may be used for purposes related to the quality assurance of data generated linked to the study vaccine or the disease under study, such as for maintenance of assays described in this protocol and comparison between analytical methods and/or laboratories.

Information on further investigations and their rationale can be obtained from GSK Biologicals.

Any sample testing will be done in line with the consent of the individual subject.
Refer also to the Investigator Agreement, where it is noted that the investigator cannot perform any other biological assays except those described in the protocol or its amendment(s).

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If additional testing is performed, the marker priority ranking given in Section 5.7.4 may be changed.

Collected samples will be stored for a maximum of 20 years (counting from when the last subject performed the last study visit), unless local rules, regulations or guidelines require different timeframes or different procedures, which will then be in line with the subject consent. These extra requirements need to be communicated formally to and discussed and agreed with GSK Biologicals.

### 5.7.1. Use of specified study materials

When materials are provided by GSK Biologicals, it is MANDATORY that all clinical samples (including serum samples) be collected and stored exclusively using those materials in the appropriate manner. The use of other materials could result in the exclusion of the subject from the ATP analysis (See Section 9.4 for the definition of study cohorts/ data sets to be analysed). The investigator must ensure that his/her personnel and the laboratory(ies) under his/her supervision comply with this requirement. However, when GSK Biologicals does not provide material for collecting and storing clinical samples, appropriate materials from the investigator's site must be used. Refer to the Module on Clinical Trial Supplies in the SPM.

### 5.7.2. Biological samples

The different biological samples collected in the study, the quantities needed, the units and the timepoints are described in Table 8.

## Table 8 Biological samples

| Sample type | Quantity <br> (approximate vol.) | Unit | Timepoint | Sub-cohort Name ${ }^{*}$ |
| :--- | :--- | :--- | :--- | :--- |
| Blood (Humoral immunity) | 8 | mL | Visit 1, 2, 3, 4 and 5 | All subjects |
| Blood (Cell-mediated immunity) | 30 | mL | Visit 1, 2, 3 and 5 | CMI sub-cohort |

* Refer to Section 4.1 for sub-cohort description / Refer to Section 5.2.3 for subset description.

For female subjects of childbearing potential, a urine specimen will be collected at the Pre-vaccination Visit, Visit 1 (Month 0) and Visit 2 (Month 1). In case a serum pregnancy test is required by country, local or ethics committee regulation, a blood sample will be collected at Visit 1 (Month 0) and Visit 2 (Month 1) instead and used for the test per local guidance.

### 5.7.3. Laboratory assays

Please refer to APPENDIX A for a detailed description of the assays performed in the study. Please refer to APPENDIX B for the address of the clinical laboratories used for sample analysis.

Laboratory assays, which will be used in this study, are summarised in Table 9 (Humoral Immunity) and Table 10 (CMI), respectively.

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Table $9 \quad$ Humoral Immunity (Antibody determination) (Amended: 11 August 2014)

| System | Component | Method | Kit $/$ <br> Manufacturer | Unit | Cut-off | Laboratory |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| Serum | Varicella Zoster <br> Virus.Glycoprotei <br> nE Ab. IgG | ELISA | NA | $\mathrm{mIU} / \mathrm{mL}$ | $\mathbf{9 7}$ | GSK <br> Biologicals* |

* GSK Biologicals laboratory refers to the Global Vaccines Clinical Laboratories (GVCL) in Rixensart, Belgium; Wavre, Belgium; Laval, Canada.
gE = Glycoprotein E; Ab = Antibody; IgG = Immunoglobulin class G; ELISA = Enzyme-linked Immunosorbent Assay;
NA = Not applicable; $\mathrm{mL}=$ millilitre; mIU = milli international unit.
Table 10 Cell-Mediated Immunity (CMI) (Amended: 11 August 2014)

| System | Component | Challenge | Method | Unit | Cut-off | Laboratory |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| PBMC | CD4.polypositives <br> CD40L+IL2+TNFa+IF <br> ${N g^{*}}$ | gE | ICS | Events | N/A | CEVAC** |

*CD4.polypositives CD40L+IL2+TNFa+IFNg = CD4+ T-cells expressing at least 2 activation markers (from among IFN- $\gamma$, IL-2, TNF- $\alpha$ and CD4OL)
** University of Ghent, Belgium
PBMC $=$ Peripheral blood mononuclear cells
gE = Glycoprotein E; ICS = Intracellular cytokine staining
The GSK Biologicals’ clinical laboratories have established a Quality System supported by procedures. The activities of GSK Biologicals' clinical laboratories are audited regularly for quality assessment by an internal (sponsor-dependent) but laboratoryindependent Quality Department.

### 5.7.4. Biological samples evaluation

### 5.7.4.1. Immunological read-outs

The plan for immunogenicity testing on samples obtained is shown in Table 11.
For all subjects anti-gE Abs will be measured by ELISA at specified timepoints.
For subjects included in the CMI sub-cohort, the gE specific CMI response will be measured at specified timepoints.

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Table 11 Immunological read-outs

| Blood sampling timepoint |  |  | Sub-cohort/Subset Name | Marker |
| :---: | :---: | :---: | :---: | :---: |
| Visit no | Timing | Month |  |  |
| Visit 1 | Pre-Vacc | 0 | Humoral immune response (all subjects) | Ab gE ELISA |
|  |  |  | CMI sub-cohort | ICS gE |
| Visit 2 | Post-Vacc 1 | 1 | Humoral immune response (all subjects) | Ab gE ELISA |
|  |  |  | CMI sub-cohort | ICS gE |
| Visit 3 | Post-Vacc 2 | 2 | Humoral immune response (all subjects) | Ab gE ELISA |
|  |  |  | CMI sub-cohort | ICS gE |
| Visit 4* | Post-Vacc 2 | $\begin{gathered} 6 \\ \text { (Months } 4 \text { to 13) } \\ \hline \end{gathered}$ | Humoral immune response (applicable subjects**) | Ab gE ELISA |
| Visit 5 | Post-Vacc 2 | 13 | Humoral immune response (all subjects) | Ab gE ELISA |
|  |  |  | CMI sub-cohort | ICS gE |

* Visit 4 will occur within Months 4 to 13 for a Blood Sampling at the start of the last cycle of chemotherapy. This visit will coincide with the subject's lowest immune status.
${ }^{* *}$ Applicable subjects will be eligible for Visit 4 if their last cycle of chemotherapy is at least two months after the previous Blood Sampling (V3/M2).
Vacc = Vaccination; $\mathrm{CMI}=$ Cell-Mediated Immunity; $\mathrm{Ab}=$ Antibody; $\mathrm{gE}=$ Glycoprotein E;
ELISA = Enzyme-linked Immunosorbent Assay; ICS = Intracellular cytokine staining
Additional testing (e.g., anti-VZV Ab measurements, neutralizing Ab responses or gE or VZV specific CMI measurements on available blood samples) may be performed if deemed appropriate by GSK Biologicals should any findings in the present study, or in other studies, indicate that further investigation of the immunogenicity of the vaccine is warranted. In this case, a priority ranking for the order of testing will be added in case there is not enough material to perform all proposed testing.


### 5.7.5. Immunological correlates of protection

No generally accepted immunological correlate of protection has been demonstrated so far for the antigen(s) used in the candidate vaccine and/or licensed comparator.

## 6. STUDY VACCINE/ PLACEBO AND ADMINISTRATION

### 6.1. Description of study vaccine/ placebo

The Quality Control Standards and Requirements the candidate vaccine are described in separate Quality Assurance documents (e.g. release protocols, certificate of analysis) and the required approvals have been obtained.

The vaccines are labelled and packed according to applicable regulatory requirements.
The characteristics of the study vaccine $\mathrm{HZ} /$ su and placebo are as detailed in Table 12.

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Table 12 Study vaccine/ placebo

| Treatment name | Product name | Formulation | Presentation | Volume to be administered | Number of doses |
| :---: | :---: | :---: | :---: | :---: | :---: |
| HZ/su | VZV gE | $50 \mu \mathrm{~g} \mathrm{gE}$ per 0.5 mL of reconstituted vaccine | Lyophilised pellet in a monodose vial | 0.5 mL | 2 |
|  | ASO1B | MPL, QS21 and liposome ( $50 \mu \mathrm{~g} \mathrm{MPL}$ and $50 \mu \mathrm{~g}$ QS21) per 0.5 mL of reconstituted vaccine | Liquid in a monodose vial |  |  |
| Placebo | Lyophilised sucrose cake | 20 mg sucrose per 0.5 mL of reconstituted placebo | lyophilised pellet in a monodose vial | 0.5 mL | 2 |
|  | Saline ( NaCl ) solution for reconstitution | 150 mM NaCl solution (water for injection) | Liquid in a monodose vial |  |  |
| $\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster subunit vaccine; gE: recombinant purified Glycoprotein E; ASO1B: Adjuvant System AS01B; VZV: Varicella Zoster Virus; NaCl: Sodium Chloride; MPL: 3-O-desacyl-4'-monophosphoryl lipid A QS21: Quillaja saponaria Molina, fraction 21 (purified saponin extract from the South American tree) |  |  |  |  |  |

There is a slight difference in appearance between the diluents used for the vaccine and placebo ( $\mathrm{AS} 01_{\mathrm{B}}$ and saline solution) as well as between the reconstituted vaccine and placebo and therefore this study is conducted in an observer-blind manner. Refer to the SPM for details regarding vaccine supply.

### 6.2. Storage and handling of study vaccine/ placebo

The study vaccine/ placebo must be stored at the respective label storage temperature conditions in a safe and locked place. Access to the storage space should be limited to authorized study personnel. The storage conditions will be assessed during pre-study activities under the responsibility of the sponsor study contact. The storage temperature should be continuously monitored with calibrated (if not validated) temperature monitoring device(s) and recorded. Refer to the Module on Clinical Trial Supplies in the SPM for more details on storage of the study vaccine/ placebo.

Temperature excursions must be reported in degree Celsius.
Any temperature excursion outside the range of 0.0 to $+8.0^{\circ} \mathrm{C}$ (for +2 to $+8^{\circ} \mathrm{C} /+36$ to $+46^{\circ} \mathrm{F}$ label storage condition) impacting investigational medicinal products (IMPs) must be reported in the appropriate (electronic) temperature excursion decision form ([e]TDF). The impacted IMPs must not be used and must be stored in quarantine at label temperature conditions until usage approval has been obtained from the sponsor.

In case of temperature excursion below $+2.0^{\circ} \mathrm{C}$ down to $0.0^{\circ} \mathrm{C}$ impacting IMP(s) there is no need to report in (e)TDF, but adequate actions must be taken to restore the +2 to $+8^{\circ} \mathrm{C} /+36$ to $+46^{\circ} \mathrm{F}$ label storage temperature conditions. The impacted IMP(s) may still be administered, but the site should avoid re-occurrence of such temperature excursion.

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Refer to the Module on Clinical Trial Supplies in the SPM for more details on actions to take.

Refer to the Module on Clinical Trial Supplies in the SPM for details and instructions on the temperature excursion reporting and usage decision process, packaging and accountability of the study vaccine/ placebo.

### 6.3. Dosage and administration of study vaccine/ placebo

Refer to the SPM for details regarding the reconstitution of HZ/su vaccine and placebo.
After removal of the vaccine components or placebo components from the temperature monitored refrigerator, the vaccine or placebo should be reconstituted and administered within 6 hours, and should be kept at room temperature (between $2^{\circ} \mathrm{C} / 36^{\circ} \mathrm{F}$ and $\left.30^{\circ} \mathrm{C} / 86^{\circ} \mathrm{F}\right)$.

Vaccine/placebo will be administered as indicated in Table 13.
The reconstituted vaccine or placebo $(0.5 \mathrm{~mL})$ should be administered by IM injection into the deltoid muscle of the non-dominant arm using a standard aseptic technique. In rare situations when there is no alternative, the injection may be given in the different arm.

Notes:

- In case of contraindication to the administration in the non-dominant arm (e.g., arm radiotherapy for breast cancer) the dominant arm should be used.
- In case of bleeding risk(s), the vaccine should only be administered, if according to the investigator, it can be with reasonable safety by this route. A fine adapted needle should be used for the vaccination and firm pressure applied to the site, without rubbing, for $\geq 2$ minutes. The subject should be informed concerning the risk for hematoma from the injection.
Table 13 Dosage and administration

| Type of contact and timepoint | Study group | Treatment name | Volume to be administered | Route ${ }^{1}$ | Site ${ }^{2}$ | Side ${ }^{3}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Visit 1 (Day 0) | HZ/su-PreChemo | HZ/su | 0.5 mL | IM | D | N-D |
| Visit 2 (Month 1) |  |  |  |  |  |  |
| Visit 1 Day 0) | Placeb-PreChemo | Placebo |  |  |  |  |
| Visit 2 (Month 1) |  |  |  |  |  |  |
| Visit 1 (Day 0) | HZ/su-OnChemo | HZ/su |  |  |  |  |
| Visit 2 (Month 1) |  |  |  |  |  |  |
| Visit 1 (Day 0) | Placeb-OnChemo | Placebo |  |  |  |  |
| Visit 2 (Month 1) |  |  |  |  |  |  |

HZ/su = Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb = Placebo; mL = millilitre,
${ }^{1}$ Intramuscular (IM)
${ }^{2}$ Deltoid (D)
${ }^{3}$ Non-dominant (N-D).

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### 6.4. Replacement of unusable vaccine/ placebo doses

In addition to the vaccine/ placebo doses provided for the planned number of subjects (including over-randomisation when applicable), at least $5 \%$ additional vaccine/placebo doses will be supplied to replace those that are unusable (i.e., cracked, broken).

The investigator will use SBIR to obtain a new treatment number that will be used as a replacement. The replacement numbers will be allocated by dose. The system will ensure, in a blinded manner, that the replacement vials match the formulation the subject was assigned to by randomisation.

### 6.5. Contraindications to subsequent vaccination

The following events constitute absolute contraindications to further administration of $\mathrm{HZ} /$ su study vaccine or placebo. If any of these events occur during the study, the subject must not receive additional doses of vaccine but may continue other study procedures at the discretion of the investigator (see Section 7.5).

- Anaphylaxis following the administration of vaccine.
- Pregnancy (see Section 7.2.1).
- If the subject experiences an SAE judged to be vaccine-related by the investigator.

The following events constitute contraindications to administration of HZ/su study vaccine or placebo at that point in time; if any of these events occur at the time scheduled for vaccination, the subject may be vaccinated at a later date, within the time window specified in the protocol (see Section 5.5), or the subject may be withdrawn at the discretion of the investigator (see Section 7.5).

- Acute disease at the time of vaccination. Acute disease is defined as the presence of a moderate or severe illness with or without fever, but excludes the underlying malignancy for which the subject is included in the present study as well as the expected symptoms/signs associated with that disease or its treatment.
- Any condition which, in the judgment of the investigator would make intramuscular injection unsafe.
- All vaccines can be administered to persons with a minor illness such as diarrhoea, mild upper respiratory infection with or without low-grade febrile illness, i.e., oral temperature $<37.5^{\circ} \mathrm{C}\left(99.5^{\circ} \mathrm{F}\right) /$ axillary temperature $<37.5^{\circ} \mathrm{C}\left(99.5^{\circ} \mathrm{F}\right)$.

Note: Refer to Section 5.6.11 for instruction that any subject with an event of HZ between Visit 1 and Visit 2 should not receive the second dose.

### 6.6. Concomitant medication/ vaccination

At each study visit/contact, the investigator should question the subject about any medication/product taken and vaccination received by the subject.

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### 6.6.1. Recording of concomitant medications/products and concomitant vaccination

The following concomitant medications/ vaccines must be recorded in the eCRF if administered during the indicated recording period:

- Previous HZ vaccination.
- All concomitant medications, except vitamins and dietary supplements, administered at any time during the period starting with the administration of each dose of study vaccine/ placebo and ending 30 days (Days 0-29) after each dose of study vaccine/placebo.
- Prophylactic medication (i.e. medication administered in the absence of ANY symptom and in anticipation of a reaction to the vaccination).
E.g., an anti-pyretic is considered to be prophylactic when it is given in the absence of fever and any other symptom, to prevent fever from occurring [fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ on oral, axillary or tympanic setting, or $\geq 38.0^{\circ} \mathrm{C}$ $/ 100.4^{\circ} \mathrm{F}$ on rectal setting].
- Any concomitant medication/product/vaccine listed in Section 6.6.2.
- Any concomitant medication/product/vaccine relevant to a SAE* or administered at any time during the study period for the treatment of a SAE*.
* SAEs that are required to be reported per protocol.
- Any concomitant medication/product/vaccine/treatment which could interfere with the immune response should be recorded during the entire study period.
- Any concomitant medication/ product/vaccine/treatment as part of a chemotherapy should be recorded during the entire study period.


### 6.6.2. Concomitant medications/ vaccines that may lead to the elimination of a subject from ATP analyses

The use of the following concomitant medications/products/vaccines will not require withdrawal of the subject from the study but may determine a subject's evaluability in the ATP analysis for a specific timepoint. See Section 9.4 for study cohorts/ data sets to be analysed.

- Chronic administration and/or planned administration of systemic glucocorticoids (defined as prednisone $\geq 20 \mathrm{mg} /$ day, or equivalent, for more than 14 consecutive days in total) within one month prior to the first vaccine dose and up to Visit 3 (Month 2); and one month prior to subsequent blood sampling at Visits 4 and 5. Inhaled, intra-articularly injected, and topical steroids are allowed. (Amended: 11 August 2014)
- Administration of any vaccine against varicella or HZ other than the study vaccine during the study period;
- Administration of a vaccine not foreseen by the study protocol starting 30 days before the first dose of study vaccine until 30 days after the last dose of study


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vaccine. However, licensed non-replicating vaccines (e.g., inactivated and subunit vaccines, including inactivated and subunit influenza vaccines, and pneumococcal conjugate vaccines) may be administered within 8 days prior to or within 14 days after either dose of study vaccine;
A detailed, comprehensive list of reasons for elimination from ATP analyses will be established at the time of data cleaning.

### 6.7. Intercurrent medical conditions that may lead to elimination of a subject from ATP analyses

At each study visit subsequent to the first vaccination visit, it must be verified if the subject has experienced or is experiencing any intercurrent medical condition. If it is the case, the condition(s) must be recorded in the eCRF. Intercurrent medical conditions will be recorded in AE/SAE screens as appropriate.

Intercurrent medical conditions are clinical events during the course of the study which might alter or confound the interpretation of the immunologic (not safety) assessments of the protocol. In regards to humoral gE assessments, this includes any clinical event that might increase or decrease the measurement of anti-gE antibodies, such as protein losing conditions in which the loss of gammaglobulin or total proteins might underestimate the subject's gE response (e.g. protein losing enteropathy, proteinuria, or cachexia). Additional examples would be conditions that would cause the administration of exogenous gE antibodies, resulting in an overestimate of the subject's anti-gE antibody response to HZ/su vaccination, such as conditions requiring the use of intravenous immunoglobulin (IVIg) or blood products. (Amended: 11 August 2014)

The occurrence of HZ is an intercurrent medical condition, as the anti-gE antibody formed in response to active shingles cannot be distinguished from the anti-gE antibody formed in response to vaccination. The reporting period for cases of HZ will be from Month 0 to study end. (Amended: 11 August 2014)

For the CMI sub-cohort, in regards to measuring their cellular immunity, intercurrent medical conditions will be active viral infections that may alter CD4+ T cell counts and/or responses. Examples, not exhaustive, of such acute viral infections would include acute Hepatitis A, acute Hepatitis B, new onset HIV, and potentially acute CMV and/or EBV infections. (Amended: 11 August 2014)

Subjects may be eliminated from the ATP cohort for immunogenicity if, during the study, they incur a condition that has the capability of confounding their immune response to the study vaccine or its interpretation (e.g., cases of HZ up to study end).

## 7. SAFETY

The investigator or site staff is/are responsible for the detection, documentation and reporting of events meeting the criteria and definition of an adverse event (AE) or serious adverse event (SAE) as provided in this protocol.

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Each subject will be instructed to contact the investigator immediately should they/the subject manifest any signs or symptoms they perceive as serious.

### 7.1. Safety definitions

### 7.1.1. Definition of an adverse event

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse.

## Examples of an AE include:

- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition.
- New conditions detected or diagnosed after investigational product administration even though they may have been present prior to the start of the study.
- Signs, symptoms, or the clinical sequelae of a suspected interaction.
- Signs, symptoms, or the clinical sequelae of a suspected overdose of either investigational product or a concurrent medication (overdose per se should not be reported as an AE/SAE).
- Signs, symptoms temporally associated with vaccine administration.
- Pre- or post-treatment events that occur as a result of protocol-mandated procedures (i.e. invasive procedures, modification of subject's previous therapeutic regimen).

AEs to be recorded as endpoints (solicited AEs) are described in Section 7.1.3. All other AEs will be recorded as UNSOLICITED AEs.

## Examples of an AE DO NOT include:

- Medical or surgical procedures (e.g., endoscopy, appendectomy); the condition that leads to the procedure is an AE.
- Situations where an untoward medical occurrence did not occur (e.g., social and/or convenience admission to a hospital, admission for routine examination).
- Anticipated day-to-day fluctuations of pre-existing disease(s) or condition(s) present or detected at the start of the study that do not worsen.
Example of events to be recorded in the medical history section of the eCRF:
- Pre-existing conditions or signs and/or symptoms present in a subject prior to the first study vaccination. These events will be recorded in the medical history section of the eCRF.


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### 7.1.2. Definition of a serious adverse event

A serious adverse event is any untoward medical occurrence that:
a. Results in death,
b. Is life-threatening,

Note: The term 'life-threatening' in the definition of 'serious' refers to an event in which the subject was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, had it been more severe.
c. Requires hospitalisation or prolongation of existing hospitalisation,

Note: In general, hospitalisation signifies that the subject has been admitted at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or in an out-patient setting. Complications that occur during hospitalisation are also considered AEs. If a complication prolongs hospitalisation or fulfils any other serious criteria, the event will also be considered serious. When in doubt as to whether 'hospitalisation' occurred or was necessary, the AE should be considered serious.
Hospitalisation for elective treatment of a pre-existing condition (known or diagnosed prior to informed consent signature) that did not worsen from baseline is NOT considered an AE.
d. Results in disability/incapacity, OR

Note: The term disability means a substantial disruption of a person's ability to conduct normal life functions. This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhoea, influenza like illness, and accidental trauma (e.g. sprained ankle) which may interfere or prevent everyday life functions but do not constitute a substantial disruption.
e. Is a congenital anomaly/birth defect in the offspring of a study subject.

Medical or scientific judgement should be exercised in deciding whether reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the subject or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These should also be considered serious. Examples of such events are invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation.

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### 7.1.3. Solicited adverse events

### 7.1.3.1. Solicited local (injection-site) adverse events

The local (injection-site) AEs described in Table 14 will be solicited.

## Table 14 Solicited local adverse events

| Solicited local AEs |
| :--- |
| Pain at injection site |
| Redness at injection site |
| Swelling at injection site |

### 7.1.3.2. Solicited general adverse events

The general AEs described in Table 15 will be solicited.
Table 15 Solicited general adverse events

| Solicited general AEs |
| :--- |
| Fever |
| Headache |
| Fatigue |
| Myalgia |
| Gastrointestinal symptoms ${ }^{\dagger}$ |
| Shivering |
| ${ }^{\dagger}$ Gastrointestinal symptoms include nausea, vomiting, diarrhoea and/or abdominal pain. |

Note: Temperature will be recorded in the evening. Should additional temperature measurements be performed at other times of day, the highest temperature will be recorded in the eCRF.

### 7.1.4. Clinical laboratory parameters and other abnormal assessments qualifying as adverse events or serious adverse events

In absence of diagnosis, abnormal laboratory findings (e.g. clinical chemistry, haematology, urinalysis) or other abnormal assessments that are judged by the investigator to be both clinically significant and unexpected, considering the specific underlying disease and chemotherapy, will be recorded as either an AE or SAE as based on whether they meet the definition of an AE or SAE (refer to Sections 7.1.1 and 7.1.2). Clinically significant abnormal laboratory findings or other abnormal assessments that are present at baseline and following the start of the study, significantly worsen as judged by the investigator and are also unexpected, considering the underlying disease and chemotherapy, will also be reported as AEs or SAEs. (Amended: 11 August 2014)

The investigator will exercise his or her medical and scientific judgement in deciding whether an abnormal laboratory finding or other abnormal assessment is clinically significant.

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### 7.1.5. Adverse events of specific interest

### 7.1.5.1. Potential immune-mediated diseases

Potential immune-mediated diseases (pIMDs) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology. AEs that need to be recorded and reported as pIMDs include those listed in Table 16.

However, the investigator will exercise his/her medical and scientific judgement in deciding whether other diseases have an autoimmune origin (i.e., pathophysiology involving systemic or organ-specific pathogenic autoantibodies) and should also be recorded as a pIMD.

Table 16 List of potential immune-mediated diseases (Amended: 11 August 2014)

| Neuroinflammatory disorders |  | Musculosk | isorders | Skin disorders |
| :---: | :---: | :---: | :---: | :---: |
| - Cranial nerve disorders, including paralyses/paresis (e.g. Bell's palsy) <br> - Optic neuritis <br> - Multiple sclerosis <br> - Transverse myelitis <br> - Guillain-Barré syndrome, including Miller Fisher syndrome and other variants <br> - Acute disseminated encephalomyelitis, including site specific variants: e.g. non-infectious encephalitis, encephalomyelitis, myelitis, myeloradiculoneuritis <br> - Myasthenia gravis, including LambertEaton myasthenic syndrome <br> - Immune-mediated peripheral neuropathies and plexopathies, (including chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy and polyneuropathies associated with monoclonal gammopathy). <br> - Narcolepsy |  | - Systemic lupus erythematosus and associated conditions <br> - Systematic Scleroderma (Systematic sclerosis), including diffuse systemic form and CREST syndrome <br> - Idiophatic inflammatory myopathies, including Dermatomyositis, Polymyositis <br> - Antisynthetase syndrome <br> - Rheumatoid arthritis and associated conditions, including Juvenile chronic arthritis and Still's disease <br> - Polymyalgia rheumatic <br> - Spondyloarthritis, including ankylosing spondylitis, reactive arthritis (Reiter's Syndrome) and undifferentiated spondyloarthritis <br> - Psoriatic arthropathy <br> - Relapsing polychondritis <br> - Mixed connective tissue disorder |  | - Psoriasis <br> - Vitiligo <br> - Erythema nodosum <br> - Autoimmune bullous skin diseases (including pemphigus, pemphigoid and dermatitis herpetiformis) <br> - Alopecia areata <br> - Lichen planus <br> - Sweet's syndrome <br> - Localised Scleroderma (Morphoea) |
| Liver disorders | Gastrointestinal disorders |  | Endocrine disorders |  |
| - Autoimmune hepatitis <br> - Primary biliary cirrhosis <br> - Primary sclerosing cholangitis <br> - Autoimmune cholangitis | - Inflammatory Bowel disease, including Crohn's disease, ulcerative colitis, microscopic colitis, ulcerative proctitis <br> - Celiac disease <br> - Autoimmune pancreatitis |  | - Autoimmune thyroiditis (including Hashimoto thyroiditis) <br> - Grave's or Basedow's disease <br> - Diabetes mellitus type I <br> - Addison's disease <br> - Polyglandular autoimmune syndrome <br> - Autoimmune hypophysitis |  |

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| Vasculitides | Blood disorders | Others |
| :---: | :---: | :---: |
| - Large vessels vasculitis including: giant cell arteritis such as Takayasu's arteritis and temporal arteritis. <br> - Medium sized and/or small vessels vasculitis including: polyarteritis nodosa, Kawasaki's disease, microscopic polyangiitis, Wegener's granulomatosis, Churg-Strauss syndrome (allergic granulomatous angiitis), Buerger's disease (thromboangiitis obliterans), necrotizing vasculitis and anti-neutrophil cytoplasmic antibody (ANCA) positive vasculitis (type unspecified), Henoch-Schonlein purpura, Behcet's syndrome, leukocytoclastic vasculitis. | - Autoimmune hemolytic anemia <br> - Autoimmune thrombocytopenia <br> - Antiphospholipid syndrome <br> - Pernicious anemia <br> - Autoimmune aplastic anemia <br> - Autoimmune neutropenia <br> - Autoimmune pancytopenia | - Autoimmune glomerulonephritis (including IgA nephropathy, glomerulonephritis rapidly progressive, membranous glomerulonephritis, membranoproliferative glomerulonephritis, and mesangioproliferative glomerulonephritis) <br> - Ocular autoimmune diseases (including autoimmune uveitis and autoimmune retinopathy <br> - Autoimmune myocarditis/cardiomyopathy <br> - Sarcoidosis <br> - Stevens-Johnson syndrome <br> - Sjögren's syndrome <br> - Idiopathic pulmonary fibrosis <br> - Goodpasture syndrome <br> - Raynaud's phenomenon |

When there is enough evidence to make any of the above diagnoses, the AE must be reported as a pIMD. Symptoms, signs or conditions which might (or might not) represent the above diagnoses, should be recorded and reported as AEs but not as pIMDs until the final or definitive diagnosis has been determined, and alternative diagnoses have been eliminated or shown to be less likely.

In order to facilitate the documentation of pIMDs in the eCRF, a pIMD standard questionnaire and a list of preferred terms (PTs) and PT codes corresponding to the above diagnoses will be available to investigators at study start.

### 7.2. Events or outcomes not qualifying as adverse events or serious adverse events

### 7.2.1. Pregnancy

Female subjects who are pregnant or lactating at the time of vaccination must not receive additional doses of study vaccine/placebo but may continue other study procedures at the discretion of the investigator.

While pregnancy itself is not considered an AE or SAE, any adverse pregnancy outcome or complication or elective termination of a pregnancy for medical reasons will be recorded and reported as an AE or a SAE.

Note: The pregnancy itself should always be recorded on an electronic pregnancy report. Pregnancy which occurs prior to first vaccination does not need to be reported on an electronic pregnancy report.

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The following should always be considered as SAE and will be reported as described in Sections 7.4.1 and 7.4.3:

- Spontaneous pregnancy loss, including:
- spontaneous abortion, (spontaneous pregnancy loss before/at 22 weeks of gestation)
- ectopic and molar pregnancy
- stillbirth (intrauterine death of foetus after 22 weeks of gestation).

Note: the 22 weeks cut-off in gestational age is based on WHO-ICD 10 noted in the European Medicines Agency (EMA) Guideline on pregnancy exposure [EMA, 2006]. It is recognized that national regulations might be different.

- Any early neonatal death (i.e. death of a live born infant occurring within the first 7 days of life).
- Any congenital anomaly or birth defect (as per [CDC MACDP] guidelines) identified in the offspring of a study subject (either during pregnancy, at birth or later) regardless of whether the foetus is delivered dead or alive. This includes anomalies identified by prenatal ultrasound, amniocentesis or examination of the products of conception after elective or spontaneous abortion.
Furthermore, any SAE occurring as a result of a post-study pregnancy AND considered by the investigator to be reasonably related to the investigational vaccine(s)/product(s) will be reported to GSK Biologicals as described in Section 7.4.3. While the investigator is not obligated to actively seek this information from former study participants, he/she may learn of a pregnancy through spontaneous reporting.


### 7.3. Detecting and recording adverse events, serious adverse events and pregnancies

### 7.3.1. Time period for detecting and recording adverse events, serious adverse events and pregnancies

All AEs starting within 30 days following administration of each dose of study vaccine/ placebo must be recorded into the appropriate section of the eCRF, irrespective of intensity or whether or not they are considered vaccination-related. (Amended: 11 August 2014)

The time period for collecting and recording SAEs will begin at the first receipt of study vaccine/placebo and will end at Month 13 (study end), i.e., approximately 12 months following administration of the last dose of study vaccine/ placebo for each subject. See Section 7.4 for instructions on reporting of SAEs.

In addition to the above-mentioned reporting requirements and in order to fulfil international reporting obligations, SAEs that are related to study participation (i.e. protocol-mandated procedures, invasive tests, a change from existing therapy) or are related to a concurrent GSK medication/vaccine will be collected and recorded from the

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The time period for collecting and recording pregnancies will begin at the first receipt of study vaccine/ placebo and will end at Month 13 (study end), i.e., approximately 12 months following administration of the last dose of study vaccine/placebo. See Section 7.4 for instructions on reporting of pregnancies.

The time period for collecting and recording of pIMDs will begin at the first receipt of study vaccine/ placebo and will end at Month 13 (study end), i.e., approximately 12 months following administration of the last dose of study vaccine/placebo. See Section 7.4 for instructions on reporting of pIMDs.

Intercurrent medical conditions (see Section 6.7) will be recorded from Month 0 until study end. Intercurrent medical conditions will be recorded in AE/SAE screens as appropriate.

The occurrence of HZ will constitute an $\mathrm{AE} / \mathrm{SAE}$ as appropriate. The reporting period for cases of HZ will be from Month 0 to study end.

An overview of the protocol-required reporting periods for AEs, AEs leading to withdrawal, SAEs, pIMDs, pregnancies, and intercurrent medical conditions, (including HZ ) is given in Table 17.

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Table 17 Reporting periods for adverse events, AEs leading to withdrawal, serious adverse events, plMDs, pregnancies and intercurrent medical conditions, (including HZ)

| Study activity | Prevaccination visit | Dose 1 (Visit 1) | 7 days Post Dose 1 | 30 days Post Dose 1 | Dose 2 <br> (Visit 2) | 7 days Post Dose 2 | 30 days Post Dose 2 | Study conclusion (Visit 5) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Up to -30 days | Month 0 |  |  | Month 1 |  |  | Month 13 ${ }^{\dagger}$ |
| Timing of reporting |  | Day 0 | Day 6 | Day 29 | Day 0 | Day 6 | Day 29 |  |
| Solicited local and general AEs ${ }^{\text {a }}$ |  |  |  |  |  |  |  |  |
| Unsolicited AEs ${ }^{\text {a }}$ |  |  |  |  |  |  |  |  |
| SAEs ${ }^{\text {b }}$ |  |  |  |  |  |  |  |  |
| SAEs related to study participation or concurrent GSK medication/vaccine ${ }^{b}$ |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |

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| Study activity | Prevaccination visit | Dose 1 (Visit 1) | 7 days Post Dose 1 | 30 days Post Dose 1 | Dose 2 <br> (Visit 2) | 7 days Post Dose 2 | 30 days Post Dose 2 | Study conclusion (Visit 5) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Up to -30 days | Month 0 |  |  | Month 1 |  |  | Month 13 ${ }^{\dagger}$ |
| Timing of reporting |  | Day 0 | Day 6 | Day 29 | Day 0 | Day 6 | Day 29 |  |
| plMDs |  |  |  |  |  |  |  |  |
| Pregnancies ${ }^{\text {c }}$ |  |  |  |  |  |  |  |  |
| Recording of intercurrent medical conditions including HZ (see Section 6.7) d |  |  |  |  |  |  |  |  |

$\dagger$ Month 13 (Visit 5) occurs approximately 12 months after the second vaccination. The date of the second vaccination at Visit 2 is taken as reference to determine the applicable allowed interval between Visit 2 and Visit 5 .
a For each solicited and unsolicited symptom the subject experiences during the applicable reporting period, the subject will be asked if he/she received medical attention defined as hospitalisation, an emergency room visit or a visit to or from medical personnel (medical doctor) for any reason and this information will be recorded in the eCRF.
${ }^{b}$ SAEs related to study participation, or a concurrent GSK medication/vaccine will be recorded from the time the subject consents to participate in the study until she/he is discharged from the study (Section 7.3.1),
${ }^{\text {c P Pregnancy testing at the Pre-vaccination visit will be done only using urine samples. For any pregnancy testing prior to first vaccination (specifically at the Pre-vaccination Visit or }}$ at Visit 1), the results will be collected but not reported to the safety database, i.e., the occurrence of pregnancy has to be reported to the sponsor only after vaccine administration. ${ }^{d}$ Intercurrent medical conditions will be recorded in AE/SAE screens as appropriate. The occurrence of HZ is an intercurrent medical condition. The reporting period for cases of HZ will be from Month 0 to study end.

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### 7.3.2. Post-Study adverse events and serious adverse events

A post-study $\mathrm{AE} / \mathrm{SAE}$ is defined as any event that occurs outside of the $\mathrm{AE} / \mathrm{SAE}$ reporting period defined in Table 17. Investigators are not obligated to actively seek AEs or SAEs in former study participants. However, if the investigator learns of any SAE at any time after a subject has been discharged from the study, and he/she considers the event reasonably related to the investigational vaccine/product, the investigator will promptly notify the Study Contact for Reporting SAEs.

### 7.3.3. Evaluation of adverse events and serious adverse events

### 7.3.3.1. Active questioning to detect adverse events and serious adverse events

As a consistent method of collecting AEs, the subject should be asked a non-leading question such as:
'Have you felt different in any way since receiving the vaccine or since the previous visit? ${ }^{\prime}$

When an AE/SAE occurs, it is the responsibility of the investigator to review all documentation (e.g. hospital progress notes, laboratory, and diagnostics reports) relative to the event. The investigator will then record all relevant information regarding an $\mathrm{AE} / \mathrm{SAE}$ on the eCRF or SAE screens as applicable. It is not acceptable for the investigator to send photocopies of the subject's medical records to GSK Biologicals instead of the appropriate completed AE/SAE screens in the eCRF. However, there may be instances when copies of medical records for certain cases are requested by GSK Biologicals. In this instance, all subject identifiers will be blinded on the copies of the medical records prior to submission to GSK Biologicals.

The investigator will attempt to establish a diagnosis pertaining to the event based on signs, symptoms, and/or other clinical information. In such cases, the diagnosis should be documented as the $\mathrm{AE} / \mathrm{SAE}$ and not the individual signs/symptoms.

### 7.3.3.2. Assessment of adverse events

### 7.3.3.2.1. Assessment of intensity

The intensity of the following solicited AEs will be assessed as described in Table 18.

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Table 18 Intensity scales for solicited symptoms

| Adverse Event | Intensity grade | Parameter |
| :---: | :---: | :---: |
| Pain at injection site | 0 | None |
|  | 1 | Mild: Any pain neither interfering with nor preventing normal every day activities |
|  | 2 | Moderate: Painful when limb is moved and interferes with every day activities |
|  | 3 | Severe: Significant pain at rest. Prevents normal every day activities |
| Redness at injection site |  | Record greatest surface diameter in mm |
| Swelling at injection site |  | Record greatest surface diameter in mm |
| Fever* |  | Record temperature in ${ }^{\circ} \mathrm{C} /{ }^{\circ} \mathrm{F}$ |
| Headache | 0 | Normal |
|  | 1 | Mild: Headache that is easily tolerated |
|  | 2 | Moderate: Headache that interferes with normal activity |
|  | 3 | Severe: Headache that prevents normal activity |
| Fatigue | 0 | Normal |
|  | 1 | Mild: Fatigue that is easily tolerated |
|  | 2 | Moderate: Fatigue that interferes with normal activity |
|  | 3 | Severe: Fatigue that prevents normal activity |
| Gastrointestinal symptoms (nausea, vomiting, diarrhoea and/or abdominal pain) | 0 | Gastrointestinal symptoms normal |
|  | 1 | Mild: Gastrointestinal symptoms that are easily tolerated |
|  | 2 | Moderate: Gastrointestinal symptoms that interfere with normal activity |
|  | 3 | Severe: Gastrointestinal symptoms that prevent normal activity |
| Myalgia | 0 | Normal |
|  | 1 | Mild: Myalgia that is easily tolerated |
|  | 2 | Moderate: Myalgia that interferes with normal activity |
|  | 3 | Severe: Myalgia that prevents normal activity |
| Shivering | 0 | None |
|  | 1 | Shivering that is easily tolerated |
|  | 2 | Shivering that interferes with normal activity |
|  | 3 | Shivering that prevents normal activity |

${ }^{*}$ Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ on oral, axillary or tympanic setting, or $\geq 38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$ on rectal setting. The preferred route for recording temperature in this study will be oral.

The maximum intensity of local injection site redness/swelling will be scored at GSK Biologicals using GSK Biologicals’ standard grading scale based on the United States (US) Food and Drug Administration (FDA) guidelines for Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers enrolled in Preventive Vaccine Clinical Trials" [FDA, 2007].

$$
\begin{array}{lll}
0 & : & <20 \mathrm{~mm} \text { diameter } \\
1 & : & \geq 20 \mathrm{~mm} \text { to } \leq 50 \mathrm{~mm} \text { diameter } \\
2 & : & >50 \mathrm{~mm} \text { to } \leq 100 \mathrm{~mm} \text { diameter } \\
3 & : & >100 \mathrm{~mm} \text { diameter }
\end{array}
$$

The investigator will assess the maximum intensity that occurred over the duration of the event for all unsolicited AEs (including SAEs) recorded during the study. The assessment will be based on the investigator's clinical judgement.

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The intensity should be assigned to one of the following categories:

| 1 (mild) $=$ | An AE which is easily tolerated by the subject, causing minimal <br> discomfort and not interfering with everyday activities. |
| :--- | :--- |
| 2 (moderate) $=$ | An AE which is sufficiently discomforting to interfere with <br> normal everyday activities. |
| 3 (severe) $=$ | An AE which prevents normal, everyday activities. Such an AE <br> would, for example prevent attendance at work and would <br> necessitate the administration of medication or other medical <br> treatment. |

An AE that is assessed as Grade 3 (severe) should not be confused with a SAE. Grade 3 is a category used for rating the intensity of an event; and both AEs and SAEs can be assessed as Grade 3. An event is defined as 'serious' when it meets one of the predefined outcomes as described in Section 7.1.2.

### 7.3.3.2.2. Assessment of causality

The investigator is obligated to assess the relationship between investigational product and the occurrence of each AE/SAE. The investigator will use clinical judgement to determine the relationship. Alternative plausible causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors, and the temporal relationship of the event to the investigational product will be considered and investigated. The investigator will also consult the Investigator Brochure (IB) to determine his/her assessment.

There may be situations when a SAE has occurred and the investigator has minimal information to include in the initial report to GSK Biologicals. However, it is very important that the investigator always makes an assessment of causality for every event prior to submission of the SAE report to GSK Biologicals. The investigator may change his/her opinion of causality in light of follow-up information and update the SAE information accordingly. The causality assessment is one of the criteria used when determining regulatory reporting requirements.

In case of concomitant administration of multiple vaccines, it may not be possible to determine the causal relationship of general AEs to the individual vaccines administered. The investigator should, therefore, assess whether the AE could be causally related to vaccination rather than to the individual vaccines.

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All solicited local (injection site) reactions will be considered causally related to vaccination. Causality of all other AEs should be assessed by the investigator using the following question:

Is there a reasonable possibility that the AE may have been caused by the investigational vaccine/product?

YES : There is a reasonable possibility that the vaccine(s) contributed to the AE.

NO : There is no reasonable possibility that the AE is causally related to the administration of the study vaccine(s). There are other, more likely causes and administration of the study vaccine(s) is not suspected to have contributed to the AE.

If an event meets the criteria to be determined as 'serious' (see Section 7.1.2), additional examinations/tests will be performed by the investigator in order to determine ALL possible contributing factors for each SAE.

Possible contributing factors include:

- Medical history.
- Other medication.
- Protocol required procedure.
- Other procedure not required by the protocol.
- Lack of efficacy of the vaccine, if applicable.
- Erroneous administration.
- Other cause (specify).


### 7.3.3.3. Assessment of outcomes

The investigator will assess the outcome of all unsolicited AEs (including SAEs) recorded during the study as:

- Recovered/resolved.
- Recovering/resolving.
- Not recovered/not resolved.
- Recovered with sequelae/resolved with sequelae.
- Fatal (SAEs only).


### 7.3.3.4. Medically attended visits

For each solicited and unsolicited symptom the subject experiences, during the applicable reporting period (see Table 17), the subject/subject's parent(s)/LAR(s) will be asked if he/she /the subject received medical attention defined as hospitalisation, or an otherwise

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unscheduled visit to or from medical personnel for any reason, including emergency room visits. This information will be recorded in the eCRF.

### 7.4. Reporting of serious adverse events, pregnancies, and other events

### 7.4.1. Prompt reporting of serious adverse events, pregnancies, and other events to GSK Biologicals

SAEs that occur in the time period defined in Section 7.3 will be reported promptly to GSK within the timeframes described in Table 19, once the investigator determines that the event meets the protocol definition of a SAE.

Pregnancies that occur in the time period defined in Section 7.3 will be reported promptly to GSK within the timeframes described in Table 19, once the investigator becomes aware of the pregnancy.
pIMDs that occur in the time period defined in Section 7.3 will be reported promptly to GSK within the timeframes described in Table 19, once the investigator becomes aware of the pIMD.

Table 19 Timeframes for submitting serious adverse event, pregnancy and other events reports to GSK Biologicals

|  | Initial Reports |  | Follow-up Information on a Previous Report |  |
| :---: | :---: | :---: | :---: | :---: |
| Type of Event | Time Frame | Documents | Time Frame | Documents |
| All SAEs | 24 hours* | SAE screen | 24 hours* | SAE screen |
| Pregnancy | 2 weeks* | electronic pregnancy report | 2 weeks* | electronic pregnancy report |
| pIMDs | 24 hours** | SAE screen | 24 hours** | SAE screen |

* Time frame allowed after receipt or awareness of the information.
**Timeframe allowed after the diagnosis is established and known to the investigator


### 7.4.2. Contact information for reporting serious adverse events and

 other events to GSK Biologicals| Back-up Study Contact for Reporting SAEs |
| :--- |
| 24/24 hour and 7/7 day availability: |
| GSK Biologicals Clinical Safety \& Pharmacovigilance |
| Fax: PPD $\quad$ or PPD |

### 7.4.3. Completion and transmission of SAE reports to GSK Biologicals

Once an investigator becomes aware that a SAE has occurred in a study subject, the investigator (or designate) must complete the information in the electronic SAE screens of the eCRF WITHIN 24 HOURS. The SAE screens will always be completed as thoroughly as possible with all available details of the event. Even if the investigator does not have all information regarding a SAE, the SAE screens should still be completed

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within 24 hours. Once additional relevant information is received, the report should be updated WITHIN 24 HOURS.

The investigator will always provide an assessment of causality at the time of the initial report.

### 7.4.3.1. Back-up system in case the electronic SAE reporting system does not work

If the electronic SAE reporting system does not work, the investigator (or designate) must complete, then date and sign a paper SAE report and fax it to the GSK Biologicals Clinical Safety and Pharmacovigilance department within 24 hours.

This back-up system should only be used if the electronic SAE reporting system is not working and NOT if the system is slow. As soon as the electronic SAE reporting system is working again, the investigator (or designate) must complete the electronic SAE report within 24 hours. The final valid information for regulatory reporting will be the information reported through the electronic SAE reporting system.

### 7.4.4. Completion and transmission of pregnancy reports to GSK Biologicals

Once the investigator becomes aware that a subject is pregnant, the investigator (or designate) must complete the required information onto the electronic pregnancy report WITHIN 2 WEEKS.

Note: Conventionally, the estimated gestational age (EGA) of a pregnancy is dated from the first day of the last menstrual period (LMP) of the cycle in which a woman conceives. If the LMP is uncertain or unknown, dating of EGA and the estimated date of delivery (EDD) should be estimated by ultrasound examination and recorded in the pregnancy report.

### 7.4.5. Reporting of pIMDs to GSK Biologicals

Once onset of a new pIMD or exacerbation of a pre-existing pIMD is diagnosed (serious or non-serious) in a study subject, the investigator (or designate) must complete the information in the electronic SAE report WITHIN 24 HOURS after he/she becomes aware of the diagnosis. A field on the SAE report allows to specify that the event is a pIMD and whether it is serious or non-serious. The SAE report will always be completed as thoroughly as possible with all available details of the event, in accordance with the pIMD standard questionnaire provided. Even if the investigator does not have all information regarding a pIMD, the report should still be completed within 24 hours. Once additional relevant information is received, the report should be updated WITHIN 24 HOURS.

The investigator will always provide an assessment of causality at the time of the initial report.

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Refer to Section 7.4.3.1 for back-up system in case the electronic SAE reporting system does not work.

### 7.4.6. Updating of SAE, pregnancy, and pIMD information after freezing of the subject's eCRF

When additional SAE, pregnancy, or pIMD information is received after freezing of the subject's eCRF, new or updated information should be recorded on a paper report, with all changes signed and dated by the investigator. The updated report should be faxed to the GSK Biologicals Clinical Safety and Pharmacovigilance department or to the Study Contact for Reporting SAEs (refer to the Sponsor Information Sheet) within the designated reporting time frames specified in Table 19.

### 7.4.7. Regulatory reporting requirements for serious adverse events

The investigator will promptly report all SAEs to GSK in accordance with the procedures detailed in Section 7.4.1. GSK Biologicals has a legal responsibility to promptly notify, as appropriate, both the local regulatory authority and other regulatory agencies about the safety of a product under clinical investigation. Prompt notification of SAEs by the investigator to the Study Contact for Reporting SAEs is essential so that legal obligations and ethical responsibilities towards the safety of other subjects are met.

Investigator safety reports are prepared according to the current GSK policy and are forwarded to investigators as necessary. An investigator safety report is prepared for a $\mathrm{SAE}(\mathrm{s})$ that is both attributable to the investigational vaccine/product and unexpected. The purpose of the report is to fulfil specific regulatory and GCP requirements, regarding the product under investigation.

### 7.5. Follow-up of adverse events, serious adverse events, and pregnancies

### 7.5.1. Follow-up of adverse events and serious adverse events

### 7.5.1.1. Follow-up during the study

After the initial $\mathrm{AE} / \mathrm{SAE}$ report, the investigator is required to proactively follow each subject and provide additional relevant information on the subject's condition to GSK Biologicals (within 24 hours for SAEs; refer to Table 19).

All SAEs and pIMDs (serious or non-serious) at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving will be reviewed at subsequent visits/contacts until the end of the study.

All AEs documented at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving will be reviewed at subsequent visits/contacts until 30 days after the last vaccination.

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### 7.5.1.2. Follow-up after the subject is discharged from the study

The investigator will follow subjects:

- with SAEs, pIMDs (serious or non-serious), or subjects withdrawn from the study as a result of an AE, until the event has resolved, subsided, stabilised, disappeared, or until the event is otherwise explained, or the subject is lost to follow-up.
If the investigator receives additional relevant information on a previously reported SAE, he/she will provide this information to GSK Biologicals using a paper SAE and/or pregnancy report as applicable.

GSK Biologicals may request that the investigator performs or arranges the conduct of additional clinical examinations/tests and/or evaluations to elucidate as fully as possible the nature and/or causality of the AE or SAE. The investigator is obliged to assist. If a subject dies during participation in the study or during a recognised follow-up period, GSK Biologicals will be provided with any available post-mortem findings, including histopathology.

### 7.5.2. Follow-up of pregnancies

Pregnant subjects will be followed to determine the outcome of the pregnancy. At the end of the pregnancy, whether full-term or premature, information on the status of the mother and child will be forwarded to GSK Biologicals using the electronic pregnancy report and the SAE report if applicable. Generally, the follow-up period doesn't need to be longer than six to eight weeks after the estimated date of delivery.

Regardless of the reporting period for SAEs for this study, if the pregnancy outcome is a SAE, it should always be reported as SAE.

### 7.6. Treatment of adverse events

Treatment of any AE is at the sole discretion of the investigator and according to current good medical practice. Any medication administered for the treatment of an AE should be recorded in the subject's eCRF (refer to Section 6.6).

### 7.7. Unblinding

GSK Biologicals' policy (which incorporates ICH E2A guidance, EU Clinical Trial Directive and US Federal Regulations) is to unblind the report of any SAE which is unexpected and attributable/suspected to be attributable to the investigational vaccine/product, prior to regulatory reporting. The GSK Biologicals' Central Safety Physician is responsible for unblinding the treatment assignment in accordance with the specified timeframes for expedited reporting of SAEs (refer to Section 7.4.1).

### 7.8. Emergency unblinding

Unblinding of a subject's individual treatment code should occur only in the case of a medical emergency, or in the event of a serious medical condition, when knowledge of

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the study treatment is essential for the clinical management or welfare of the subject, as judged by the investigator.

The emergency unblinding process consists of the automated Internet-based system SIBR that allows the investigator to have unrestricted, immediate and direct access to the subject's individual study treatment.

The investigator has the option of contacting a GSK Biologicals' On-call Central Safety Physician (or Backup) if he/she needs medical advice or needs the support of GSK to perform the unblinding (i.e., he/she cannot access the automated Internet-based system).

Any emergency unblinding must be fully documented by using the Emergency Unblinding Documentation Form, which must be appropriately completed by the investigator and sent within 24 hours to GSK Biologicals.
GSK Biologicals' Contact information for Emergency Unblinding

\[\)|  24/24 hour and  $7 / 7 \text { day availability }$ |
| :--- |
|  GSK Biologicals' Central Safety Physician:  |
|  Outside US/Canada:  |
|  PPD  |
|  USK Biologicals Central Safety Physician on-call)  |
|  US/Canada only:  |
|  PPD GSK Biologicals Central Safety Physician on-call)  |
|  GSK Biologicals' Central Safety Physician Back-up:  |
|  Outside US/Canada  |
|  PPD  |
|  US/Canada only:  |
|  PPD  |
|  Emergency Unblinding Documentation Form transmission:  |
|  Outside US \& Canada:  |
|  Fax: PPD  |
|  US/Canada only:  |
|  Fax: PPD  |

\]

### 7.9. Subject card

Study subjects must be provided with the address and telephone number of the main contact for information about the clinical study.

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The investigator (or designate) must therefore provide a "subject card" to each subject. In an emergency situation this card serves to inform the responsible attending physician that the subject is in a clinical study and that relevant information may be obtained by contacting the investigator.

Subjects must be instructed to keep subject cards in their possession at all times.

### 7.10. Safety monitoring

Safety reviews will be performed by an iSRC. This iSRC will include as core members a GSK Biologicals' Safety Physician, a Clinical Development Manager (CDM) and a Biostatistician, that are not otherwise involved in the conduct of the project, in order to maintain the observer-blind to the treatment codes amongst project-related personnel until the final analysis of data. The iSRC will review the safety data and any findings that could have an impact on the safety of the subjects. These reviews will be conducted on unblinded data.

## 8. SUBJECT COMPLETION AND WITHDRAWAL

### 8.1. Subject completion

A subject who returns for the concluding visit/is available for the concluding contact foreseen in the protocol is considered to have completed the study.

### 8.2. Subject withdrawal

Only subjects withdrawn at the Pre vaccination visit and who are no longer eligible at Visit 1 will be replaced. All the other withdrawals will not be replaced.

### 8.2.1. Subject withdrawal from the study

From an analysis perspective, a 'withdrawal' from the study refers to any subject who did not come back for the concluding visit/was not available for the concluding contact foreseen in the protocol.

All data collected until the date of withdrawal/last contact of the subject will be used for the analysis.

A subject is considered a 'withdrawal' from the study when no study procedure has occurred, no follow-up has been performed and no further information has been collected for this subject from the date of withdrawal/last contact.

Investigators will make an attempt to contact those subjects who do not return for scheduled visits or follow-up.

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Information relative to the withdrawal will be documented in the eCRF. The investigator will document whether the decision to withdraw a subject from the study was made by the subject himself/herself, or by the investigator, as well as which of the following possible reasons was responsible for withdrawal:

- Serious adverse event.
- Non-serious adverse event.
- Protocol violation (specify).
- Consent withdrawal, not due to an adverse event*.
- Moved from the study area.
- Lost to follow-up.
- Other (specify).
*In case a subject is withdrawn from the study because he/she/the subject's parent(s) has withdrawn consent, the investigator will document the reason for withdrawal of consent, if specified by the subject, in the CRF.

Subjects who are withdrawn from the study because of SAEs/AEs must be clearly distinguished from subjects who are withdrawn for other reasons. Investigators will follow subjects who are withdrawn from the study as result of a SAE/AE until resolution of the event (see Section 7.5.1.2).

### 8.2.2. Subject withdrawal from investigational vaccine/ placebo

A 'withdrawal' from the investigational vaccine/ placebo refers to any subject who does not receive the complete treatment, i.e. when no further planned dose is administered from the date of withdrawal. A subject withdrawn from the investigational vaccine/ placebo may not necessarily be withdrawn from the study as further study procedures or follow-up may be performed (safety or immunogenicity) if planned in the study protocol.

Information relative to premature discontinuation of the investigational vaccine/ placebo will be documented on the Vaccine Administration page/screen of the eCRF. The investigator will document whether the decision to discontinue further vaccination/treatment was made by the subject himself/herself, or by the investigator, as well as which of the following possible reasons was responsible for withdrawal:

- Serious adverse event.
- Non-serious adverse event.
- Other (specify).


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## 9. STATISTICAL METHODS

### 9.1. Primary endpoints

- Anti-gE humoral immunogenicity with respect to components of the study/investigational vaccine.
- Anti-gE Ab concentrations as determined by ELISA at Month 2.
- Occurrence of solicited local and general symptoms.
- Occurrence, intensity and duration of each solicited local symptom within 7 days (Days 0-6) after each vaccination.
- Occurrence, intensity, duration and relationship to vaccination of each solicited general symptom within 7 days (Days 0-6) after each vaccination.
- Occurrence of unsolicited adverse events (AEs).
- Occurrence, intensity and relationship to vaccination of unsolicited AEs during 30 days (Days 0-29) after each vaccination, according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence of serious Adverse Events (SAEs).
- Occurrence and relationship to vaccination of SAEs up to 30 days post last vaccination.
- Occurrence of AEs of specific interest.
- Occurrence and relationship to vaccination of any potential Immune Mediated Diseases (pIMDs) up to 30 days post last vaccination.


### 9.2. Secondary endpoints

- For immunogenicity with respect to components of the study/investigational vaccine.
- Anti-gE Ab concentrations as determined by ELISA at Month 0, Month 1, Month 2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13.
- Vaccine response for anti-gE Abs at Month 1, Month 2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13.
- Frequencies of gE-specific CD4+ T-cells, expressing at least 2 activation markers (from among IFN- $\gamma$, IL-2, TNF- $\alpha$ and CD40 L), as determined by in vitro intracellular cytokine staining (ICS), at Month 0, Month 1, Month 2, and Month 13.
- Vaccine response for gE-specific CD4+ T-cells expressing at least 2 activation markers (from among IFN- $\gamma$, IL-2, TNF- $\alpha$ and CD40L), as determined by in vitro ICS, at Month 1, Month 2 and Month 13.


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- Occurrence of Serious Adverse Events (SAEs).
- Occurrence and relationship to vaccination of SAEs during the period starting after 30 days post last vaccination until study end.
- Occurrence of AEs of specific interest.
- Occurrence of any pIMDs during the period starting after 30 days post last vaccination until study end.


### 9.3. Determination of sample size

### 9.3.1. Sample size assumptions for humoral immune response endpoint

Assumptions used were based on anti-gE humoral immunogenicity data obtained in study ZOSTER-001 for subjects who received 2 doses of $\mathrm{HZ} /$ su vaccine ( $\mathrm{gE}_{[50 \mu \mathrm{~g}]} / \mathrm{AS} 01_{\mathrm{B}}$ ). The humoral immune response to vaccine was assessed in comparison to the placebo group using anti-gE Ab concentrations. In the ZOSTER-001 study, the fold increase observed post dose 2 in the HZ/su group as compared with placebo is approximately 28 -fold for anti-gE Abs. The Decimal Logarithm $\left(\log _{10}\right)$ standard deviation observed in ZOSTER001 is approximately 0.76 in the placebo group, and 1.12 after 2 doses of $\mathrm{HZ} / \mathrm{su}$.
Accounting for an anticipated higher variability in the current study that could be due to different chemotherapeutic regimens, the standard deviation used in the computation has been multiplied by 1.1.

A 12.5 -fold increase over placebo and a minimum of 3-fold increase in geometric mean as lower limit have been assumed for the analyses on PreChemo subjects.

The type 1 error to $2.5 \%$ one-sided has been used.
Table 20 presents the assumptions used and the power obtained for the primary objective related to immunogenicity.

Table 20 Power calculations for a T-test for Relevant Superiority in PreChemo Groups

| Power | N1/N2 evaluable | Equivalence Margin (E) $\left[\log _{10}(3-\right.$ fold)] | Assumed Difference <br> (D) $\left[\log _{10}(12.5-\right.$ fold)] | Significance level |  | Standard Deviation ( $\log _{10}$ of value) |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | Alpha | Beta |  |  |
|  |  |  |  |  |  | Vaccine | Placebo |
| 0.90599 | 67/67 | 0.477 | 1.097 | 0.025 | 0.09401 | 1.232 | 0.836 |

$\mathrm{N} 1, \mathrm{~N} 2$ : number of evaluable subjects receiving vaccine (N1) and placebo (N2)
$\log _{10}=$ Decimal Logarithm
To obtain a power of at least $90 \%$ to see a minimum of 3-fold increase as lower limit in anti-gE humoral immune response over placebo, assuming a 12.5 fold increase between placebo to $\mathrm{HZ} / \mathrm{su}, 67$ evaluable subjects per treatment group are needed.

A sample size of 93 subjects is needed assuming a $27 \%$ rate from drop-out and nonevaluable subjects at Month 2. (Amended 11 August 2014)

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The vaccine response rate observed in the overall autologous HCT population post-dose 2 , in the HZ/su group of study ZOSTER-001, is $86 \%$ for anti-gE Ab. Table 21 presents the power to demonstrate that the vaccine response in the HZ/su PreChemo Group is significantly greater than $60 \%$.

Table 21 Power calculations for a One-sided binomial test for Relevant Superiority in PreChemo Groups (Amended: 11 August 2014)

| Power | N evaluable | Vaccine response |  | Significance level |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  |  | Lower limit | Assumed | Alpha 1-Sided | Beta |
| $>0.9273$ | 67 | 0.6 | 0.80 | 0.025 | 0.0727 |

An 8-fold increase over placebo and a minimum of 3-fold increase in geometric mean as lower limit of the $95 \%$ CI have been assumed for the analyses on all subjects.

Table 22 and Table 23 present the assumptions used and the power obtained for the secondary objectives related to immunogenicity for all subjects (OnChemo and PreChemo subjects).

Table 22 Power calculations for a T-test for Relevant Superiority in all subjects

| Power | N1/N2 evaluable | Equivalence Margin <br> (E) $\left[\log _{10}\right.$ <br> (3-fold)] | Actual Difference <br> (D) $\left[\log _{10}\right.$ <br> (8-fold)] | Significance level |  | Standard Deviation ( $\log _{10}$ of value) |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | Alpha | Beta | Vaccine | Placebo |
| 0.71961 | 84/84 | 0.477 | 0.903 | 0.025 | 0.28039 | 1.232 | 0.836 |

N 1 , N2: number of evaluable subjects receiving vaccine (N1) and placebo (N2)
$\log _{10}=$ Decimal Logarithm
The 84 evaluable subjects per treatment group provide at least $71 \%$ power to see a minimum of 3-fold increases in anti-gE humoral immune response over placebo. Assuming a 27\% rate from drop-out and non-evaluable subjects at Month 2, 232 subjects should be enrolled. (Amended: 11 August 2014)

Table $23 \quad \begin{aligned} & \text { Power calculations for a One-sided binomial test for Relevant } \\ & \text { Superiority in all subjects }\end{aligned}$ Superiority in all subjects

| Power | N evaluable | Vaccine response |  | Significance level |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  |  | Lower limit | Assumed | Alpha 1-Sided | Beta |
| 0.44 | 84 | 0.6 | 0.70 | 0.025 | 0.56 |

The 84 evaluable subjects in the HZ/su group provide at least $44 \%$ power to demonstrate that the vaccine response in the $\mathrm{HZ} /$ su group (all subjects) is significantly greater than $60 \%$. Assuming a $27 \%$ rate from drop-out and non-evaluable subjects at Month 2, 116 subjects should be enrolled in the HZ/su group. (Amended: 11 August 2014)

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### 9.3.2. Sample size assumptions for CMI

### 9.3.2.1. Assumptions and background information for CMI

Assumptions to estimate the number of subjects to be included in the CMI sub-cohort in study ZOSTER-028 were based on gE-specific CMI data obtained in study ZOSTER-001 for subjects who received two doses of $\mathrm{HZ} / \mathrm{su}$ vaccine.

### 9.3.2.2. Number of subjects in the CMI sub-cohort

Assumptions used were based on CMI results (frequency of CD4+ T-cells expressing at least two activation markers from among IFN- $\gamma$, IL-2, TNF- $\alpha$ and CD40L) from ZOSTER-001 for adult autologous HCT subjects who received two doses of HZ/su. The CMI response was assessed in comparison to the control group (placebo). The increase observed post-dose 2 in study ZOSTER-001 in the HZ/su group as compared with placebo is at least 9 -fold after induction with gE. The natural logarithm (ln) standard deviation observed in ZOSTER-001 is about 1.49. The standard deviation used in the computation has been multiplied by 1.5 due to an expected higher variability in this population. Therefore, a 5 -fold increase over control with a lower limit above 1 has been assumed. The type 1 error of $2.5 \%$ one-sided has been used.

Table 24 presents the number of subjects under vaccine (N1) and placebo (N2) required to demonstrate a significant increase over placebo in frequency of gE-specific CD4+ T-cells producing at least 2 activation markers. At least 30 evaluable subjects per treatment group (only PreChemo Groups) are needed to reach approximately $78 \%$ power.

Table 24 Power calculations for the CMI sub-cohort

| Power | N1/N2 | Equivalence margin (E) $\ln$ (1) | Actual <br> difference (D) <br> In (5) | Significance level |  | Standard Deviation (In of value) |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | Alpha | beta | SD1 | SD2 |
| 0.78283 | 30/30 | 0 | 1.6 | 0.25 | 0.21717 | 2.2 | 2.2 |
| 0.84348 | 35/35 | 0 | 1.6 | 0.25 | 0.15652 | 2.2 | 2.2 |
| 0.88871 | 40/40 | 0 | 1.6 | 0.025 | 0.11129 | 2.2 | 2.2 |
| 0.92181 | 45/45 | 0 | 1.6 | 0.025 | 0.07819 | 2.2 | 2.2 |

In = Natural Logarithm; SD = Standard Deviation
Assuming an $\boldsymbol{\sim} 20 \%$ rate from drop-out and non-evaluable subjects at Month 2, the total number of subjects enrolled into the sub-cohort should be $\sim 38$ per group. (Amended: 11 August 2014)
The vaccine response observed in the overall HCT population post-dose 2 , in the HZ/su group of study ZOSTER-001, is $80 \%$ for gE -specific CD4[2+] T cell frequencies. Table 25 presents the power to demonstrate that the vaccine response in the HZ/su group is significantly greater than $50 \%$.

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## Table 25 Power calculations for a One-sided binomial test for Relevant Superiority

| Power | N evaluable | Vaccine response |  | Significance level |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  |  | Lower limit | Assumed | Alpha 1-Sided | Beta |
| 0.8034 | 30 | 0.5 | 0.75 | 0.025 | 0.1966 |
| $\mathbf{0 . 9 3 8 9}$ | 30 | 0.5 | 0.80 | 0.025 | 0.0611 |
| 0.9903 | 30 | 0.5 | 0.85 | 0.025 | 0.0097 |

### 9.4. Study cohorts/ data sets to be analysed

### 9.4.1. Total vaccinated cohort

The Total Vaccinated cohort (TVC) will include all vaccinated subjects with respect to the vaccine actually administered.

The TVC for analysis of immunogenicity will include vaccinated subjects for whom data related to immunogenicity endpoints are available.

The TVC for analysis of safety will include all subjects with at least one vaccine administered.

The TVC for analysis of reactogenicity will include all subjects with at least one vaccine administration documented.

### 9.4.2. According-to-protocol cohort for analysis of safety for the active phase (or for the extended safety follow up) (Amended: 11 August 2014)

The According To Protocol (ATP) cohort for analysis of safety will include all subjects:

- who have received at least one dose of study vaccine/ placebo according to their random assignment;
- for whom administration site of study vaccine/ placebo is known;
- who have not received other vaccine forbidden in the protocol during the active phase (or during the entire study period);
- for whom the randomisation code has not been broken during the active phase (or during the entire study period).


### 9.4.3. According-to-protocol cohort for analysis of immunogenicity (or for persistence)

The ATPc for analysis of immunogenicity will include all evaluable subjects from the ATP cohort for safety analysis:

- Who meet all eligibility criteria (refer to Sections 4.2 and 4.3).
- Who comply with the procedures and intervals defined in the protocol for the active phase (for persistence). The intervals between vaccinations (dose 1 to dose 2) and


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between dose 2 and blood sample at Visit 3 (dose 2 to 1 month post dose 2 visit) for inclusion in the ATP cohort for immunogenicity/persistence will be defined respectively as 30-84 days and 21-63 days (see Table 26). The immune ATPc analysis will be based on the allowed intervals for Visit $1 \rightarrow$ Visit 2, Visit $2 \rightarrow$ Visit 3, and Visit $2 \rightarrow$ Visit 5. (Amended: 11 August 2014)
Table 26 Intervals between study visits for the ATP cohort for analysis of immunogenicity (Amended: 11 August 2014)

| Interval between visits | Allowed interval for the ATP cohort for analysis of immunogenicity |
| :---: | :---: |
| Visit $1 \rightarrow$ Visit 2 | $30-84$ days |
| Visit $2 \rightarrow$ Visit 3 | $21-63$ days |
| Visit $2 \rightarrow$ Visit 5 | $335-425$ days |

- Who do not meet any of the criteria for elimination from an ATP analysis during the active phase (during the entire study period for persistence) as listed in Section 6.6.2,
- Who did not receive a product leading to elimination from an ATP analysis during the active phase (during the entire study period for persistence) as listed in Section 6.6.2,
- Who did not present with a medical condition leading to elimination from an ATP analysis during the active phase (during the entire study period for persistence) as listed Section 6.7.

For whom data concerning immunogenicity endpoint measures are available during the active phase (during the entire study period for persistence).

### 9.5. Derived and transformed data

### 9.5.1. Handling of missing data

For a given subject and a given measurement, missing or non-evaluable measurements will not be imputed for the primary analysis. The missing endpoint and censoring are supposed to occur independently, and the pattern of the missing value(s) being either Missing Completely At Random (MCAR) or Missing At Random (MAR) only.

For the analysis of solicited symptoms, missing or non-evaluable measurements will not be replaced. Therefore the analysis of the solicited symptoms based on the TVC will include only subjects/doses with documented safety data (i.e., symptom screen/sheet completed).

For the analysis of unsolicited AEs/SAEs/concomitant medication, all vaccinated subjects will be considered and subjects who did not report an event will be considered as subjects without an event.

### 9.5.2. Humoral immune response

- A seronegative subject is a subject whose Ab concentration is below the cut-off value.


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- A seropositive subject is a subject whose Ab concentration is greater than or equal to the cut-off value.
- The seropositive ity rate is defined as the percentage of seropositive subjects.
- The vaccine response rate for anti-gE is defined as the percentage of subjects who have at least a:
- 4-fold increase in the anti-gE antibodies concentration as compared to the prevaccination anti-gE antibodies concentration, for subjects who are seropositive at baseline, or,
- 4-fold increase in the anti-gE antibodies concentration as compared to the antigE antibodies cut-off value for seropositivity, for subjects who are seronegative at baseline. (Amended: 11 August 2014)
- The Geometric Mean Concentrations (GMCs) calculations are performed by taking the anti-log of the mean of the log concentration transformations. For descriptive statistics only, Ab concentrations below the cut-off of the assay $(97 \mathrm{mIU} / \mathrm{mL}$; see Table 9) will be given an arbitrary value equal to half the cut-off for the purpose of GMC calculation. (Amended: 11 August 2014)


### 9.5.3. Cellular-mediated immune response

- For the inferential analysis, the frequency of CD4+ T-cells producing at least 2 activation markers (IFN- $\gamma$, IL-2, TNF- $\alpha$ and/or CD40L, termed CD4 [2+]) upon in vitro stimulation with the gE-antigen (induction condition) is calculated by adding an offset of 0.5 to the number of activated CD4 T-cells (numerator) divided by the total number of CD4 T-cells involved (denominator). A similar calculation will be made for the frequency of CD4 [2+] upon in vitro stimulation in medium only (background condition). (Amended: 11 August 2014)

$n_{\text {Induction }}^{2+}=$ number of CD4 T -cells secreting at least 2 activation markers after induction with the gE - antigen
$n_{\text {Background }}^{2+}=$ number of CD4 T-cells secreting at least 2 activation markers in the medium conditions
$N^{C D 4}=$ Total number of CD4 T-cells involved in the assay (induction of background)
- For the descriptive analyses, the frequency of CD4[2+] T-cells upon in vitro stimulation with the antigen (induction condition) is calculated by dividing the number of activated CD4[2+] T-cells (numerator) over the total number of CD4 Tcells involved (denominator). The same calculation will be performed for the frequency computation for any kinds of cells and for each individual activation marker as appropriate. (Amended: 11 August 2014)
Freq $\underset{\text { Induction }}{C D 4[2+]}=\frac{n_{\text {Induction }}^{2+}}{N_{\text {Induction }}^{\text {CD }}}$
$n_{\text {Induction }}^{2+}=$ number of CD4 T - cells secreting at least 2 activation s markers after inductions with the antigen
$N^{C D 4}=$ Total number of CD4 T - cells involved in the assay (induction )


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- The frequency of $\mathbf{g E}$-specific CD4 T-cells for each individual subject is calculated as the difference between the frequency of CD4 [2+], upon in vitro stimulation with the gE -antigen (induction condition) minus the frequency of (CD4 [2+] upon in vitro stimulation in medium only (background condition). The differences less or equal to one (1) are imputed to 1 gE -specific CD4[2+] T-cell per $\mathbf{1 0}^{6}$ CD4+ $\boldsymbol{T}$-cells. The same calculation will be performed for the frequency computation for any kinds of cells and for each individual activation marker as appropriate. (Amended: 11 August 2014)

Freq $q_{\text {Specific }}^{C D 4[2+]}=\frac{n_{\text {Induction }}^{2+}}{N_{\text {Induction }}^{C D 4}}-\frac{n_{\text {Background }}^{2+}}{N_{\text {Background }}^{C D 4}}$
if $\frac{n_{\text {Induction }}^{2+}}{N_{\text {Induction }}^{C D 4}}>1+\frac{n_{\text {Background }}^{2+}}{N_{\text {Background }}^{C D 4}}$
Freq ${ }_{\text {Specific }}^{C D 4[2+]}=1$
$n_{\text {Induction }}^{2+}=$ number of CD4 T - cells secreting at least 2 activation markers after induction with the gE - antigen
$n_{\text {Background }}^{2+}=$ number of CD4 T-cells secreting at least 2 activation markers in the medium conditions
$N^{C D 4}=$ Total number of CD4 T-cells involved in the assay (induction of background )

- The GM frequency calculations are performed by taking the anti-log of the mean of the log frequency transformations;
- The CMI vaccine response to $g E$ will be based on the gE-specific data as computed above. The lower limit of linearity ( $\boldsymbol{L} \boldsymbol{L} \boldsymbol{L}$ ) for the assay ( 320 positive events $/ 10^{6}$ CD4+ T-cells) will be used as threshold for vaccine response assessment. The vaccine response is defined as the percentage of subjects who have at least a:
- 2-fold increase as compared to the $\boldsymbol{L} \boldsymbol{L} \boldsymbol{L}$, for subjects with pre-vaccination T-cell frequencies below the $\boldsymbol{L L} \boldsymbol{L}$.
- 2-fold increase as compared to pre-vaccination T-cell frequencies, for subjects with pre-vaccination above the $\boldsymbol{L} \boldsymbol{L} \boldsymbol{L}$.
(Amended: 11 August 2014)


### 9.6. Conduct of analysis

Any deviation(s) or change(s) from the original statistical plan outlined in the protocol will be described and justified in the final study report.

### 9.7. Analysis of demographics

Demographic characteristics (age, gender, geographic ancestry and ethnicity) will be tabulated per treatment group.

The mean age (plus range and standard deviation) of the enrolled subjects, as a whole, and per treatment group will be calculated.

The distribution of subjects enrolled among the study sites will be tabulated as a whole and per treatment group.

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The same tabulation will be performed by age strata and by duration between the first dose and the start of chemotherapy cycle.

### 9.8. Analysis of immunogenicity (Amended: 11 August 2014)

The primary analysis will be based on the ATPc for analysis of immunogenicity which will be relevant and consistent with the actual clinical course of these immunocompromised individuals (see Table 26).

If the percentage of enrolled subjects excluded from the immune ATPc is more than $5 \%$, a second analysis based on the TVc will be performed to complement the ATP analysis.

All descriptive immunogenicity analyses will be performed by age strata and by duration between the first dose and the start of chemotherapy cycle (PreChemo and OnChemo) as appropriate. This will be further detailed in the Statistical Analysis Plan (SAP).

### 9.8.1. Humoral immune response

Within groups assessment (Amended: 11 August 2014)
Descriptive statistics of the following parameters will be tabulated by vaccine group:

- Seropositivity rate with exact $95 \% \mathrm{CI}$;
- GMC with 95\% CI;
- Vaccine response rate with exact $95 \% \mathrm{CI}$;


## Between groups assessment

A repeated measurement model will be used to assess the geometric mean fold increase over placebo at Month 2. The statistical and immunological assumptions underlying the use of the models below will be described in the Statistical Analysis Plan (SAP).
(Amended: 11 August 2014)
A likelihood-based method will be used to analyze post-vaccination log-transformed antigE antibody concentrations (Month 1 to Month 2). (Amended: 11 August 2014)

The fixed-effect model will include the means for all levels of the visit by treatment interaction effect and for the 2 levels of first vaccination schedule. A separate parameter for each level of the interaction of the visit by the pre-vaccination log-transformed antibody concentrations (Month 0 ) will be included as a continuous covariate.

The goodness-of-fit Bayesian information criterion (BIC) and Akaike information criteria AIC statistics will be used to assess the need of a separate residual variance for placebo group or for each treatment group. Preference will be given to a simpler model. Geometric means of Month 2 post-vaccination antibody concentrations will be calculated conditionally to the means of the log-transformed concentrations at pre-vaccination calculated across the treatment groups. Adjusted means and difference of means between vaccines and placebo will be calculated together with 2 -sided confidence intervals and back-transformed to the original units to provide GMCs and GM ratios.

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### 9.8.2. Cell-mediated immune response

## Within groups assessment (Amended: 11 August 2014)

Descriptive statistics of the following parameters will be tabulated by vaccine group at all timepoints:

- descriptive statistics of the frequency of CD4+ T-cells secreting at least two activation markers (from among IFN- $\gamma$, IL-2, TNF- $\alpha, \mathrm{CD} 40 \mathrm{~L}$ ) for gE -specific ( $N$, mean, standard deviation [SD], min, Q1, median, Q3, max);
- proportion of responders with exact $95 \% \mathrm{CI}$.


## Between groups assessment

A repeated measurement model will be used to assess the geometric mean ratio over placebo at month 2. (Amended: 11 August 2014)

The statistical and immunological assumptions underlying the use of the models below will be described in the SAP.

A likelihood-based method will be used to analyze the post-vaccination log-transformed frequencies of CD4+ T-cells s secreting at least 2 cytokines following induction with gE (CD4[2+]). The placebo and HZ/su treatment groups only will be included in the main analysis. (Amended: 11 August 2014)

The fixed-effect model will include the means for all levels of the treatment effect by visits interaction and the 2 levels of the time of the first vaccination relative to the chemotherapy schedule. The continuous covariates will include: a separate parameter for each level of the interaction of the visits by the pre-vaccination log-transformed CD4[2+] T cell frequency following induction with gE (Month 0 ) and the post-vaccination logtransformed CD4 T cell frequency under the background condition.

The goodness of fit Bayesian Information Criterion (BIC) and Akaike Information Criteria (AIC) statistics will be used to assess the need of a separate residual variance for placebo group or for each treatment group in the primary model above. Preference will be given to a simpler model. In sensitivity analyses, the likelihood ratio test will be used to test the need for other significant fixed effects that would alter the conclusions made using the primary model.

Geometric means (GMs) of Month 2 post-vaccination CD4[2+] T cell frequency following induction with gE , will be calculated conditionally to the means of the prevaccination log-transformed $\mathrm{CD} 4[2+] \mathrm{T}$ cell frequency following induction with gE and the post-vaccination log-transformed CD4[2+] T cell frequency under background conditions, both overall means calculated across the treatment groups. Adjusted means and difference of means between vaccines and placebo will be calculated together with 2sided confidence intervals and back-transformed to the original units to provide frequency GMs and frequency GM ratios.

The geometric means calculated as described above provide the effect of the vaccine on the sum of both antigen-specific and non-specific CD4[2+] frequencies.

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The same model as described above will be used to analyze the log-transformed ratio between induction frequency and background frequency of CD4[2+]. Least-square means and difference of least-squares means will then be back-transformed and used to provide estimates for the frequency difference divided by background ([induction - background] / background). The log-transformation of the ratios of these estimates between treatments will be calculated together with confidence intervals according to the delta-method (error propagation method). (Amended: 11 August 2014)

$$
\begin{aligned}
\hat{Z}_{k} & =\operatorname{Exp}\left(\hat{Y}_{k}-\bar{x}\right)-1=\frac{\operatorname{Exp}\left(\hat{Y}_{k}\right)-\operatorname{Exp}(\bar{x})}{\operatorname{Exp}(\bar{x})} \\
\log _{e}\left(\frac{\hat{Z}_{k_{2}}}{\hat{Z}_{k_{1}}}\right)= & \log _{e}\left(\frac{\operatorname{Exp}\left(\hat{Y}_{k_{2}}\right)-\operatorname{Exp}(\bar{x})}{\operatorname{Exp}\left(\hat{Y}_{k_{1}}\right)-\operatorname{Exp}(\bar{x})}\right) \\
Y_{k} & =\text { least - squares mean of log - transformed frequency following induction with antigen } \\
& \text { for treatment } k \\
\bar{x} & =\text { mean of log - transformed background frequency post - vaccination } \\
\hat{Z}_{k} & =\text { mean increase in CD } 4_{\text {Specific }}^{2+} \text { for treatment } k, \text { relative to mean background frequency } .
\end{aligned}
$$

### 9.9. Analysis of safety

The primary analysis for safety will be based on the TVc. A second analysis based on the ATPc will be performed to complement the TVc analysis.

All safety analyses might be performed by age strata and by duration between the first dose and the start of chemotherapy cycle.

When appropriate, tabulations will be presented overall and by time of occurrence relative to last vaccination (e.g., using windows such as Days $0-6$, Days $0-29$ and more than 30 days post-vaccination).

The results for the analysis of safety will be tabulated as:

- The percentage of subjects with at least one local solicited AE, with at least one general solicited $\boldsymbol{A E}$ and with any solicited AE during the solicited 7-day follow-up period will be tabulated with exact $95 \%$ Confidence Intervals (CI) after each vaccine dose and overall; (Amended: 11 August 2014)
- The percentage of subjects reporting each individual solicited local and general AE during the solicited 7-day-follow-up period will be tabulated with exact $95 \% \mathrm{CI}$;
- For all solicited symptoms, the same tabulation will be performed for grade 3 solicited AEs and for solicited general AEs with relationship to vaccination;
- The proportion of subjects with at least one report of unsolicited AE classified by the Medical Dictionary for Regulatory Activities (MedDRA) Preferred Terms and reported up to 30 days after each vaccination will be tabulated with exact $95 \% \mathrm{CI}$;
- The same tabulation will be performed for grade 3 unsolicited AEs and for unsolicited AEs with a relationship to vaccination. The proportion of AEs resulting in a medically attended visit will also be tabulated;


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- Total number/percentages of doses (per dose and overall) followed by AEs will be tabulated;
- Number of subjects with pIMDs as listed in Section 7.1.5.1 will be tabulated;
- SAEs and withdrawal due to $\mathrm{AE}(\mathrm{s})$ will be described in detail.


### 9.10. Interpretation of analyses

With respect to primary and secondary confirmatory objectives, a hierarchical procedure will be applied to control the Type I error. The objectives will be assessed sequentially in order of ascending rank as indicated in Table 27. We will continue to assess the objectives until an objective is not met. At this point, we will proceed with descriptive analyses of the remaining endpoints.

All confirmatory objectives will be assessed at a 2-sided 5\% type I error rate.
Table 27 List of ranked confirmatory objectives

| Rank | Objectives (primary/secondary: nominal $\alpha=2.5 \%$ one-sided) |
| :--- | :--- |
| 1 | To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the <br> HZ/su vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy (PreChemo <br> Groups only). (primary: nominal a $=2.5 \%$ one-sided). |
| 2 | To evaluate vaccine response rate in anti-gE humoral immunogenicity responses at Month 2, following a <br> two-dose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy <br> (PreChemo Groups only). (secondary: nominal $a=2.5 \%$ one-sided). |
| 3 | To evaluate gE-specific CD4+ T-cell immunogenicity responses at Month 2, following a two-dose <br> administration of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours receiving <br> chemotherapy (PreChemo Groups only) (in the CMI sub-cohort). (secondary: nominal a $=2.5 \%$ one-sided). |
| 4 | To evaluate vaccine response rate in gE-specific CD4+ T-cell mediated immunogenicity at Month 2, <br> following a two-dose administration of the HZ/su vaccine in subjects with solid tumours receiving <br> chemotherapy (PreChemo Groups only) (in the CMI sub-cohort). (secondary: nominal a $=2.5 \%$ one-sided). |
| 5 | To evaluate the anti-gE humoral immunogenicity response at Month 2, following a two-dose administration <br> of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (all <br> subjects). (secondary: nominal $\alpha=2.5 \%$ one-sided). |
| 6 | To evaluate vaccine response rate in anti-gE humoral immunogenicity responses at Month 2, following a <br> two-dose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (all <br> subjects receiving the HZ/su vaccine). (secondary: nominal $a=2.5 \%$ one-sided). |

### 9.11. Conduct of analyses

Any deviation(s) or change(s) from the original statistical plan outlined in this protocol will be described and justified in the final study report.

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### 9.11.1. Sequence of analyses (Amended: 11 August 2014)

Unblinded evaluation of safety for the subjects (with coded group names) will be performed by the iSRC on a regular basis. Operational details for iSRC will be provided in the iSRC Charter.

## Two formal analyses are planned: a first analysis and an end of study analysis.

The first analysis of immunogenicity and reactogenicity/safety data will be performed when all data up to and including Month 2 ( 30 days post dose 2 ) will be available after completion of Visit 3. A study report will be written.

The end of study analysis of persistence of immunogenicity and safety data will be performed when all data up to and including Month 13 will be available. An end of study report will be written which will present data from the entire study.

### 9.11.2. Statistical considerations for interim analysis

No interim analysis has been planned.

## 10. ADMINISTRATIVE MATTERS

To comply with ICH GCP administrative obligations relating to data collection, monitoring, archiving data, audits, confidentiality and publications must be fulfilled.

### 10.1. Remote Data Entry instructions

Remote Data Entry (RDE), a validated computer application, will be used as the method for data collection.

In all cases, subject initials will not be collected nor transmitted to GSK. Subject data necessary for analysis and reporting will be entered/transmitted into a validated database or data system. Clinical data management will be performed in accordance with applicable GSK standards and data cleaning procedures.

While completed eCRFs are reviewed by a GSK Biologicals' Site Monitor at the study site, omissions or inconsistencies detected by subsequent eCRF review may necessitate clarification or correction of omissions or inconsistencies with documentation and approval by the investigator or appropriately qualified designee. In all cases, the investigator remains accountable for the study data.

The investigator will be provided with a CD-ROM of the final version of the data generated at the investigational site once the database is archived and the study report is complete and approved by all parties.

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### 10.2. Study Monitoring by GSK Biologicals

GSK will monitor the study to verify that, amongst others, the:

- Data are authentic, accurate, and complete.
- Safety and rights of subjects are being protected.
- Study is conducted in accordance with the currently approved protocol, any other study agreements, GCP and all applicable regulatory requirements.
The investigator and the head of the medical institution (where applicable) agrees to allow the monitor direct access to all relevant documents.

The investigator must ensure provision of reasonable time, space and qualified personnel for monitoring visits.

Direct access to all study-site related and source data is mandatory for the purpose of monitoring review. The monitor will perform a RDE review and a Source Document Verification (SDV). By SDV we understand verifying RDE entries by comparing them with the source data that will be made available by the investigator for this purpose.

The Source Documentation Agreement Form describes the source data for the different data in the RDE. This document should be completed and signed by the site monitor and investigator and should be filed in the monitor's and investigator's study file. Any data item for which the RDE will serve as the source must be identified, agreed and documented in the source documentation agreement form.

For RDE, the monitor will mark completed and approved screens at each visit.
Upon completion or premature discontinuation of the study, the monitor will conduct site closure activities with the investigator or site staff, as appropriate, in accordance with applicable regulations, GCP, and GSK procedures.

### 10.3. Record retention

Following closure of the study, the investigator must maintain all site study records (except for those required by local regulations to be maintained elsewhere) in a safe and secure location. The records must be easily accessible, when needed (e.g. audit or inspection), and must be available for review in conjunction with assessment of the facility, supporting systems, and staff. Where permitted by applicable laws/regulations or institutional policy, some or all of these records can be maintained in a validated format other than hard copy (e.g. microfiche, scanned, electronic); however, caution needs to be exercised before such action is taken. The investigator must ensure that all reproductions are legible and are a true and accurate copy of the original and meet accessibility and retrieval standards, including re-generating a hard copy, if required. Furthermore, the investigator must ensure that an acceptable back-up of the reproductions exists and that there is an acceptable quality control procedure in place for making these reproductions.

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GSK will inform the investigator/institution of the time period for retaining these records to comply with all applicable regulatory requirements. However, the investigator/institution should seek the written approval of the sponsor before proceeding with the disposal of these records. The minimum retention time will meet the strictest standard applicable to a particular site, as dictated by ICH GCP, any institutional requirements, applicable laws or regulations, or GSK standards/procedures; otherwise, the minimum retention period will default to 15 years.

The investigator/institution must notify GSK of any changes in the archival arrangements, including, but not limited to archival at an off-site facility, transfer of ownership of the records in the event the investigator leaves the site.

### 10.4. Quality assurance

To ensure compliance with GCP and all applicable regulatory requirements, GSK may conduct a quality assurance audit. Regulatory agencies may also conduct a regulatory inspection of this study. Such audits/inspections can occur at any time during or after completion of the study. If an audit or inspection occurs, the investigator and institution agree to allow the auditor/inspector direct access to all relevant documents and to allocate his/her time and the time of his/her staff to the auditor/inspector to discuss findings and any relevant issues.

### 10.5. Posting of information on publicly available clinical trial registers and publication policy

Study information from this protocol will be posted on publicly available clinical trial registers before enrollment of subjects begins.

Summaries of the results of GSK interventional studies (phase I-IV) are posted on publicly available results registers within 12 months of the primary completion date for studies of authorised vaccines and 18 months for studies of non-authorised vaccines.

GSK also aims to publish the results of these studies in the searchable, peer reviewed scientific literature. Manuscripts are submitted for publication within 24 months of the last subject's last visit.

### 10.6. Provision of study results to investigators

Where required by applicable regulatory requirements, an investigator signatory will be identified for the approval of the study report. The investigator will be provided reasonable access to statistical tables, figures, and relevant reports and will have the opportunity to review the complete study results at a GSK site or other mutuallyagreeable location.

GSK Biologicals will also provide the investigator with the full summary of the study results. The investigator is encouraged to share the summary results with the study subjects, as appropriate.

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## 11. COUNTRY SPECIFIC REQUIREMENTS

### 11.1. Country-specific age of legal consent

Countries will comply with eligibility criteria as described in Sections 4.2 and 4.3 of the protocol. In some countries participating in the study ZOSTER-028, in accordance with local regulations, the age of legal consent is higher than 18 years (see Table 28).

Table 28 Age of legal consent by country

| Country | Age of legal consent (YOA) |
| :--- | :---: |
| Canada (Alberta, Manitoba, Ontario, Prince Edward Island, Quebec and <br> Saskatchewan) | 18 |
| Canada (British Columbia, New Brunswick, Newfoundland and Labrador, | 19 |
| Nova Scotia, Nunavut, North West Territories and Yukon Territories) |  |
| France | 18 |
| Spain | 18 |
| South-Korea | 20 |
| UK | 16 |

$\mathrm{YOA}=\mathrm{Years}$ of Age

### 11.2. Requirements for France

This section includes all the requirements of the French law ( $\mathrm{n}^{\circ} 2004-806$ of 9th August 2004), and identifies, item per item, the mandatory modifications or additional information to the study protocol.

Concerning the «STUDY POPULATION»

- In line with the local regulatory requirements, the following text in section "OTHER STUDY ELIGIBILITY CRITERIA CONSIDERATIONS" is added:

A subject will be eligible for inclusion in this study if he /she is either affiliated to or beneficiary of a social security category.
It is the investigator's responsibility to ensure and to document (in source document patient notes) that the patient is either affiliated to or beneficiary of a social security category.

Concerning the "DATA ANALYSIS AND STATISTICAL CONSIDERATIONS" and specially in the "SAMPLE SIZE ASSUMPTION"
The expected number of patients to be recruited in France is declared to the French regulatory authority.

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## Concerning the "STUDY CONDUCT CONSIDERATIONS"

In section "Regulatory and Ethical Considerations, Including the Informed Consent Process"

- Concerning the process for informing the patient or his/her legally authorised representative, the following text is added:

French Patient Informed Consent form is a document in triplicate which summarises the main features of the study and allows collection of the patient's written consent. It also contains a reference to the authorisation of Afssaps and the approval from the French Ethic committee and the maintenance of confidentiality of the returned consent form by GSK France.

- Concerning the process for obtaining subject informed consent:
- When biomedical research is carried out on a minor / on an adult in the care of a "tutelle" guardian, consent is given by their legal representative and, if the committee mentioned in article L. 1123-1 considers that the research in question, because of the gravity of the restraints or the specificity of the medical acts involved, entails a serious risk of affecting their private life or the integrity of their body, by the family council if it has been instated, or by the judge of "tutelle" guardians.
- When biomedical research is carried out on an adult in the care of a "curatelle" guardian, consent is given by the subject assisted by his guardian.

However, if the adult in the care of a "curatelle" guardian is invited to participate in research which the committee mentioned in article L. 1123-1 considers, because of the gravity of the restraints or the specificity of the medical acts involved, to entail a serious risk of affecting their private life or the integrity of their body, the matter is submitted to the judge of guardians who decides whether the adult is capable of giving his consent. In the case of incapacity, the judge will decide whether or not to authorise the biomedical research.

- When biomedical research, which complies with the conditions laid down in article L. 1121-8, is considered for an adult incapable of expressing his consent and not under a legal protection order, consent is given by a person of confidence as defined in article L. 1111-6 and, failing this, by a person who maintains close and stable links with the subject. However, if the committee mentioned in article L. 1123-1 considers that the research in question, because of the gravity of the restraints or the specificity of the medical acts involved, entails a serious risk of affecting their private life or the integrity of their body, consent is given by the judge of guardians.
- Concerning the management of the Patient Informed Consent forms, the following text is added:

The first copy of the Patient Informed Consent form is kept by the investigator. The second copy is kept by the Medical Direction of GlaxoSmithKline France and the last copy is given to the patient or his/her legally authorised representative.

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The second copy of all the consent forms will be collected by the investigator under the Clinical Research Assistant's (CRA's) control, and placed in a sealed envelope bearing only:

- the study number,
- the identification of the Centre : name of the principal investigator and centre number),
- the number of informed consents,
- the date,
- and the principal investigator's signature.

Then, the CRA hands the sealed envelope over to the Medical Direction, for confidential recording, under the responsibility of the Medical Director.

In section concerning the "DEMOGRAPHIC DATA" the following text is added:
In accordance with the data-processing and freedom French law dated on 6th of January 1978 modified on the 6th of August 2004 - article 8, the ethnic origin can only be collected if the collection of this data is justified within the framework of this study.

In section concerning the "TESTING OF BIOLOGICAL SAMPLES" the following text is added:

In accordance with Article L1211-2 of the French Public Health Code, a biological sample without identified purpose at the time of the sample and patient's preliminary information is not authorized.

In section concerning the "NOTIFICATION TO THE HOSPITAL DIRECTOR" the following text is added:

In accordance with Article L1123-13 of the Public Health Code, the Hospital Director is informed of the commitment to the trial in his establishment. The Hospital Director is supplied with the protocol and any information needed for the financial disposition, the name of the investigator(s), the number of sites involved in his establishment and the estimated time schedule of the trial (R.1123-63).

In section concerning the "INFORMATION TO THE HOSPITAL PHARMACIST" the following text is added:
In accordance with Article R.1123-64 of the Public Health Code, the Hospital Pharmacist is informed of the commitment to the trial in his establishment. The Pharmacist is supplied with a copy of the protocol (which allows him to dispense the drug(s) of the trial according to the trial methodology), all information concerning the product(s) of the trial (e.g. included in the CIB), the name of the investigator(s), the number of sites involved in his establishment and the estimated time schedule of the trial.

In section "DATA MANAGEMENT" the following text is added:
Within the framework of this clinical trial, data regarding the identity of the investigators and/or co-investigators and/or the pharmacist if applicable, involved in this clinical trial, and data regarding the patients recruited in this clinical trial (patient number, treatment

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number, patient status with respect to the clinical trial, dates of visit, medical data) will be collected and computerised in GSK data bases by GlaxoSmithKline Laboratory or on its behalf, for reasons of follow up, clinical trial management and using the results of said clinical trial. According to the Act $n^{\circ} 78-17$ of $6^{\text {th }}$ January 1978 further modified, each of these people aforesaid has a right of access, correction and opposition on their own data through GlaxoSmithKline Laboratory (Clinical Operations Department).

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## APPENDIX A LABORATORY ASSAYS

## Specific Ab (anti-gE) measurements

Anti-gE ELISA: Anti-gE Ab concentrations will be measured using an anti-gE ELISA. Diluted blood serum samples of study subjects will be added to microtitre wells precoated with gE antigen. Secondary peroxidase-conjugated anti-human Abs will be added, which bind to the primary human anti-gE Abs. After incubation of the microtitre wells with a chromogen substrate solution, the enzymatic reaction will be stopped. Optical densities will be recorded and anti-gE Ab concentrations are calculated from a standard curve. The assay cut-off is $97 \mathrm{mIU} / \mathrm{mL}$. The assay will be performed on human serum at GSK Biologicals' laboratory or another laboratory designated by GSK Biologicals.

## (Amended: 11 August 2014)

## Intracellular cytokine staining (ICS)

CMI responses will be performed by CEVAC-Ghent on thawed Peripheral Blood Mononuclear Cells (PBMCs) by ICS. The assay will be performed on samples collected during the course of the study. This assay provides information on the frequency of CD4+ T-cells responding to culture medium or antigens (gE peptide pool) by secreting cytokine molecules involved in immunity such as IFN- $\gamma$, IL-2, TNF- $\alpha$, and CD40L.

## (Amended: 11 August 2014)

Briefly, PBMC collected from the subjects are stimulated for two hours using culture medium (for evaluation of the non-specific response), a pool of overlapping peptides covering the entire sequence of the vaccine antigen gE . Then, an intracellular block (brefeldin A) is added to inhibit cytokine secretion for a subsequent overnight incubation. Cells are then harvested, stained for surface markers (CD3, CD4 and CD8) and fixed. The fixed cells are then permeabilised and stained with anti-cytokine Abs, washed and analysed by cytofluorometry.

The results of ICS assays are expressed as the frequency of specific CD4 T cells per million total CD4 T cells.

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## APPENDIX B CLINICAL LABORATORIES

Table 29 GSK Biologicals' laboratories

| Laboratory | Address |
| :--- | :--- |
| GSK Biologicals Global Vaccine Clinical <br> Laboratory, Rixensart | Biospecimen Reception - B7/44 <br> Rue de I'Institut, 89 - B-1330 Rixensart - Belgium |
| GSK Biologicals Global Vaccine Clinical <br> Laboratory, North America- Laval | Biospecimen Reception - Clinical Serology <br> 525 Cartier blvd West - Laval - Quebec - Canada - H7V 3S8 |
| GSK Biologicals Global Vaccine Clinical <br> Laboratory, Wavre-Nord Noir Epine | Avenue Fleming, 20 - B-1300 Wavre - Belgium |
| GSK = GlaxoSmithKline. |  |

Table $30 \quad$ Outsourced laboratories

| Laboratory | Address |
| :--- | :--- |
| CEVAC - University of Ghent | De Pintelaan, 185 Ghent - Belgium |
| CEVAC $=$ Centre for Vaccination. |  |

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## APPENDIX C AMENDMENTS AND ADMINISTRATIVE CHANGES TO THE PROTOCOL

| GlaxoSmithKline Biologicals <br> Clinical Research \& Development <br> Protocol Amendment 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
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| eTrack study number <br> and Abbreviated Title 116427 (ZOSTER-028) <br> IND number BB-IND 13879 <br> EudraCT number 2012-002966-11 <br> Amendment number: Amendment 1 <br> Amendment date: 19 November 2012 <br> Co-ordinating author: PPD $\quad$ Manpower Business Solutions for GSK Biologicals <br> Rationale/background for changes: <br> - Subjects in the ZOSTER-028 study will be randomised into two groups based on the vaccination schedule in relation to the start of chemotherapy. The OnChemo subjects receive their first HZ/su vaccination at start of chemotherapy, while the PreChemo subjects receive their first $\mathrm{HZ} / \mathrm{su}$ vaccination at least 10 days before start of chemotherapy. The previous design had these two groups at an equal size. <br> - New unpublished data from studies with other GSK candidate vaccines indicate that giving the first vaccination at the start of chemotherapy can lead to a decreased/suppressed immune response, possibly due to steroids used concomitantly in high doses to prevent nausea and vomiting. The primary objective on immunogenicity in the ZOSTER-028 is confirmatory and aims to evaluate the anti-gE humoral immunogenicity response. To increase the chance of success in obtaining a significant immune response with $\mathrm{HZ} / \mathrm{su}$, the primary objective for immunogenicity will be evaluated only in the PreChemo Group. For this reason, the study groups have been changed by enlarging the proportion of PreChemo subjects to maintain a $90 \%$ power for the primary immunogenicity objective: instead of a 1:1 ratio ( 100 subjects in each group), the PreChemo:OnChemo ratio, will now be $4: 1(\mathrm{~N}=168 / 42)$. The $\mathrm{HZ} / \mathrm{su}:$ Placebo ratio is maintained as $1: 1$. Thus the overall study N was increased by $5 \%$ ( 10 subjects) in order to have $90 \%$ power for the primary immunogenicity objective. A |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
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comparison of the Old and New N values for the study is indicated below.

|  | Old N | New N | Old CMI <br> Sub-cohort | New CMI <br> Sub-cohort |
| ---: | :---: | :---: | :---: | :---: |
| HZ PreChemo | 50 | 84 | 19 | 38 |
| Placebo PreChemo | 50 | 84 | 19 | 38 |
| HZ OnChemo | 50 | 21 | 19 | 0 |
| Placebo OnChemo | 50 | 21 | 19 | 0 |
| TOTAL | $\mathbf{2 0 0}$ | $\mathbf{2 1 0}$ | $\mathbf{7 6}$ | $\mathbf{7 6}$ |

## The following updates have been made:

- The primary objective for immunogenicity response (based on Geometric Mean [GM] ratios) following the $\mathrm{HZ} / \mathrm{su}$ vaccination compared to placebo will now be evaluated only in the PreChemo Groups.
- The secondary objectives have now been qualified to evaluate immunogenicity in either the PreChemo Groups (Vaccine Response Rates [VRR] in anti-gE humoral immunogenicity responses and VRR and GM ratio in gE-specific CellularMediated Immunity [CMI]) or in all study subjects (VRR and GM ratio in anti-gE humoral immunogenicity responses).
- The CMI sub-cohort will now only be recruited in the PreChemo Groups.
- Changes have been made to Section 9.3.1 since an error in the calculation (logarithm transformation) of a criteria value and one assumptions was discovered in the sample size assumptions for the humoral immune response endpoint. In order to correct the error, the following calculation modifications have been performed:
- For the criteria value, the wrong value natural logarithm $(\ln (3)=1.099)$ has been replaced by decimal logarithm $\left(\log _{10}(3)=0.477\right)$.
- The assumed fold increase has been re-evaluated to 12.5 , due to the change in the population assessed (PreChemo only) for the primary immunogenicity objective, and due to new data from another HZ/su study in an immunocompromised population, showing a higher fold increase, and therefore the previous value $(\ln (5.5)=1.705)$ has been replaced by $\left(\log _{10}(12.5)=1.097\right)$.
- The overall sample size was increased by adding 10 subjects in order to maintain the power for the primary immunogenicity objective at $90 \%$.
- The updates supporting these study design changes have been made in:
- Synopsis Table 1,
- The Section 3 Study Design Overview Figure,
- Table 1,
- Table 5,
- Table 26,
- Treatment allocation in Section 3,


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- Section 4.1 Number of subjects,
- Section 5.2.2.2.1. Study group and treatment number allocation,
- Section 9.3 Determination of sample size.
- The timepoint for evaluation of the primary objective for safety/reactogenicity has been reworded for clarity ('up to 30 days post last vaccination' instead of 'up to month 2').
- The word "humoral" has been removed from the first Secondary Endpoint in the Synopsis and Section 9.2.
- The inclusion criteria for subject age in Section 4.2, now also include the requirement that the subject must also have reached the age of legal consent at the time of study entry i.e., when informed consent is signed.
- It is now indicated that the Pre-vaccination visit is mandatory in 3 places: 1.) under duration of the study, 2.) footnote under Table 6 List of study procedures and 3.) Section 5.6.1. Procedures during the Pre-vaccination visit. This visit can still occur on the same day as Visit 1.
- It has been clarified in the footnotes in 2 places what happens when the variable study Visit 4 occurs at Month 13: 1.) under the Section 3 Study Design Overview Figure; and 2.) Table 6 List of Study procedures.
- The statement "Any condition which, in the judgment of the investigator would make intramuscular injection unsafe" has been added to Sections 4.3 Exclusion criteria for enrolment and 6.5 Contraindications to subsequent vaccination.
- Notes about contraindication of vaccine administration to the non-dominant arm and to subjects with potential bleeding risk(s) have been added to the end of Section 6.3. Dosage and administration of study vaccine/ placebo.
- The change: 'At Visit 1, all subjects will be "informed of" instead of "educated to recognize" the signs and symptoms of typical HZ' has been made in Section 5.4.1. and footnote $h$ of Table 6.
- Edits to footnotes and changes to symbol placements were done for Tables 4, 6 and 17.
- Country specific requirements from France have been added to Section 11.2.
- Typographical errors have been corrected in Section 6.7, Section 7.1.5.1. (Table 17) and Section 7.4.3.

Amended text has been included in bold italics and deleted text in strikethrough in the following sections:

## Synopsis

| Contributing authors | $\bullet$ | PPD | Project Study |
| :--- | :--- | :--- | :--- |
|  |  | Statistician |  |
| Rationale for the study | $\bullet$ | Rationale for the study design |  |

Subjects in the ZOSTER-028 study will initially be
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| and study design | CONFIDENTIAL |
| :---: | :---: |
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|  | randomised into two groups based on the vaccination |
|  | schedule in relation to the start of chemotherapy. The |
|  | OnChemo group receives their first $\mathrm{HZ} / \mathbf{s u}$ vaccination |
|  | at start of chemotherapy, while the PreChemo group |
|  | receives their first HZ/su vaccination at least 10 days |
|  | before start of chemotherapy. Unpublished data with |
|  | other GSK candidate vaccines indicates that |
|  | vaccination at the start of chemotherapy can lead to a |
|  |  |
|  | decreased/suppressed immune response, possibly due |
|  | to steroids used concomitantly in high doses to prevent |
|  | nausea and vomiting. Therefore, the primary objective |
|  | linked to immunogenicity will be assessed in the |
|  | PreChemo groups only. For this reason, the study |
|  | groups will be allocated 4:1 (168/42) |
|  | PreChemo:OnChemo. |

## Objectives

## Co-Primary

- To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).


## Criteria to be used:

The objective is met if the lower limit of the $95 \%$ confidence interval (CI) of the Geometric Mean (GM) ratio (HZ/su PreChemo groups over placebo PreChemo groups) in anti-gE ELISA antibody concentrations is greater than 3 .

- To evaluate the safety and reactogenicity following administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine as compared to placebo up to Menth $2 \mathbf{3 0}$ days post last vaccination in subjects with solid tumours receiving chemotherapy.


## Secondary

- To evaluate vaccine response rate in anti-gE humoral immunogenicity responses at Month 2, following a twodose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).


## Criteria to be used:

The objective is met if the lower limit of the $95 \%$ CI of the vaccine response rate for anti-gE ELISA antibody concentrations at Month 2 in the HZ/su vaceine PreChemo group is at least $60 \%$.

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- To evaluate gE-specific CD4+ T-cell immunogenicity responses at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only) (in the CMI sub-cohort).

Criteria to be used:
The objective is met if the lower limit of the $95 \%$ CI of the GM ratio (HZ/su vaccine-PreChemo groups over placebo PreChemo groups) in gE-specific CD4+ T-cell frequencies at Month 2 is greater than 1.

- To evaluate vaccine response rate in gE-specific CD4+ T-cell mediated immunogenicity at Month 2, following a two-dose administration of the HZ/su vaccine in subjects with solid tumours receiving chemotherapy (PreChemo Groups only) (in the CMI sub-cohort).
Criteria to be used:
The objective is met if the lower limit of the $95 \%$ CI of the vaccine response rate for gE -specific CD4+ T-cell frequencies at Month 2 in the HZ/su vaccine PreChemo group is at least $50 \%$.
- To evaluate the anti-gE humoral immunogenicity response at Month 2, following a two-dose administration of the $H Z / s u$ vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (all subjects).

Criteria to be used:
The objective is met if the lower limit of the 95\% confidence interval (CI) of the Geometric Mean (GM) ratio (HZ/su group over placebo group) in anti-gE ELISA antibody concentrations is greater than 3.

- To evaluate vaccine response rate in anti-gE humoral immunogenicity responses at Month 2, following a twodose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (all subjects receiving the HZ/su vaccine).
Criteria to be used:
The objective is met if the lower limit of the 95\% CI of the vaccine response rate for anti-gE ELISA antibody concentrations at Month 2 in the HZ/su group is at least 60\%.


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- To characterize anti-gE humoral immunogenicity responses at Month 0, Month 1, Month2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13 within the HZ/su and placebo groups.
- To characterize gE-specific CD4+ T-cell mediated immunogenicity responses at Month 0 , Month 1, Month2, and Month 13 within the HZ/su and placebo groups (Pre Chemo Groups only) (in the CMI subcohort).

Synopsis Table 1Study groups and epochs foreseen in the study

| Study groups | Number of subjects | Age (Min.)* | Epoch |
| :---: | :---: | :---: | :---: |
|  |  |  | Epoch 001 |
| HZ/su-PreChemo | 5084 | 18 years | $\bullet$ |
| Placeb-PreChemo | 5084 | 18 years | $\bullet$ |
| HZ/su-OnChemo | 5021 | 18 years | $\bullet$ |
| Placeb-OnChemo | 5021 | 18 years | $\bullet$ |

$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb $=$ Placebo;
Min. $=$ Minimum
*And above the legal age of consent (see Table 27)

- Treatment allocation:

Eligible subjects will be randomised to the investigational HZ/su vaccine or placebo (1:1 ratio) and to first vaccination at least 10 days (up to 1 month) before start of chemotherapy or at start of the first (or second) chemotherapy cycle ( $1-4: 1$ ratio).

- Biological samples to be collected:
- Blood samples (approximately 8 mL ) will be collected from all subjects at Visits 1, 2, 3, 4 and 5. Blood samples will be used to assess humoral immune responses by $A b \mathrm{gE}$ ELISA with respect to the study/investigational vaccine in all subjects.


## Number of subjects

Target enrolment is approximately $200-210$ eligible adults diagnosed with solid tumours receiving chemotherapy.

## Endpoints Secondary

- For hemeratimmunogenicity with respect to components of the study/investigational vaccine.
- Anti-gE Ab concentrations as determined by ELISA at Month 0, Month 1, Month2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13.


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APPENDIX CAMENDMENTS AND ADMINISTRATIVE CHANGES TO THE PROTOCOL

## List of abbreviations

| In: | Natural Logarithm |
| :--- | :--- |
| $\log _{10}:$ | Decimal Logarithm |
| LS: | Least Squares |
| SD: | Standard Deviation |
| VRR: | Vaccine Response Rates |

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## Section 1 Introduction

## Section 1.2 Rationale for the study and study design

Subjects in the ZOSTER-028 study will initially be randomised into two groups based on the vaccination schedule in relation to the start of chemotherapy. The OnChemo group receives their first HZ/su vaccination at start of chemotherapy, while the PreChemo group receives their first HZ/su vaccination at least 10 days before start of chemotherapy. Unpublished data with other GSK candidate vaccines indicates that vaccination at the start of chemotherapy can lead to a decreased/suppressed immune response, possibly due to steroids used concomitantly in high doses to prevent nausea and vomiting. Therefore, the primary objective linked to immunogenicity will be assessed in the PreChemo groups only. For this reason, the study groups will be allocated 4:1 (168/42) PreChemo:OnChemo.

## Section 2 Objectives

## Section 2.1 Co-primary objectives

- To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).
Criteria to be used:
The objective is met if the lower limit of the $95 \%$ confidence interval (CI) of the Geometric Mean (GM) ratio (HZ/su PreChemo groups over placebo PreChemo groups) in anti-gE ELISA antibody concentrations is greater than 3.
- To evaluate the safety and reactogenicity following administration of the HZ/su vaccine as compared to placebo up to Month $2 \mathbf{3 0}$ days post last vaccination in subjects with solid tumours receiving chemotherapy.


## Section 2.2 Secondary objectives

- To evaluate vaccine response rate in anti-gE humoral immunogenicity responses at Month 2, following a two-dose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).
Criteria to be used:
The objective is met if the lower limit of the $95 \%$ CI of the vaccine response rate for anti-gE ELISA antibody concentrations at Month 2 in the HZ/su vaceine-PreChemo group is at least $60 \%$.


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- To evaluate gE-specific CD4+ T-cell immunogenicity responses at Month 2, following a two-dose administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only) (in the CMI sub-cohort).
Criteria to be used:
The objective is met if the lower limit of the $95 \% \mathrm{CI}$ of the GM ratio (HZ/su vaceine PreChemo groups over placebo PreChemo groups) in gE-specific CD4+ T-cell frequencies at Month 2 is greater than 1.
- To evaluate vaccine response rate in gE-specific CD4+ T-cell mediated immunogenicity at Month 2, following a two-dose administration of the HZ/su vaccine in subjects with solid tumours receiving chemotherapy (PreChemo Groups only) (in the CMI sub-cohort).

Criteria to be used:
The objective is met if the lower limit of the $95 \%$ CI of the vaccine response rate for gE-specific CD4+ T-cell frequencies at Month 2 in the HZ/su *aceine-PreChemo group is at least $50 \%$.

- To evaluate the anti-gE humoral immunogenicity response at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (all subjects).
Criteria to be used:
The objective is met if the lower limit of the 95\% confidence interval (CI) of the Geometric Mean (GM) ratio (HZ/su group over placebo group) in anti-gE ELISA antibody concentrations is greater than 3.
- To evaluate vaccine response rate in anti-gE humoral immunogenicity responses at Month 2, following a two-dose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy (all subjects receiving the HZ/su vaccine).
Criteria to be used:
The objective is met if the lower limit of the $95 \%$ CI of the vaccine response rate for anti-gE ELISA antibody concentrations at Month 2 in the HZ/su group is at least 60\%.
- To characterize anti-gE humoral immunogenicity responses at Month 0, Month 1, Month2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13 within the HZ/su and placebo groups.
- To characterize gE-specific CD4+ T-cell mediated immunogenicity responses at Month 0, Month 1, and Month 13 within the HZ/su and placebo groups (PreChemo Groups only) (in the CMI sub-cohort).

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## Section 3 Study design overview


** The second dose of study vaccine/ placebo must be administered between 1 and 2 months after the first vaccination AND at the at the first day (allowing a window of $+/-1$ day) of a subsequent cycle of chemotherapy.
$\Delta$ Should Visit 4 coincide with Month 13, the Visit 5 procedures will be conducted (including a Blood Sampling for CMI).
$¥$ Blood samples ( $\sim 8 \mathrm{~mL}$ ) will be collected from all subjects at Visit $1,2,3$, first day of last chemotherapy cycle at Visit 4 and Visit 5 to evaluate humoral immune responses by a gE ELISA.

- Duration of the study:

Each subject will be followed at least until he/she completes Visit 5 (i.e., until Month 13, approximately 12 months after the second dose of study vaccine/ placebo). The first vaccination visit at Month 0 (Visit 1) will be preceded by a mandatory Prevaccination visit that will take place from 30 days prior to Visit 1 up to the day of Visit 1 (the Pre-vaccination visit can occur on the same day as Visit 1).

- Study groups:


## Table 1 Study groups and epochs foreseen in the study

| Study groups | Number of subjects | Age (Min.) $^{*}$ | Epoch |
| :---: | :---: | :---: | :---: |
|  |  | Epoch 001 |  |
| HZ/su-PreChemo | 5084 | 18 years | $\bullet$ |
| Placeb-PreChemo | 5084 | 18 years | $\bullet$ |
| HZ/su-OnChemo | 5021 | 18 years | $\bullet$ |
| Placeb-OnChemo | 5021 | 18 years | $\bullet$ |

$\mathrm{HZ} /$ su $=$ Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb = Placebo; Min. $=$ Minimum
*And above the legal age of consent (see Table 27)

- Treatment allocation:

Eligible subjects will be randomised to two treatment groups: investigational HZ/su vaccine or placebo (1:1); and to two vaccination strata: first vaccination at least 10 days before start of chemotherapy, or at the start of the first (or second)

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chemotherapy cycle ( $14: 1$ ). The overall ratio of these 4 equal study groups will be 1:1 4:4:1:1 (see Table 5).

- Biological samples to be collected:
- Blood samples (approximately 8 mL ) will be collected from all subjects at Visits $1,2,3,4$ and 5 . Blood samples will be used to assess humoral immune responses by Ab gE ELISA with respect to the study/investigational vaccine in all subjects.


## Section 4 Study cohort

## Section 4.1 Number of subjects

Target enrolment is approximately $200-210$ eligible adults ( 50 per study group/ 100 per treatment group) diagnosed with solid tumours receiving chemotherapy. Taking into account a projected $20 \%$ rate from drop-out and non-evaluable subjects at Month 2, the number of evaluable subjects is estimated to be 160-168 (80-84 per treatment group). See Section 9.3 for a description of the criteria used in the determination of sample size.
Refer to Sections 4.2 and 4.3 for eligibility criteria.

## Table 4 Sub-cohorts

| Sub-cohort name | Description | Estimated number of <br> enrolled subjects |
| :--- | :--- | :---: |
| CMI sub-cohort* | Blood samples (approximately 30 mL ) collected at Visits <br> $1,2,3$ and 5 will be analysed to assess CMI response | 76 |

* This CMI sub-cohort will be comprised exclusively of subjects from the PreChemo Groups.

Table 5 Number of subjects required for enrolment

| Vaccination Start stratum | Study groups | Number of subjects |  |
| :--- | :--- | :---: | :---: |
|  |  | Overall <br> $\mathbf{N}$ | CMI sub-cohort <br> $\mathbf{N}$ |
| First Vaccination <br> at least 10 days before start of chemotherapy cycle | HZ/su-PreChemo | 50.84 | 1838 |
|  | Placeb-PreChemo | 50.84 | 1838 |
|  | HZ/su-OnChemo | 50.21 | 180 |
|  | Placeb-OnChemo | 50.21 | 180 |
|  | Total | 200.210 | 76 |

## Section 4.2 Inclusion criteria for enrolment

- A male or female aged 18 years or older (and has reached the age of legal consent) at the time of study entry (i.e., when informed consent is signed); (Refer to Section 11.1 for country-specific age of legal consent);


## Section 4.3 Exclusion criteria for enrolment

- Any condition which, in the judgment of the investigator would make intramuscular injection unsafe;


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## Section 5 Conduct of the study

## Section 5.2.2.2.1 Study group and treatment number allocation

Target enrolment is approximately $200-210$ eligible adults diagnosed with solid tumours receiving chemotherapy. During the Pre-vaccination visit eligible subjects will be randomised to the investigational $\mathrm{HZ} / \mathrm{su}$ vaccine or placebo according to a $1: 1$ ratio (vaccine:placebo), and to first vaccination at least 10 days before start of chemotherapy or at start of the first (or second) chemotherapy cycle ( $44: 1$ ). The overall ratio of these 4 equal study groups will be $1: 1-4: 4: 1: 1$.

## Section 5.2.3 Allocation of subjects to assay subsets (CMI sub-cohort)

The CMI analyses will be performed at specified timepoints for subjects included in the CMI sub-cohort (Refer to Table 4). This CMI sub-cohort will be comprised exclusively of subjects from the PreChemo Groups. This is a subgroup of the subjects in the study in selected countries at designated sites that have access to a peripheral blood mononuclear cells (PBMC) processing facility within the acceptable time window from sample collection to PBMC processing.

## Section 5.4.1 Suspected HZ cases

At Visit 1, all subjects will be edueated to recognize informed of the signs and symptoms of typical HZ.

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## Section 5.5 Outline of study procedures

Table 6 List of study procedures

| Epoch | Epoch 001 |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of contact | Pre- vaccination Visit $t$ | Visit 1* | Visit 2** | Visit 3 | Visit 4*** | Month 5 Phone Contact | Month 9 Phone Contact | Visit $5^{\boldsymbol{4}}$ |
| Timepoints | $\begin{array}{\|c\|} \hline \text { Up to }-30 \\ \text { to }-10 \text { days } \\ \hline \end{array}$ | Month 0 ${ }^{\text {² }}$ | Month 1 ${ }^{\text {k* }}$ | Month 2 | Month 6*** (Months 4 to 13) | Month 5 | Month 9 | Month 13 |
| Sampling timepoints |  | Pre-Vacc | Post-Vacc 1 | Post-Vacc 2 | Post-Vacc 2 |  |  | Post-Vacc 2 |
| Blood sampling (approximately 8 mL ) for ELISA humoral immune response from all subjects |  | - | - | - | - |  |  | - |
| Recording of any concomitant medication//product/vaccine/treatment which could impact the immune response or is part of a chemotherapy 9 |  | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | - | $\bullet$ |
| Reporting of intercurrent medical conditions including HZ h |  | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Reporting of serious adverse events (SAEs) ${ }^{g}$ |  | $\bullet$ - ${ }^{\text {i }}$ | $\bullet$ | - | $\bullet$ | - | - | $\bullet$ |
| Reporting of SAEs related to study participation or to a concurrent GSK medication/vaccine ig | - | $\bullet$ | - | - | - | - | $\bullet$ | - |
| Reporting of pregnancies |  | - ${ }^{i j}$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Reporting of potential immune-mediated diseases (pIMDs) ig |  | - ${ }^{\text {i }}$ | - | - | - | - | - | - |

$\dagger$ The Pre-vaccination visit is mandatory and can occur on the same day as Visit 1. If thero is no the Pre-vaccination visit occurs on the same day as Visit 1 ,
all procedures indicated under the Pre-vaccination visit will be performed and recorded in the eCRF at Visit 1.
${ }^{\Delta}$ Should Visit 4 coincide with Month 13, it will be recorded as Visit 5 in the eCRF, i.e., the Visit 5 procedures will be conducted (including a Blood Sampling for CMI) and Visit 5 will be the visit recorded using the special Visit 5 tick-box in the eCRF indicating that Visit 5 has superseded Visit 4.
${ }^{d}$ Subjects will be instructed to contact their study site immediately if the subject develops any symptoms suggestive of HZ '(At Visit 1 , subject will beducad with regard to the signs and symptoms of HZ ), if the subject manifests any symptoms he/she perceive as serious and, in case of pregnancy for women of childbearing potential
${ }^{\mathrm{h}}$ Refer to Section 6.7 for details regarding intercurrent medical conditions. The occurrence of HZ is an intercurrent medical condition. At Visit 1 , all subjects will be educated to ecognize informed of the signs and symptoms of typical HZ
For each AE/SAE the subject experionces, during the applicable reporting poriod, the subject will be asked if holsho recoived medical altention defined as
hospitalisation, an emergency room visit or a visit to or from medical porsonnol (medical doctor) for any reason and this information will be recorded in the eCRF
ji Study procedure to be assessed only after administration of vaccine at Visit 1.

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Table $7 \quad$ Intervals between study visits

* If it is not possible for a subject to have the Pre-vaccination visit prior to the day of Visit 1 ; $t$ The Pre-vaccination visit can occur on the same day as Visit 1.
** The second dose of study vaccine/ placebo mustwill be administered between 1 andto 2 months after the first vaccinationdose AND at the first day (allowing a window of $+/-1$ day) of a subsequent cycle of chemotherapy.


## Section 5.6.1 Procedures during the pre-vaccination visit

The mandatory Pre-vaccination visit should take place prior to the day of Visit 1. If the Pre-vaccination visit occurs, it should take place between 30 and 10 days prior to the day of Visit 1. Procedures occurring at the Pre-vaccination visit, will be recorded in the eCRF, with the exception of a positive Pre-vaccination pregnancy test (see Section 7.2.1). The Pre-vaccination visit can occur on the same day as Visit 1.

## Section 5.6.1.5 Recording of AEs, SAEs related to study participation or GSK concomitant medication/vaccination

Refer to Section 7.3 for procedures for the investigator to record AEs, SAEs and pregnancies. Refer to Section 7.4 for guidelines on how to report AEs, SAEs, and pregnancies to GSK Biologicals. Up toFrom the time of informed consent until the first vaccination at Visit 1, SAEs related to study participation or GSK concomitant medication/vaccination are to be reported.

## Section 5.6.10 Sampling

- A volume of approximately 8 mL of whole blood will be collected from all subjects at Visits 1, 2, 3, 4 and 5. Blood samples will be used to assess humoral immune responses by Ab gE ELISA with respect to the study/investigational vaccine in all subjects.


## Section 5.6.13 Recording of AEs, SAEs, pregnancies and pIMDs

- For subjects who are illiterate or who need assistance with completion of diary cards, refer to Section 5.8 of the SPM for guidelines on assistance in subject diary card completion.


## Section 5.7.2 Biological samples

Table 8 Biological samples

| Sample type | Quantity <br> (approximate vol.) | Unit | Timepoint | Sub-cohort <br> Name $^{*}$ |
| :--- | :--- | :--- | :--- | :--- |
| Blood (Humoral <br> immunologyimmunity) | 8 | mL | Visit 1, 2, 3, 4 and 5 | All subjects |
| Blood (Cell-mediated <br> immunologyimmunity) | 30 | mL | Visit 1, 2, 3 and 5 | CMI sub-cohort |

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## Section 6 Study vaccine/ placebo and administration

## Section 6.3 Dosage and administration of study vaccine/ placebo

## Notes:

- In case of contraindication to the administration in the non-dominant arm (e.g., arm radiotherapy for breast cancer) the dominant arm should be used
- In case of bleeding risk(s), the vaccine should only be administered, if according to the investigator, it can be with reasonable safety by this route. A fine adapted needle should be used for the vaccination and firm pressure applied to the site, without rubbing, for $\geq 2$ minutes. The subject should be informed concerning the risk for hematoma from the injection.


## Section 6.5 Contraindications to subsequent vaccination

- Any condition which, in the judgment of the investigator would make intramuscular injection unsafe.
- All vaccines can be administered to persons with a minor illness such as diarrhoea, mild upper respiratory infection with or without low-grade febrile illness, i.e., oral temperature $<37.5^{\circ} \mathrm{C}\left(99.5^{\circ} \mathrm{F}\right)$ / Aaxillary temperature $<37.5^{\circ} \mathrm{C}\left(99.5^{\circ} \mathrm{F}\right)$.


## Section 6.6.2 Concomitant medications/ vaccines that may lead to the elimination of a subject from ATP analyses

- Administration of a vaccine not foreseen by the study protocol during the study starting 30 days before the first dose of study vaccine until 30 days after the last dose of study vaccine. However, licensed non-replicating vaccines (e.g., inactivated and subunit vaccines, including inactivated and subunit influenza vaccines, and pneumococcal conjugate vaccines) may be administered up to 8 days prior to dose 2 and/or at least 14 days after anywithin 8 days prior to or within 14 days after either dose of study vaccine;


## Section 6.7 Intercurrent medical conditions that may lead to elimination of a subject from ATP analyses

The oceurrence of HZ is an intereurrent medical condition. The reporting period for cases of HZ will be from Month 0 to study end.

## Section 7 Safety



For each AE and SAE-solicited and unsolicited symptom the subject experiences during the applicable reporting period, the subject will be asked if he/she received medical attention defined as hospitalisation, an emergency room visit or a visit to or from medical personnel (medical doctor) for any reason and this information will be recorded in the eCRF.
SAEs that are related to the GSK study vaccine will be recorded from Month 0 until study conclusion
${ }^{c b}$ SAEs related to study participation, tor a concurrent GSK medication/vaccine will be reported during the entire study period recorded from the time the subject consents to participate in the study until she/he is discharged from the study (Section 7.3.1).
${ }^{\text {dc }}$ Pregnancy testing at the Pre-vaccination visit will be done only using urine samples. For any pregnancy testing prior to first vaccination (specifically at the Pre-vaccination Visit or at Visit 1), the results will be collected but not reported to the safety database, i.e., the occurrence of pregnancy has to be reported to the sponsor only after vaccine
administration.
Intercurrent medical conditions will be recorded in AE/SAE screens as appropriate. The occurrence of HZ is an intercurrent medical condition. The reporting period for cases of HZ will be from Month 0 to study end.

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## Section 7.4.3 Completion and transmission of SAE reports to GSK Biologicals

Once an investigator becomes aware that a SAE has occurred in a study subject, the investigator (or designate) must complete the information in the electronic SAE screens of the eCRF WITHIN 24 HOURS. The SAESAE screens will always be completed as thoroughly as possible with all available details of the event. Even if the investigator does not have all information regarding a SAE, the SAE screens should still be completed within 24 hours. Once additional relevant information is received, the report should be updated WITHIN 24 HOURS.

## Section 9 Statistical methods

## Section 9.2 Secondary endpoints

- For hemoralimmunogenicity with respect to components of the study/investigational vaccine.
- Anti-gE Ab concentrations as determined by ELISA at Month 0, Month 1, Month2, Month 6 (Visit 4, at the start of the last cycle of chemotherapy between months 4 and 13) and Month 13.


## Section 9.3 Determination of sample size

## Section 9.3.1 Sample size assumptions for humoral immune response endpoint

Assumptions used were based on anti-gE humoral immunogenicity data obtained in study ZOSTER-001 for subjects who received 2 doses of $\mathrm{HZ} /$ su vaccine $\left(\mathrm{gE}_{[50 \mu \mathrm{~g}]} / \mathrm{AS} 01_{\mathrm{B}}\right.$ ). The humoral immune response to vaccine was assessed in comparison to the placebo group using anti-gE Ab concentrations. In the ZOSTER-001 study, the minimumfold increase observed post dose 2 in the HZ/su group as compared with placebo is approximately 9 $\mathbf{2 8}$-fold for anti-gE Abs. The Decimal Logarithm ( $\boldsymbol{\operatorname { l o g }}_{10}$ ) standard deviation observed in ZOSTER-001 is approximately 0.76 in the placebo group, and 1.12 after 2 doses of $\mathrm{HZ} / \mathrm{su}$. Accounting for an anticipated higher variability in the current study that could be due to , as compared to study ZOSTER 001, due to an anticipated heterogeneous population with different underlying malignancies and-different chemotherapeutic regimens, the standard deviation used in the computation has been multiplied by 1.1.

A 5.512.5-fold increase over placebo and a minimum of 3-fold increase in geometric mean as lower limit have been assumed for the analyses on PreChemo subjects.

Table 20 presents the assumptions used and the power obtained using several seenarios of sample size for the primary objective related to immunogenicity.

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Table 20 Power calculations for a T-test for Relevant Superiority in PreChemo Groups

| Power | N1/N2 evaluable | Equivalence Margin <br> (E) $\left[\log _{10}(3-\right.$ fold)] | Actual <br> Assumed Difference <br> (D) (5.5) $\left[\log _{10}\right.$ <br> (12.5-fold)] | Significance level |  | Standard Deviation ( $\log _{10}$ of value) |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | Alpha | Beta |  |  |
|  |  |  |  |  |  | Vaccine | Placebo |
| 0.91585 | $70 / 70$ | 1.4 | 1.7 | 0.025 | 0.08415 | 1.2 | 0.8 |
| 0.94649 | 80180 | 1.4 | 1.7 | 0.025 | 0.05351 | 1.2 | 0.8 |
| 0.96647 | $20 / 90$ | 1.4 | 1.7 | 0.025 | 0.03353 | 1.2 | 0.8 |
| 0.97927 | 100/100 | 1.4 | 1.7 | 0.025 | 0.02073 | 1.2 | 0.8 |
| 0.90599 | 67/67 | 0.477 | 1.097 | 0.025 | 0.09401 | 1.232 | 0.836 |

$\mathrm{N} 1, \mathrm{~N} 2$ : number of evaluable subjects receiving vaccine (N1) and placebo (N2)
Log $_{10}=$ Decimal Logarithm
To obtain a power of at least $\mathbf{9 0} \%$ to see a minimum of 3-fold increase as lower limit in anti-gE humoral immune response over placebo, assuming a $\mathbf{1 2 . 5}$ fold increase between placebo to HZ/su, 67 evaluable subjects per treatment group are needed.

A sample size of 84 subjects is needed assuming a 20\% rate from drop-out and nonevaluable subjects at Month 2.

The vaccine response rate observed in the overall autologous HCT population post-dose 2 , in the HZ/su group of study ZOSTER-001, is $86 \%$ for anti-gE Ab. Table 21 presents the power to demonstrate that the vaccine response in the HZ/su group PreChemo Group is significantly greater than $60 \%$.

Table 21 Power calculations for a One-sided binomial test for Relevant Superiority in PreChemo Groups

| Power | N evaluable | Vaccine response |  | Significance level |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  |  | Lower limit | Assumed | Alpha 1-Sided | Beta |
| 0.9995 | 80 | 0.6 | 0.85 | 0.025 | 0.0005 |
| 0.9783 | 80 | 0.6 | 0.80 | 0.025 | 0.0217 |
| 0.8184 | 80 | 0.6 | 0.75 | 0.025 | 0.1819 |
| $>0.9273$ | 67 | 0.6 | $\mathbf{0 . 8 0}$ | $\mathbf{0 . 0 2 5}$ | $\mathbf{0 . 0 0 3 7}$ |

An 8-fold increase over placebo and a minimum of 3-fold increase in geometric mean as lower limit of the $\mathbf{9 5 \%}$ CI have been assumed for the analyses on all subjects.

Table 22 and Table 23 present the assumptions used and the power obtained for the secondary objectives related to immunogenicity for all subjects (OnChemo and PreChemo subjects).

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Table 22
Power calculations for a T-test for Relevant Superiority in all subjects

| Power | N1/N2 evaluable | Equivalence Margin <br> (E) $\left[\log _{10}\right.$ <br> (3-fold)] | Actual Difference <br> (D) $\left[\log _{10}\right.$ (8-fold)] | Significance level |  | Standard Deviation ( $\log _{10}$ of value) |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | Alpha | Beta | Vaccine | Placebo |
| 0.71961 | 84/84 | 0.477 | 0.903 | 0.025 | 0.28039 | 1.232 | 0.836 |

N1, N2: number of evaluable subjects receiving vaccine (N1) and placebo (N2)
Log $_{10}=$ Decimal Logarithm
The 84 evaluable subjects per treatment group provide at least 71\% power to see a minimum of 3-fold increases in anti-gE humoral immune response over placebo assuming a 20\% rate from drop-out and non-evaluable subjects at Month 2.

Table23 Power calculations for a One-sided binomial test for Relevant Superiority in all subjects

| Power | N evaluable | Vaccine response |  | Significance level |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  |  | Lower limit | Assumed | Alpha 1-Sided | Beta |
| 0.44 | 84 | 0.6 | 0.70 | 0.025 | 0.56 |

The 84 evaluable subjects in the $H Z / s u$ group provide at least $44 \%$ power to demonstrate that the vaccine response in the HZ/su group (all subjects) is significantly greater than 60\% assuming a 20\% rate from drop-out and non-evaluable subjects at Month 2.

## Section 9.3.2.2 Number of subjects in the CMI sub-cohort

Assumptions used were based on CMI results (frequency of CD4+ T-cells expressing at least two activation markers from among IFN- $\gamma$, IL-2, TNF- $\alpha$ and CD40L) from ZOSTER-001 for adult autologous HCT subjects who received two doses of HZ/su. The CMI response was assessed in comparison to the control group (placebo). The increase observed post-dose 2 in study ZosterZOSTER-001 in the HZ/su group as compared with placebo is at least 9-fold after induction with gE. The natural logarithm (ln) standard deviation observed in ZOSTER-001 is about 1.49. The standard deviation used in the computation has been multiplied by 1.5 due to an expected higher variability in this population. Therefore, a 5-fold increase over control with a lower limit above 1 has been assumed. The type 1 error of $2.5 \%$ one-sided has been used.

Table 2224 presents the number of subjects under vaccine (N1) and placebo (N2) required to demonstrate a significant increase over placebo in frequency of gE-specific CD4+ T-cells producing at least 2 activation markers. At least 30 evaluable subjects per treatment group (only PreChemo Groups) are needed to reach approximately 78\% power.

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Table 22-24 Power calculations for the CMI sub-cohort

| Power | N1/N2 | Equivalence <br> margin (E) <br> $\ln$ (1) | Actual <br> difference (D) <br> In (5) | Significance level |  | Standard $\notin$ Deviation (In of value) |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | Alpha | beta | SD1 | SD2 |
| 0.78283 | 30/30 | 0 | 1.6 | 0.25 | 0.21717 | 2.2 | 2.2 |
| 0.84348 | 35/35 | 0 | 1.6 | 0.25 | 0.15652 | 2.2 | 2.2 |
| 0.88871 | 40/40 | 0 | 1.6 | 0.025 | 0.11129 | 2.2 | 2.2 |
| 0.92181 | 45/45 | 0 | 1.6 | 0.025 | 0.07819 | 2.2 | 2.2 |

In = Natural Logarithm; SD = Standard Deviation
The vaccine response observed in the overall HCT population post-dose 2, in the HZ/su group of study ZOSTER-001, is $80 \%$ for gE -specific CD4[2+] T cell frequencies. Table 2325 presents the power to demonstrate that the vaccine response in the HZ/su group is significantly greater than $50 \%$.

Table 23-25 Power calculations for a One-sided binomial test for Relevant Superiority

## Section 9.8 Analysis of immunogenicity

All immunogenicity analyses will be performed by age strata and by duration between the first dose and the start of chemotherapy cycle (PreChemo and OnChemo).

## Section 9.8.1 Humoral immune response

Descriptive statistics (N, mean, standard deviation [SD], min, Q1, median, Q3, max) of the following parameters will be tabulated by waceine group treatment group and by study group for the analyses performed on all subjects:

## Section 9.8.2 Cell-mediated immune response

## Within groups assessment

- descriptive statisties of the frequency of $\mathrm{CD} 4+\mathrm{T}$ cells secreting each individual activation marker in addition to one other marker (from among IFN $\gamma$, H 2, TNF $\alpha, \mathrm{CD} 40 \mathrm{~L}$ ) for gE -specific;


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## Section 9.10 Interpretation of analyses

With respect to primary and secondary confirmatory objectives, a hierarchical procedure will be applied to control the Type I error. The objectives will be assessed sequentially in order of ascending rank as indicated in Table 24-26.

Table 24-26 List of ranked confirmatory objectives

| Rank | Objectives (primary/secondary: nominal $\alpha=$ 2.5\% one-sided) |
| :--- | :--- |
| 1 | To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the <br> HZ/su vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy (PreChemo <br> Groups only). (primary: nominal a $=2.5 \%$ one-sided). |
| 2 | To evaluate vaccine response rate in anti-gE humoral immunogenicity responses at Month 2, following a <br> two-dose administration of the HZ/su vaccine, in subjects with solid tumours receiving chemotherapy <br> (PreChemo Groups only) (secondary: nominal a = 2.5\% one-sided). |
| 3 | To evaluate gE-specific CD4+ T-cell immunogenicity responses at Month 2, following a two-dose <br> administration of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours receiving <br> chemotherapy (PreChemo Groups only) (in the CMI sub-cohort) (secondary: nominal a $=2.5 \%$ one-sided). |
| 4 | To evaluate vaccine response rate in gE-specific CD4+ T-cell mediated immunogenicity at Month 2, <br> following a two-dose administration of the HZ/su vaccine in subjects with solid tumours receiving <br> chemotherapy (PreChemo Groups only) (in the CMI sub-cohort) (secondary: nominal a $=2.5 \%$ one-sided). |
| 5 | To evaluate the anti-gE humoral immunogenicity response at Month 2, following a two-dose <br> administration of the HZ/su vaccine, as compared to placebo, in subjects with solid tumours <br> receiving chemotherapy (all subjects). (secondary: nominal $\alpha=2.5 \%$ one-sided). |
| 6 | To evaluate vaccine response rate in anti-gE humoral immunogenicity responses at Month 2, <br> following a two-dose administration of the HZ/su vaccine, in subjects with solid tumours receiving <br> chemotherapy (all subjects receiving the HZ/su vaccine). (secondary: nominal $\alpha=2.5 \%$ one-sided). |

## Section 11 Country specific requirements

## Section 11.1 Country-specific age of legal consent

Countries will comply with eligibility criteria as described in Sections 4.2 and 4.3 of the protocol. In some countries participating in the study ZOSTER-028, in accordance with local regulations, the age of legal consent is higher than 18 years (see Table 27).

Table 27 Age of legal consent by country

## Section 11.1 Requirements for France

This appendix includes all the requirements of the French law ( $n^{\circ}$ 2004-806 of 9th August 2004), and identifies, item per item, the mandatory modifications or additional information to the study protocol.

Concerning the «STUDY POPULATION»

- In line with the local regulatory requirements, the following text in section " OTHER STUDY ELIGIBILITY CRITERIA CONSIDERATIONS " is added:

A subject will be eligible for inclusion in this study if he /she is either affiliated to or beneficiary of a social security category.

It is the investigator's responsibility to ensure and to document (in source document - patient notes) that the patient is either affiliated to or beneficiary of a social security category.

Concerning the " DATA ANALYSIS AND STATISTICAL CONSIDERATIONS " and specially in the "SAMPLE SIZE ASSUMPTION"

The expected number of patients to be recruited in France is declared to the French regulatory authority.

## Concerning the "STUDY CONDUCT CONSIDERATIONS "

In section" Regulatory and Ethical Considerations, Including the Informed Consent Process "

- Concerning the process for informing the patient or his/her legally authorised representative, the following text is added:
French Patient Informed Consent form is a document in triplicate which summarises the main features of the study and allows collection of the patient's written consent. It also contains a reference to the authorisation of Afssaps and the approval from the French Ethic committee and the maintenance of confidentiality of the returned consent form by GSK France.
- Concerning the process for obtaining subject informed consent:
- When biomedical research is carried out on a minor / on an adult in the care of a "tutelle" guardian, consent is given by their legal representative and, if the committee mentioned in article L. 1123-1 considers that the research in question, because of the gravity of the restraints or the specificity of the medical acts involved, entails a serious risk of affecting their private life or the integrity of their body, by the family council if it has been instated, or by the judge of "tutelle" guardians.
- When biomedical research is carried out on an adult in the care of a "curatelle" guardian, consent is given by the subject assisted by his guardian.
However, if the adult in the care of a "curatelle" guardian is invited to participate in research which the committee mentioned in article L. 1123-1 considers, because of the gravity of the restraints or the specificity of the medical acts involved, to entail a serious risk of affecting their private life or the integrity of their body, the matter is submitted to the judge of guardians who decides whether the adult is capable of giving his consent. In the case of incapacity, the judge will decide whether or not to authorise the biomedical research.


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- When biomedical research, which complies with the conditions laid down in article L. 1121-8, is considered for an adult incapable of expressing his consent and not under a legal protection order, consent is given by a person of confidence as defined in article L. 1111-6 and, failing this, by a person who maintains close and stable links with the subject. However, if the committee mentioned in article L. 1123-1 considers that the research in question, because of the gravity of the restraints or the specificity of the medical acts involved, entails a serious risk of affecting their private life or the integrity of their body, consent is given by the judge of guardians.
- Concerning the management of the Patient Informed Consent forms, the following text is added:

The first copy of the Patient Informed Consent form is kept by the investigator. The second copy is kept by the Medical Direction of GlaxoSmithKline France and the last copy is given to the patient or his/her legally authorised representative.

The second copy of all the consent forms will be collected by the investigator under the Clinical Research Assistant's (CRA's) control, and placed in a sealed envelope bearing only:

- the study number,
- the identification of the Centre : name of the principal investigator and centre number),
- the number of informed consents,
- the date,
- and the principal investigator's signature.

Then, the CRA hands the sealed envelope over to the Medical Direction, for confidential recording, under the responsibility of the Medical Director.
In section concerning the " DEMOGRAPHIC DATA " the following text is added:
In accordance with the data-processing and freedom French law dated on 6th of January 1978 modified on the 6th of August 2004 - article 8, the ethnic origin can only be collected if the collection of this data is justified within the framework of this study.

In section concerning the " TESTING OF BIOLOGICAL SAMPLES" the following text is added:

In accordance with Article L1211-2 of the French Public Health Code, a biological sample without identified purpose at the time of the sample and patient's preliminary information is not authorized.

In section concerning the " NOTIFICATION TO THE HOSPITAL DIRECTOR" the following text is added:

In accordance with Article L1123-13 of the Public Health Code, the Hospital Director is informed of the commitment to the trial in his establishment. The Hospital Director is supplied with the protocol and any information needed for the financial disposition,

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the name of the investigator(s), the number of sites involved in his establishment and the estimated time schedule of the trial (R.1123-63).

In section concerning the "INFORMATION TO THE HOSPITAL PHARMACIST" the following text is added:

In accordance with Article R.1123-64 of the Public Health Code, the Hospital Pharmacist is informed of the commitment to the trial in his establishment. The Pharmacist is supplied with a copy of the protocol (which allows him to dispense the drug(s) of the trial according to the trial methodology), all information concerning the product(s) of the trial (e.g. included in the CIB), the name of the investigator(s), the number of sites involved in his establishment and the estimated time schedule of the trial.

In section" DATA MANAGEMENT" the following text is added:
Within the framework of this clinical trial, data regarding the identity of the investigators and/or co-investigators and/or the pharmacist if applicable, involved in this clinical trial, and data regarding the patients recruited in this clinical trial (patient number, treatment number, patient status with respect to the clinical trial, dates of visit, medical data) will be collected and computerised in GSK data bases by GlaxoSmithKline Laboratory or on its behalf, for reasons of follow up, clinical trial management and using the results of said clinical trial. According to the Act $n^{\circ}$ 78-17 of $6^{\text {th }}$ January 1978 further modified, each of these people aforesaid has a right of access, correction and opposition on their own data through GlaxoSmithKline Laboratory (Clinical Operations Department).

## Appendix BClinical Laboratories

Table 25-28 GSK Biologicals' laboratories
GSK = GlaxoSmithKline .
Table 26-29 Outsourced laboratories
CEVAC $=$ Centre for Vaccination.

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modification. The increased flexibility will allow meaningful analysis of the data collected in this immunocompromised populations, where the underlying disease and implications of its treatment (such as cancer treatment schedule, side effects of the concomitant treatment) lead to a higher number of out of window visits compared to what is observed in a healthy population. (Section 9.4.3)

- Secondary to the clinical course of IC populations, the projected subject loss as cancer deaths, consent withdrawals, and non-evaluable subjects at Month 2 in Zoster-028 has been revised from $20 \%$ to $27 \%$. Therefore, the target enrolment has been changed from 210 to 232 adults diagnosed with solid tumours receiving chemotherapy. Similarly, the targeted enrolment numbers increased for the PreChemo group from 168 (84 per treatment group) to 186 ( 93 per treatment group) and for the OnChemo group from 42 ( 21 per treatment group) to 46 ( 23 per treatment group), based on the projected $27 \%$ drop-out and non-evaluable subjects at Month 2. (Synopsis rationale for study design, Synopsis table 1, Synopsis Number of subjects, Section 1.2, Table 1, Section 4.1, Table 5, Section 5.2.2.2.1, Section 9.3.1).
- Intercurrent medical conditions were clarified with examples. (Section 6.7)
- The list of potential immune-mediated diseases has been updated. (Section 7.1.5.1, Table 16)
- Temperature measurement grading scale has been removed, since all temperature measurements will be recorded. The description of the temperature analyses will be described in details in the Statistical Analysis Plan. (Section 7.3.3.2.1)
- The definition of the according-to-protocol (ATP) cohort for safety was updated.
- The definition of the ATP cohort for immunogenicity was updated. Visit 4 has been removed from the ATP cohort (ATPc) for analysis of immunogenicity as this visit does not occur for all subjects. The ATPc for analysis of immunogenicity will be now defined by Visit $1 \rightarrow$ Visit 2, Visit $2 \rightarrow$ Visit 3, and Visit $2 \rightarrow$ Visit 5. (Section 9.8)
- Statistical section was updated to describe the descriptive cell-mediated immune (CMI) response analysis, to clarify other descriptive analysis for immunogenicity and safety. (Section 9.5.3)
- The requirement for reporting an abnormal laboratory findings as an AE or SAE has been modified. Now, if the abnormal assessments are judged by the investigator to be clinically significant and unexpected, considering the specific underlying disease and chemotherapy, they are to be recorded as an AE or SAE. Abnormal laboratory results which are secondary to the clinical course of malignancies and their treatment (cytotoxic or immunosuppressive chemotherapy) are to be expected and frequently occurring for the subject population in this study. The laboratory abnormalities of interest for safety reporting in this study are those judged by the investigators to be clinically significant and unexpected, as this subset may have the possibility to be related to the study vaccine. (Section 7.1.4)
- Minor edits in other sections were made for clarification.


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Amended text has been included in bold italics and deleted text in strikethrough in the following sections:

## Cover page

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## Synopsis

Rationale for the study and study design

- Rationale for the study design

Subjects in the ZOSTER-028 study will initially be randomised into two groups based on the vaccination schedule in relation to the start of $\boldsymbol{a}$ chemotherapy cycle. The OnChemo group receives their first HZ/su vaccination at the start of $\boldsymbol{a}$ chemotherapy cycle, while the PreChemo group receives their first HZ/su vaccination at least 10 days before the start of $\boldsymbol{a}$ chemotherapy cycle. Unpublished data with other GSK candidate vaccines indicates that vaccination at the start of $\boldsymbol{a}$ chemotherapy cycle can lead to a decreased/suppressed immune response, possibly due to steroids used concomitantly

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in high doses to prevent nausea and vomiting. Therefore, the primary objective linked to immunogenicity will be assessed in the PreChemo groups only. For this reason, the study groups will be allocated $4: 1(168 / 42186 / 46)$ PreChemo:OnChemo.

## Synopsis Table 1 Study groups and epochs foreseen in the study

| Study groups | Number of subjects | Age (Min.)* | Epoch |
| :--- | :--- | :--- | :--- |
|  |  |  | Epoch 001 |
| HZ/su-PreChemo | 8493 | 18 years | $\bullet$ |
| Placeb-PreChemo | 8493 | 18 years | $\bullet$ |
| HZ/su-OnChemo | 2123 | 18 years | $\bullet$ |
| Placeb-OnChemo | 2123 | 18 years | $\bullet$ |

HZ/su $=$ Herpes Zoster subunit vaccine; Chemo $=$ Chemotherapy; Placeb $=$
Placebo; Min. = Minimum

* And above the legal age of consent (see Table 28)
- Treatment allocation:

Eligible subjects will be randomised to the investigational $\mathrm{HZ} / \mathrm{su}$ vaccine or placebo (1:1 ratio) and to the PreChemo Group, first vaccination at least 10 days (up to 1 month) before the start of $\boldsymbol{a}$ chemotherapy cycle, or OnChemo Group, first vaccination at the start of the first (or second) $\boldsymbol{a}$ chemotherapy cycle (4:1 ratio).

Number of subjects Target enrolment is approximately 210232 eligible adults diagnosed with solid tumours receiving chemotherapy.

## List of abbreviations

## ANCOVA:

## Glossary of terms

| OnChemo | OnChemo refers to the administration of first dose of <br> HZ/su vaccine simultaneous with the administration of a <br> chemotherapeutic cycle (+/-1day), i.e. vaccination is "on"" <br> top of the next chemotherapeutic cycle. |
| :--- | :--- |
| PreChemo | PreChemo refers to the administration of first dose of <br> HZ/su vaccine at least 10 days prior to a chemotherapeutic <br> cycle, i.e. vaccination is "pre" the next chemotherapeutic <br> cycle. | HZ/su vaccine simultaneous with the administration of a chemotherapeutic cycle (+/-1day), i.e. vaccination is "on" top of the next chemotherapeutic cycle.

PreChemo refers to the administration of first dose of HZ/su vaccine at least 10 days prior to a chemotherapeutic cycle, i.e. vaccination is "pre" the next chemotherapeutic cycle.

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## Trademarks

| Trademarks of the GlaxoSmithKline <br> group of companiesTrademarks not <br> owned by the GlaxoSmithKline group of <br> companies |
| :---: |
| Zostavax® (Merck \& Co., Inc.) |


| Generic description |
| :--- |
| Herpes zoster vaccine consisting of high- <br> titre live attenuated varicella-zoster virus <br> (Oka strain) |

## Section 1.2. Rationale for the study and study design

Subjects in the ZOSTER-028 study will initially be randomised into two groups based on the vaccination schedule in relation to the start of $a$ chemotherapy cycle. The OnChemo group receives their first $\mathrm{HZ} / \mathrm{su}$ vaccination at the start of $a$ chemotherapy cycle, while the PreChemo group receives their first HZ/su vaccination at least 10 days before the start of $a$ chemotherapy cycle. Unpublished data with other GSK candidate vaccines indicates that vaccination at the start of $a$ chemotherapy cycle can lead to a decreased/suppressed immune response, possibly due to steroids used concomitantly in high doses to prevent nausea and vomiting. Therefore, the primary objective linked to immunogenicity will be assessed in the PreChemo groups only. For this reason, the study groups will be allocated 4:1 (168/42186/46) PreChemo:OnChemo.

## Section 2.2. Secondary objectives

- To characterize gE-specific CD4+ T-cell mediated immunogenicity responses at Month 0, Month 1, Month 2, and Month 13 within the HZ/su and placebo groups (PreChemo Groups only) (in the CMI sub-cohort).


## Section 3. Study design overview



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- HZ/su-PreChemo and Placeb-PreChemo Groups - within a maximum of 1 month to a minimum of 10 days before the start of the firsta chemotherapy cycle.
- HZ/su-OnChemo and Placeb-OnChemo Groups - at the first day (allowing a window of $+/-1$ day) of the first (or socond)a chemotherapy cycle.

Table 1. Study groups and epochs foreseen in the study

| Study groups | Number of subjects | Age (Min.)* | Epoch |
| :--- | :--- | :--- | :--- |
|  |  | Epoch 001 |  |
| HZ/su-PreChemo | 8493 | 18 years | $\bullet$ |
| Placeb-PreChemo | 8493 | 18 years | $\bullet$ |
| HZ/su-OnChemo | 2123 | 18 years | $\bullet$ |
| Placeb-OnChemo | 2123 | 18 years | $\bullet$ |

HZ/su = Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb = Placebo;
Min. $=$ Minimum

* And above the legal age of consent (see Table 28)
- Treatment allocation:

Eligible subjects will be randomised to two treatment groups: investigational HZ/su vaccine or placebo (1:1); and to two vaccination strata: PreChemo Group, first vaccination at least 10 days before the start of $\boldsymbol{a}$ chemotherapy cycle, or OnChemo
Group, first vaccination at the start of the first (or second) $\boldsymbol{a}$ chemotherapy cycle (4:1). The overall ratio of these 4 study groups will be $4: 4: 1: 1$ (see Table 5).

## Section 4.1. Number of subjects

Target enrolment is approximately 210232 eligible adults diagnosed with solid tumours receiving chemotherapy. Taking into account a projected $20 \sim 27 \%$ rate from drop-out and non-evaluable subjects at Month 2, the number of evaluable subjects is estimated to be 168 (84 per treatment group). See Section 9.3 for a description of the criteria used in the determination of sample size. Refer to Sections 4.2 and 4.3 for eligibility criteria.

Table 5. Number of subjects required for enrolment

| Vaccination Start stratum | Study groups | Estimated Nnumber of subjects |  |
| :--- | :--- | :---: | :---: |
|  |  | Overall <br> $\mathbf{N}$ | CMI sub-cohort <br> $\mathbf{N}$ |
| First Vaccination <br> at least 10 days before the start of a chemotherapy <br> cycle | HZ/su-PreChemo | 8493 | 38 |
|  | Placeb-PreChemo | 8493 | 38 |
|  |  |  |  |
|  | HZ/su-OnChemo | 2123 | 0 |
|  | Placeb-OnChemo | 2423 | 0 |
|  | Total | 210232 | 76 |

HZ/su = Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb = Placebo

## Section 4.3. Exclusion criteria for enrolment

- Chronic administration and/or planned administration of systemic glucocorticoids (e.g.,defined as prednisone $\geq 20 \mathrm{mg} /$ day, or equivalent, for more than 14 consecutive


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days in total) within one month prior to the first vaccine dose and up to Visit 3 (Month 2). Inhaled, intra-articularly injected, and topical steroids are allowed;
Section 5.2.2.2.1. Study group and treatment number allocation
Target enrolment is approximately 210232 eligible adults diagnosed with solid tumours receiving chemotherapy. During the Pre-vaccination visit eligible subjects will be randomised to the investigational HZ/su vaccine or placebo according to a $1: 1$ ratio (vaccine:placebo), and stratified to PreChemo Group,to first vaccination at least 10 days before the start of a chemotherapy cycle or OnChemo Group, first vaccination at the start of the first (or secend) $\boldsymbol{a}$ chemotherapy cycle (4:1). The overall ratio of these 4 study groups (HZ/su-PreChemo, Placeb-PreChemo, HZ/su-OnChemo, and PlacebOnChemo) will be 4:4:1:1.

Allocation of the subject to a study group at the investigator site will be performed using a randomisation system on internet (SBIR). The randomisation algorithm will use a minimisation procedure accounting for age (18-49 YOA and $\geq 50 \mathrm{YOA}$ ), centre, country and gender (Male and Female).

## Section 5.2.3. Allocation of subjects to assay subsets (CMI sub-cohort)

The target number for the CMI sub-cohort is 76 subjects ( 30 evaluable subjects per treatment group). A randomization algorithm will be used to attribute the subjects to the sub-cohorts at the designated sites (see Table 5).

## Section 5.5. Outline of study procedures

| Epoch | Epoch 001 |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of contact | Prevaccination Visit ${ }^{\dagger}$ | Visit ${ }^{*}$ | Visit 2** | Visit 3 | Visit 4*** | Month 5 Phone Contact | Month 9 Phone Contact | Visit ${ }^{\text { }}$ |
| Timepoints | $\begin{array}{\|c\|} \hline \text { Up to }-30 \\ \text { to }-10 \text { days } \\ \hline \end{array}$ | Month 0 | Month 1 | Month 2 | Month 6 (Months 4 to 13) | Month 5 | Month 9 | Month 13 |
| Sampling timepoints |  | Pre-Vacc | Post-Vacc 1 | Post-Vacc 2 | Post-Vacc 2 |  |  | Post-Vacc 2 |
| Informed consent | - | $\mathrm{O}^{\text {a }}$ |  |  |  |  |  |  |
| Check inclusion criteria ${ }^{\text {b }}$ | - | $\bullet$ |  |  |  |  |  |  |
| Check exclusion criteria ${ }^{\text {b }}$ | $\bullet$ | - |  |  |  |  |  |  |
| Record demographic data | $\bullet$ |  |  |  |  |  |  |  |
| Randomisation | $\bullet$ |  |  |  |  |  |  |  |
| Pre-vaccination visit conclusion | - |  |  |  |  |  |  |  |
| Medical history |  | - |  |  |  |  |  |  |
| Specific subject characteristics ${ }^{\text {c }}$ |  | $\bullet$ |  |  |  |  |  |  |
| Check contraindications |  | $\bullet$ | $\bullet$ |  |  |  |  |  |
| History directed physical examination |  | 0 |  |  |  |  |  |  |
| Training on self-reporting by subjects ${ }^{\text {d }}$ | 0 | 0 | 0 | 0 | 0 |  |  |  |
| HCG pregnancy test if applicable e | - ${ }^{\text {e }}$ | - | $\bullet$ |  |  |  |  |  |
| Pre-vaccination body temperature |  | $\bullet$ | $\bullet$ |  |  |  |  |  |
| Blood sampling (approximately 8 mL ) for humoral immune response from all subjects |  | - | $\bullet$ | - | - |  |  | $\bullet$ |
| Blood sampling (approximately 30 mL ) for CMI response in CMI sub-cohort subjects only |  | $\bullet$ | $\bullet$ | - |  |  |  | $\bullet$ |
| Assignment/recording of treatment number |  | $\bullet$ | $\bullet$ |  |  |  |  |  |
| Vaccination |  | $\bullet$ | $\bullet{ }^{\text {f }}$ |  |  |  |  |  |
| Training on completion of diary cards |  | 0 | 0 |  |  |  |  |  |
| Dispensing of a diary card for solicited AEs and for unsolicited AEs and concomitant medication/vaccination to the subjects |  | 0 | 0 |  |  |  |  |  |
| Daily post-vaccination recording of solicited adverse events (Days 0-6) by subjects on diary card 9 |  | 0 | 0 | 0 |  |  |  |  |

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## Table 6. List of study procedures

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#### Abstract

| Epoch | Epoch 001 |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Type of contact | Prevaccination Visit ${ }^{\dagger}$ | Visit ${ }^{*}$ | Visit 2** | Visit 3 | Visit 4*** | Month 5 <br> Phone <br> Contact | Month 9 <br> Phone <br> Contact | Visit $5^{\boldsymbol{4}}$ |
| Timepoints | $\begin{array}{\|c\|} \hline \text { Up to }-30 \\ \text { to }-10 \text { days } \\ \hline \end{array}$ | Month 0 | Month 1 | Month 2 | Month 6 (Months 4 to 13) | Month 5 | Month 9 | Month 13 |
| Sampling timepoints |  | Pre-Vacc | Post-Vacc 1 | Post-Vacc 2 | Post-Vacc 2 |  |  | Post-Vacc 2 |
| Return of diary cards (for solicited and unsolicited symptoms) |  |  | 0 | 0 |  |  |  |  |
| Transcription of the diary card for solicited symptoms, unsolicited AE and concomitant medication and vaccination by study staff/investigator 9 |  |  | - | $\bullet$ |  |  |  |  |
| Recording of any concomitant medication//product/vaccine/treatment which could impact the immune response or is part of a chemotherapy |  | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Recording of non-serious adverse events within 30 days (Days $0-29$ ) post-vaccination, by investigator |  | $\bullet$ | - | - |  |  |  |  |
| Reporting of intercurrent medical conditions including HZ h |  | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Reporting of serious adverse events (SAEs) ${ }^{g}$ |  | $\bullet$ - | - | - | $\bullet$ | $\bullet$ | $\bullet$ | - |
| Reporting of SAEs related to study participation or to a concurrent GSK medication/vaccine $g$ | - | $\bullet$ | - | - | - | - | - | - |
| Reporting of pregnancies |  | - 1 | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Reporting of potential immune-mediated diseases (pIMDs) ${ }^{\text {g }}$ |  | $\bullet$ - | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ | $\bullet$ |
| Study analysis |  |  |  | 0 |  |  |  | 0 |
| Study conclusion |  |  |  |  |  |  |  | $\bullet$ |

Study conclusion Note: The double-line border following Month 2 indicates the analyses which will be performed on all data (i.e., data that are as clean as possible) obtained after completion of Visit 3.

Vacc = vaccination; HCG = Human Chorionic Gonadotropin; pIMDs = potential Immune-Mediated Diseases; GSK = GlaxoSmithKline; CMI $=$ Cell-Mediated Immunity; $\mathrm{HZ}=\mathrm{Herpes}$ Zoster. $\bullet$ is used to indicate a study procedure that requires documentation in the individual eCRF. - is used to indicate a study procedure that does not require documentation in the individual eCRF. $\dagger$ The Pre-vaccination visit is mandatory and can occur on the same day as Visit 1 . If the Pre-vaccination visit occurs on the same day as Visit 1 , all procedures indicated under the Pre-vaccination visit will be performed and recorded in the eCRF at Visit 1 * Visit 1 will be the day of first vaccination. ${ }^{* *}$ Visit 2 (the second dose of study vaccine/ placebo administration) will be 1 to 2 months after the first vaccination AND should be at the first day (allowing a window of $+/-1$ day) of a subsequent cycle of chemotherapy.


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*** Visit 4 will occur within Months 4 to 13 for a Blood Sampling at the start of the last cycle of chemotherapy (if at least two months after the previous Blood Sampling (V3/M2)). Thus, the timing of this particular visit will be variable depending on the subject's chemotherapy schedule and also on when they started vaccination in relation to their chemotherapeutic regimen (see Table 7). This visit will coincide with the subject's lowest immune status.
${ }^{\Delta}$ Should Visit 4 coincide with Month 13, it will be recorded as Visit 5 in the eCRF, i.e., the Visit 5 procedures will be conducted (including a Blood Sampling for CMI) and Visit 5 will be the visit recorded using the special Visit 5 tick-box in the eCRF indicating that Visit 5 has superseded Visit 4.
a If a Pre-vaccination visit occurs, informed consent will be reconfirmed at Visit 1 , if needed per local requirements.
${ }^{\text {b }}$ If study entry occurs at the Pre-vaccination visit, eligibility criteria, medical history and demographic characteristics will be checked at this visit (otherwise these will be checked at Visit 1). A check for any changes compared to the Pre-vaccination Visit will be performed at Visit 1 and recorded in the Pre-vaccination section of the eCRF. In case the subject is no longer eligible at Visit 1 , the subject will be withdrawn from the study. The reason for this will be recorded in the Pre-vaccination section of the eCRF.
${ }^{\text {c }}$ The following subject characteristics will be recorded in the eCRF for each subject at the time of enrolment:
1.Diagnosis for solid tumour malignancy;
2.Previous varicella and HZ vaccination status;
3.Evidence of prior VZV infection: when readily available, serological evidence of prior VZV infection, or else by medical history;
4. History of current and previous hospitalizations/surgery(s)/chemotherapy (based on readily available admissions and discharge for the solid tumour for which the subject is included in the study). Notes:
a. Number and dates of chemotherapy courses and cycles, and chemotherapeutic regimens;
b. Number and dates of radiotherapy courses and treatments
c. Number and dates of surgeries.
d Subjects will be instructed to contact their study site immediately if the subject develops any symptoms suggestive of HZ if the subject manifests any symptoms he/she perceive as serious and, in case of pregnancy for women of childbearing potential.
Only for women of childbearing potential. Pregnancy testing must be performed with a urine or serum sample. Serum test should only be considered, instead of a urine pregnancy test, if required by country, local or ethics committee requlations. In case, a serum pregnancy test is required, a blood sample will be collected and testing performed per local guidance. The results of the applicable test will be recorded in the eCRF. Pregnancy testing at the Pre-vaccination visit will be done only using urine samples
$t$ (a) The second dose of study vaccine/ placebo must be between 1 and 2 months after the first vaccination AND at the first day (allowing a window of $+1-1$ day) of a subsequent cycle of chemotherapy. (b) Any subject with a HZ episode between Visit 1 and Visit 2 should not receive the second dose
9 For each solicited and unsolicited symptom the subject experiences, the subject will be asked if he/she received medical attention defined as hospitalisation, an emergency room visit or a visit to or from medical personnel (medical doctor) for any reason and this information will be recorded in the eCRF. Any concomitant medication/product/vaccine/treatment which could interfere with the immune response or is part of a chemotherapy should be recorded throughout the entire stud (see Section 6.6.1).
${ }^{h}$ Refer to Section 6.7 for details regarding intercurrent medical conditions. The occurrence of HZ is an intercurrent medical condition. At Visit 1 , all subjects will be informed of the signs and symptoms of typical HZ .
Study procedure to be assessed only after administration of vaccine at Visit 1.

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## Section 5.5. Outline of study procedures

Table 7. Intervals between study visits

| Interval between visits ${ }^{1}$ | Optimal length of interval ${ }^{2}$ | Allowed interval ${ }^{3}$ (range in days) |
| :---: | :---: | :---: |
| Pre-vaccination visit ${ }^{*}$ ¢ $\rightarrow$ Visit 1 | Up to 30 to 10 days | Maximally 30 days and minimally 10 days before Visit 1 |
| Visit $1 \rightarrow$ Visit 2 (1 month) | 1-2 months**5 | 30-60 |
| Visit $2 \rightarrow$ Visit 3 (1 month) | 1 month | 30-48 |
| Visit $1 \rightarrow$ Visit 4 (between Month 4, and Month 13) ${ }^{\ddagger 7}$ | 4-13 months, Variable*** 6 | Minimally ~120 days after Visit 1 Maximally $\sim 335$ days after Visit 1 |
| Visit $3 \rightarrow$ Month 5 Phone Contact ${ }^{\dagger 7}$ | 3 months ${ }^{\ddagger 8}$ | 80-110 |
| Month 5 Phone Contact $\rightarrow$ Month 9 Phone Contact ${ }^{\dagger 7}$ (Visit $3 \rightarrow$ Month 9 Phone Contact) | 4 months ${ }^{* 9}$ (7 months) | $\begin{gathered} 110-150 \\ (190-260) \\ \hline \end{gathered}$ |
| Visit $2 \rightarrow$ Visit 5 (12 months) | 12 months\$10 | 335-425 |

${ }^{1}$ Unless otherwise specified, Visit 1 is taken as a reference to determine the applicable allowed interval between Visits 2 and 4 ; and Visit 2 is taken as a reference to determine the applicable allowed interval between Visits 3 , and 5 .
${ }^{2}$ Whenever possible the investigator should arrange study visits within this interval.
${ }^{3}$ Whenever clinically possible the investigator should arrange study visits within this interval. Subjects may not be eligible for inclusion in the ATP cohorts if they make the study visit or contact outside any of these intervals.
${ }^{\star 4}$ The Pre-vaccination visit can occur on the same day as Visit 1.
${ }^{* * 5}$ The second dose of study vaccine/ placebo must be administered between 1 and 2 months after the first vaccination AND should be at the first day (allowing a window of $+/-1$ day) of a subsequent cycle of chemotherapy. ${ }^{* * * 6}$ Visit 4 will occur within Months 4 to 13 for a Blood Sampling at the start of the last cycle of chemotherapy. (if at least two months after the previous Blood Sampling (V3/M2)). Thus, the timing of this particular visit will be variable depending on the subject's chemotherapy schedule and also on when they started vaccination in relation to their chemotherapeutic regimen (refer to Section 3). This visit will coincide with the subject's lowest immune status. ${ }^{\text {7 }}$ Should Visit 4 coincide with Month 5 or Month 9 , it will replace the Month 5 or the Month 9 Phone Contact, respectively.
${ }^{\ddagger 8}$ Visit 3 is taken here as reference to determine the applicable allowed interval up to the Month 5 Phone Contact.
${ }^{* 9}$ The Month 5 Phone Contact is taken here as reference to determine the applicable allowed interval up to the Month 9 Phone Contact (If Visit 4 coincides with the Month 5 Phone Contact, the date of Visit 3 will be used as a reference instead of Month 5).
$\$ 10$ Visit 5 occurs approximately 12 months after the second vaccination.

## Section 5.7.3. Laboratory assays

Table 9. Humoral Immunity (Antibody determination)

| System | Component | Method | Kit / <br> Manufacturer | Unit | Cut-off | Laboratory |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| SERSerum | Varicella Zoster <br> Virus.Glycoprotei <br> nE Ab.lgG | ELISA | NA | mIU/m+L | 1897 | GSK <br> Biologicals* |

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Table 10. Cell-Mediated Immunity (CMI)

| System | Component | Challenge | Method | Unit | Cut-off | Laboratory |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Peripheral Blood Mononuclear CollsPBMC | Cells CD4.All double CD40 Ligand or Interleukin-2 or Iumour Nocrosis Factor alpha or Interferon gamma CD4.polypositives CD40L+IL2+TNFa+IF $N g^{*}$ | gE | ICS | Events/10E ${ }^{6}$ Events | $320 * * N / A$ | CEVAC** |
| *CD4.polypositives CD40L+IL2+TNFa+IFNg = CD4+ T-cells expressing at least 2 activation markers (from among IFN- $\boldsymbol{\gamma}$, IL-2, TNF- $\alpha$ and CD40L) <br> ** University of Ghent, Belgium <br> ** Corresponding to the lower limit of linearity. <br> PBMC = Peripheral blood mononuclear cells <br> gE = Glycoprotein E; ICS = Intracellular cytokine staining |  |  |  |  |  |  |

Section 6.6.2. Concomitant medications/ vaccines that may lead to the elimination of a subject from ATP analyses

- Chronic administration and/or planned administration of systemic glucocorticoids (e.g.,defined as prednisone $\geq 20 \mathrm{mg} /$ day, or equivalent, for more than 14 consecutive days in total) within one month prior to the first vaccine dose and up to Visit 3 (Month 2); and one month prior to subsequent blood sampling at Visits 4 and 5. Inhaled, intra-articularly injected, and topical steroids are allowed.

Section 6.7. Intercurrent medical conditions that may lead to elimination of a subject from ATP analyses

Intercurrent medical conditions are clinical events during the course of the study which might alter or confound the interpretation of the immunologic (not safety) assessments of the protocol. In regards to humoral $g E$ assessments, this includes any clinical event that might increase or decrease the measurement of anti-gE antibodies, such as protein losing conditions in which the loss of gammaglobulin or total proteins might underestimate the subject's $g E$ response (e.g. protein losing enteropathy, proteinuria, or cachexia). Additional examples would be conditions that would cause the administration of exogenous $g E$ antibodies, resulting in an overestimate of the subject's anti-gE antibody response to HZ/su vaccination, such as conditions requiring the use of intravenous immunoglobulin (IVIg) or blood products.

The occurrence of HZ is an intercurrent medical condition, as the anti-gE antibody formed in response to active shingles cannot be distinguished from the anti-gE antibody formed in response to vaccination The reporting period for cases of HZ will be from Month 0 to study end.

For the CMI sub-cohort, in regards to measuring their cellular immunity, intercurrent medical conditions will be active viral infections that may alter CD4+ $T$ cell counts and/or responses. Examples, not exhaustive, of such acute viral infections would

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include acute Hepatitis A, acute Hepatitis B, new onset HIV, and potentially acute CMV and/or EBV infections.

Section 7.1.4. Clinical laboratory parameters and other abnormal assessments qualifying as adverse events or serious adverse events

In absence of diagnosis, abnormal laboratory findings (e.g. clinical chemistry, haematology, urinalysis) or other abnormal assessments that are judged by the investigator to be both clinically significant (and not expectedunexpected, consideringtaking into account the specific underlying disease and chemotherapy), will be recorded as either an AE or SAE ifas based on whether they meet the definition of an AE or SAE (refer to Sections 7.1.1 and 7.1.2). Clinically significant abnormal laboratory findings or other abnormal assessments that are present at baseline and significantly worsen following the start of the study, significantly worsen as judged by the investigator, and are also unexpected, considering the underlying disease and chemotherapy, will also be reported as AEs or SAEs.

## Section 7.1.5.1. Potential immune-mediated diseases

Table 16. List of potential immune-mediated diseases

| Neuroinflammatory disorders | Musculoskeletal disorders | Skin disorders |
| :---: | :---: | :---: |
| - Cranial nerve disorders, including paralyses/paresis (e.g. Bell's palsy) <br> - Optic neuritis <br> - Multiple sclerosis <br> - Transverse myelitis <br> - Guillain-Barré syndrome, including Miller Fisher syndrome and other variants <br> - Acute disseminated encephalomyelitis, including site specific variants: e.g. noninfectious encephalitis, encephalomyelitis, myelitis, myeloradiculomyelitis myeloradiculon euritis <br> - Myasthenia gravis, including LambertEaton myasthenic syndrome <br> - Immune-mediated peripheral neuropathies and plexopathies, (including chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy and polyneuropathies associated with monoclonal gammopathy). <br> - Narcolepsy | - Systemic lupus erythematosus and associated conditions <br> - Systematic Scleroderma (Systematic sclerosis), including diffuse systemic form and CREST syndrome <br> - Systemic sclerosis <br> - Idiophatic inflammatory myopathies, including Dermatomyositis, Polymyositis <br> - Polymyositis <br> - Antisynthetase syndrome <br> - Rheumatoid arthritis; and associated conditions, including Juvenile chronic arthritis and Still's disease <br> - Juvenile chronic arthritis, (including Still's disease) <br> - Polymyalgia rheumatic <br> - Spondyloarthritis, including ankylosing spondylitis, reactive arthritis (Reiter's Syndrome) and undifferentiated spondyloarthritis <br> - Psoriatic arthropathy <br> - Relapsing polychondritis <br> - Mixed connective tissue disorder | - Psoriasis <br> - Vitiligo <br> - Erythema nodosum <br> - Autoimmune bullous skin diseases (including pemphigus, pemphigoid and dermatitis herpetiformis) <br> - Cutaneous lupus erythematosus <br> - Alopecia areata <br> - Lichen planus <br> - Sweet's syndrome <br> - Localised Scleroderma (Morphoea) |

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| Liver disorders | Gastrointestinal disorders | Metabolic diseasesEndocrine disorders |
| :---: | :---: | :---: |
| - Autoimmune hepatitis <br> - Primary biliary cirrhosis <br> - Primary sclerosing cholangitis <br> - Autoimmune cholangitis | - Inflammatory Bowel disease, including Crohn's disease, ulcerative colitis, microscopic colitis, ulcerative proctitis <br> - Ulcerative colitis <br> - Ulecrative proctitis <br> - Celiac disease <br> - Autoimmune pancreatitis | - Autoimmune thyroiditis (including Hashimoto thyroiditis) <br> - Grave's or Basedow's disease <br> - Diabetes mellitus type I <br> - Addison's disease <br> - Polyglandular autoimmune syndrome <br> - Autoimmune hypophysitis |
| Vasculitides | Blood disorders | Others |
| - Large vessels vasculitis including: giant cell arteritis such as Takayasu's arteritis and temporal arteritis. <br> - Medium sized and/or small vessels vasculitis including: polyarteritis nodosa, Kawasaki's disease, microscopic polyangiitis, Wegener's granulomatosis, Churg-Strauss syndrome (allergic granulomatous angiitis), Buerger's disease (thromboangiitis obliterans), necrotizing vasculitis and anti-neutrophil cytoplasmic antibody (ANCA) positive vasculitis (type unspecified), Henoch-Schonlein purpura, Behcet's syndrome, leukocytoclastic vasculitis. | - Autoimmune hemolytic anemia <br> - Autoimmune thrombocytopenia <br> - Antiphospholipid syndrome <br> - Pernicious anemia <br> - Autoimmune aplastic anemia <br> - Autoimmune neutropenia <br> - Autoimmune pancytopenia | - Autoimmune hemolytic anemia <br> - Autoimmune thrombocytopenia <br> - Antiphospholipid syndrome <br> - Pernicious anemia <br> - Autoimmune glomerulonephritis (including $\lg A$ nephropathy, glomerulonephritis rapidly progressive, membranous glomerulonephritis, membranoproliferative glomerulonephritis, and mesangioproliferative glomerulonephritis) <br> - Ocular autoimmune diseases (including autoimmune uveitis and autoimmune retinopathy <br> - Uveitis <br> - Autoimmune myocarditis/cardiomyopathy <br> - Sarcoidosis <br> - Stevens-jJohnson syndrome <br> - Sjögren's syndrome <br> - Idiopathic pulmonary fibrosis <br> - Goodpasture syndrome <br> - Raynaud's phenomenon |

Section 7.3.1. Time period for detecting and recording adverse events, serious
adverse events and pregnancies
All AEs starting within 30 days following administration of each dose of study vaccine/ placebo must be recorded into the appropriate section of the eCRF, irrespective of intensity or whether or not they are considered vaccination-related.

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## Section 7.3.3.2.1. Assessment of intensity

Temperature (measured by oral, axillary or tympanic route) will be scored at GSK
Biologicals as follows:

$$
\begin{array}{rll}
\theta & \div & <37.5^{\circ} \mathrm{C} \\
4 & \div 37.5^{\circ} \mathrm{C} t-38.0^{\circ} \mathrm{C} \\
Z & \div 38.1^{\circ} \mathrm{Ct}-39.0^{\circ} \mathrm{C} \\
3 & \div & >39.0^{\circ} \mathrm{C}
\end{array}
$$

## Section 9.3.1. Sample size assumptions for humoral immune response endpoint

A sample size of 8493 subjects is needed assuming a $2027 \%$ rate from drop-out and nonevaluable subjects at Month 2.

Table 21. Power calculations for a One-sided binomial test for Relevant Superiority in PreChemo Groups

| Power | N evaluable | Vaccine response |  | Significance level |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  |  | Lower limit | Assumed | Alpha 1-Sided | Beta |
| $>0.9273$ | 67 | 0.6 | 0.80 | 0.025 | 0.00370 .0727 |

The 84 evaluable subjects per treatment group provide at least $71 \%$ power to see a minimum of 3 fold increases in anti-gE humoral immune response over placebo. a $A$ ssuming a $2027 \%$ rate from drop-out and non-evaluable subjects at Month 2, 232 subjects should be enrolled.

The 84 evaluable subjects in the HZ/su group provide at least $44 \%$ power to demonstrate that the vaccine response in the HZ/su group (all subjects) is significantly greater than $60 \%$. a $A$ ssuming a $2027 \%$ rate from drop-out and non-evaluable subjects at Month 2, 116 subjects should be enrolled in the HZ/su group.

Assuming an $\boldsymbol{\sim} \mathbf{2 0 \%}$ rate from drop-out and non-evaluable subjects at Month 2, the total number of subjects enrolled into the sub-cohort should be $\sim 38$ per group.

Section 9.4.2. According-to-protocol cohort for analysis of safety for the active phase (or for the extended safety follow up)

The According To Protocol (ATP) cohort for analysis of safety will include all subjects:

- who have received at least one dose of study vaccine/ placebo according to their random assignment;
- with sufficient data to perform an analysis of safety (at least one dose with safety follow - w);
- for whom administration site of study vaccine/ placebo is known;
- who have not received other medication/vaccine forbidden in the protocol during the active phase (or during the entire study period);


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- for whom the randomisation code has not been broken during the active phase (or during the entire study period).


## Section 9.4.3. According-to-protocol cohort for analysis of immunogenicity (or for persistence)

- Who comply with the procedures and intervals defined in the protocol for the active phase (for persistence blood sample)(refer to Table 7). The intervals between vaccinations (dose 1 to dose 2) and between dose 2 and blood sample at Visit 3 (dose 2 to 1 month post dose 2 visit) for inclusion in the ATP cohort for immunogenicity/persistence will be defined respectively as 30-84 days and 21-63 days (see Table 26). The immune ATPc analysis will be based on the allowed intervals for Visit $1 \rightarrow$ Visit 2, Visit $2 \rightarrow$ Visit 3, and Visit $2 \rightarrow$ Visit 5 .

Table 26. Intervals between study visits for the ATP cohort for analysis of immunogenicity

| Interval between visits | Allowed interval for the ATP cohort for analysis of immunogenicity |
| :--- | :--- |
| Visit $1 \rightarrow$ Visit 2 | $30-84$ days |
| Visit $2 \rightarrow$ Visit 3 | $21-63$ days |
| Visit $2 \rightarrow$ Visit 5 | $335-425$ days |

## Section 9.5.2. Humoral immune response

- The vaccine response rate for anti-gE is defined as the percentage of subjects who have at least a:
- at least a 4-fold increase in the anti-gE antibodies concentration as compared to the pre-vaccination anti-gE antibodies concentration, for subjects who are seropositive at baseline, or,
- a 4 -fold increase in the anti-gE antibodies concentration as compared to the antigE antibodies cut-off value for seropositivity, for subjects who are seronegative at baseline.
- The Geometric Mean Concentrations (GMCs) calculations are performed by taking the anti-log of the mean of the log concentration transformations. For descriptive statistics only, Ab concentrations below the cut-off of the assay $(4897 \mathrm{mIU} / \mathrm{mL}$; see Table 9) will be given an arbitrary value equal to half the cut-off for the purpose of GMC calculation.


## Section 9.5.3. Cellular-mediated immune response

- For the inferential analysis, Tthe frequency of CD4+ T-cells producing at least 2 activation markers (IFN-g, IL-2, TNF-a and/or CD40L, termed CD4 [2+]) upon in vitro stimulation with the gE-antigen (induction condition) is calculated by adding an offset of 0.5 to the number of activated CD4 T-cells (numerator) divided by the total number of CD4 T-cells involved (denominator). A similar calculation will be made for the frequency of CD4 [2+] upon in vitro stimulation in medium only (background


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condition). The same calculation will be performed for the frequency computation for any kinds of cells and for each individual activation marker as appropriate.

- For the descriptive analyses, the frequency of CD4[2+] T-cells upon in vitro stimulation with the antigen (induction condition) is calculated by dividing the number of activated CD4[2+] T-cells (numerator) over the total number of CD4 Tcells involved (denominator). The same calculation will be performed for the frequency computation for any kinds of cells and for each individual activation marker as appropriate.
Freq ${ }_{\text {Induction }}^{c \mathrm{c}[2+]}=\frac{n_{n_{\text {nnduction }}}^{2+}}{N_{\text {Induction }}^{\text {cot }}}$
$n_{\text {Indection }}^{2+}=$ number of CD4 $\mathrm{T}-$ cells secreting at least 2 activation s markers after inductions with the antigen
$N^{C D 4}=$ Total number of CD4 $\mathrm{T}-$ cells involved in the assay (induction )
- The frequency of gE-specific CD4 T-cells for each individual subject is calculated as the difference between the frequency of CD4 [2+], upon in vitro stimulation with the gE-antigen (induction condition) minus the frequency of (CD4 [2+] upon in vitro stimulation in medium only (background condition). The differences less or equal to one (1) are imputed to 1 gE -specific activation marker expressing CD4 T cell per $10^{6}$ CD4 T cells CD4[2+] T-cell per $10^{6}$ CD4+ T-cells. The same calculation will be performed for the frequency computation for any kinds of cells and for each individual activation marker as appropriate.
- The CMI vaccine response to gE will be based on the gE -specific data as computed above. The eut-offlower limit of linearity ( $\boldsymbol{L L} \boldsymbol{L}$ ) for the assay ( 320 positive events/ 106 CD4+ T-cells; see Table 10) and-will be used as threshold for vaccine response assessment. The vaccine response is defined as the percentage of subjects who have at least $a$ :
- 2-fold increase as compared to the eut-qfeLLL, for subjects with pre-vaccination T cell frequencies below the eut-off $\boldsymbol{L L L}$.
- 2-fold increase as compared to pre-vaccination T cell frequencies, for subjects with pre-vaccination above the eut-off $\boldsymbol{L} \boldsymbol{L L}$.


## Section 9.8. Analysis of immunogenicity

The primary analysis will be based on the ATPc for analysis of immunogenicity which will be relevant and consistent with the actual clinical course of these immunocompromised individuals (see Table 26).

If the percentage of enrolled subjects excluded from this-the immune ATPc is more than $5 \%$, a second analysis based on the TVc will be performed to complement the ATP analysis.

All descriptive immunogenicity analyses will be performed by age strata and by duration between the first dose and the start of chemotherapy cycle (PreChemo and OnChemo) as appropriate. This will be further detailed in the Statistical Analysis Plan (SAP).

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## Section 9.8.1. Humoral immune response

## Within groups assessment

Descriptive statistics of the following parameters will be tabulated by vaccine group: Descriptive statisties (N, mean, standard deviation [SD], min, Q1, median, Q3, max) of the following parameters will be tabulated by treatment group and by study group for the analyses performed on all subjects:

- Seropositivity rate with exact $95 \% \mathrm{CI}$;
- GMC with $95 \% \mathrm{CI}$;
- Vaccine response rate with exact $95 \% \mathrm{CI}$;


## Between groups assessment

A repeated measurement ANCOVA model will be used to assess the geometric mean fold increase over placebo at month 2. The statistical and immunological assumptions underlying the use of the models below will be described in the Statistical Analysis Plan (SAP).

A likelihood-based ANCOVA modelmethod will be used to analyze post-vaccination log-transformed anti-gE antibody concentrations (Month 1 to Month 2).

## Section 9.8.2. Cell-mediated immune response

## Within groups assessment

Descriptive statistics ( N , mean, standard deviation [SD], min, Q 1 , median, Q3, max) of the following parameters will be tabulated by vaccine group at all timepoints:

- descriptive statistics of the frequency of CD4+ T-cells secreting at least two activation markers (from among IFN-g, IL-2, TNF-a,CD40L) for gE-specific ( $N$, mean, standard deviation [SD], min, Q1, median, Q3, max);


## Between groups assessment

A repeated measurement ANCOVA model will be used to assess the geometric mean ratio over placebo at month 2 .

A likelihood-based Repeated Measurement Analysis of Covariance (ANCOVA) modelmethod will be used to analyze the post-vaccination log-transformed frequencies of CD4+ T-cells s secreting at least 2 cytokines following induction with gE (CD4[2+]). The placebo and HZ/su treatment groups only will be included in the main analysis.

The same ANCOVA model as described above will be used to analyze the logtransformed ratio between induction frequency and background frequency of CD4[2+]. Least-square means and difference of least-squares means will then be back-transformed and used to provide estimates for the frequency difference divided by background

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([induction - background] / background). The log-transformation of the ratios of these estimates between treatments will be calculated together with confidence intervals according to the delta-method (error propagation method).

## Section 9.9. Analysis of safety

- The percentage of subjects with at least one local solicited AE (solieited and tusolicited), with at least one general solicited $A E$ adverse event (solicited and unsolicited) and with any solicited AE during the solicited 7-day follow-up period will be tabulated with exact $95 \%$ Confidence Intervals (CI) after each vaccine dose and overall;


## Section 9.11.1. Sequence of analyses

## Two formal analyses are planned: a first analysis and an end of study analysis.

The mainfirst analysis of immunogenicity and reactogenicity/safety data will be performed when all data up to and including Month 2 (i.e., on data that are as clean as possible 30 days post dose 2 ) will be available after completion of Visit 3. A study report will be written.

The end of study analysis of persistence of immunogenicity and safety data will be performed when all data from after Month 2 up to and including Month 13 will be available-after completion of Visit 5. An annexend of study report will be written which will present data from the entire study.

## APPENDIX A LABORATORY ASSAYS

## Specific Ab (anti-gE) measurements

Anti-gE ELISA: Anti-gE Ab concentrations will be measured using an anti-gE ELISA. Diluted blood serum samples of study subjects will be added to microtitre wells precoated with gE antigen. Secondary peroxidase-conjugated anti-human Abs will be added, which bind to the primary human anti-gE Abs. After incubation of the microtitre wells with a chromogen substrate solution, the enzymatic reaction will be stopped. Optical densities will be recorded and anti-gE Ab concentrations are calculated from a standard curve. The assay cut-off is $4897 \mathrm{mIU} / \mathrm{mL}$. The assay will be performed on human serum at GSK Biologicals' laboratory or another laboratory designated by GSK Biologicals.

## Intracellular cytokine staining (ICS)

CMI responses will be performed by GSK Biologicals (or designated taboratory) CEVAC-Ghent on thawed Peripheral Blood Mononuclear Cells (PBMCs) by ICS. The assay will be performed on samples collected during the course of the study. This assay provides information on the frequency of CD4+ T-cells responding to culture medium or antigens (gE peptide pool) by secreting cytokine molecules involved in immunity such as IFN- $\gamma$, IL-2, TNF- $\alpha$, and CD40L.

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## Protocol Sponsor Signatory Approval

| eTrack study number and Abbreviated Title(s) | 116427 ZOSTER-028 |
| :---: | :---: |
| IND number | BB-IND 13879 |
| EudraCT number | 2012-002966-11 |
| Date of protocol | Final: 16 August 2012 |
| Detailed Title | A phase II/III, randomised, observer-blind, placebocontrolled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster $\mathrm{HZ} / \mathrm{su}$ candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy. |
| Sponsor signatory | Lidia Oostvogels, Director, Global Clinical Development, Vaccines |
| PPD |  |
| Signature |  |
| Date | $31 \text { Hu9 2012 }$ |

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## Protocol Amendment 1 Sponsor Signatory Approval

| eTrack study number and <br> Abbreviated Title | 116427 ZOSTER-028 |
| :--- | :--- |
| IND number | BB-IND 13879 |
| EudraCT number | $2012-002966-11$ |
| Date of protocol amendment | Amendment 1 Final: 19 November 2012 |
| Detailed Title | A phase II/III, randomised, observer-blind, placebo- <br> controlled, multicentre, clinical trial to assess the <br> immunogenicity and safety of GSK Biologicals' <br> herpes zoster HZ/su candidate vaccine when <br> administered intramuscularly on a 0 and 1 to 2 <br> months schedule to adults $\geq 18$ years of age with solid <br> tumours receiving chemotherapy. |
| Sponsor signatory | Lidia Oostvogels, Director, Global Clinical <br> Development, Vaccines |
| Signature | PPD |
| Date | $21 /$ NOV 2012 |

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## Protocol Amendment 1 Investigator Agreement

## I agree:

- To conduct the study in compliance with this protocol, any future protocol amendments or protocol administrative changes, with the terms of the clinical trial agreement and with any other study conduct procedures and/or study conduct documents provided by GlaxoSmithKline (GSK) Biologicals.
- To assume responsibility for the proper conduct of the study at this site.
- That I am aware of, and will comply with; 'Good Clinical Practice' (GCP) and all applicable regulatory requirements.
- To ensure that all persons assisting me with the study are adequately informed about the GSK Biologicals' investigational product(s) and other study-related duties and functions as described in the protocol.
- To acquire the reference ranges for laboratory tests performed locally and, if required by local regulations, obtain the laboratory's current certification or Quality Assurance procedure manual.
- To ensure that no clinical samples (including serum samples) are retained onsite or elsewhere without the approval of GSK Biologicals and the express written informed consent of the subject and/or the subject's legally acceptable representative.
- To perform no other biological assays on the clinical samples except those described in the protocol or its amendment(s).
- To co-operate with a representative of GSK Biologicals in the monitoring process of the study and in resolution of queries about the data.
- That I have been informed that certain regulatory authorities require the sponsor to obtain and supply, as necessary, details about the investigator's ownership interest in the sponsor or the investigational product(s), and more generally about his/her financial ties with the sponsor. GSK Biologicals will use and disclose the information solely for the purpose of complying with regulatory requirements.


## Hence I:

- Agree to supply GSK Biologicals with any necessary information regarding ownership interest and financial ties (including those of my spouse and dependent children).
- Agree to promptly update this information if any relevant changes occur during the course of the study and for one year following completion of the study.
- Agree that GSK Biologicals may disclose any information it has about such ownership interests and financial ties to regulatory authorities.
- Agree to provide GSK Biologicals with an updated Curriculum Vitae and other documents required by regulatory agencies for this study.

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|  | 116427 (ZOSTER-028) <br> Protocol Amendment 1 Final |  |
| eTrack study number and Abbreviated Title | 116427 ZOSTER-028 |  |
| IND number | BB-IND 13879 |  |
| EudraCT number | 2012-002966-11 |  |
| Date of protocol amendment | Amendment 1 Final: 1 | ember 2012 |
| Detailed Title | A phase II/III, random controlled, multicentre immunogenicity and herpes zoster HZ/su c administered intramus months schedule to ad tumours receiving che | observer-blind, placeboical trial to assess the of GSK Biologicals' ate vaccine when $y$ on a 0 and 1 to 2 18 years of age with solid rapy. |
| Investigator name | RAZVAN DI | ONESCU |
|  | PPD |  |
| Signature |  |  |
| Date | JAN 24201 |  |

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## Investigator name



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| Detailed Title | A phase II/III, randomised, observer-blind, placebocontrolled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster $\mathrm{HZ} /$ su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy. <br> PPD |  |
| Investigator name |  | Shelly McNal |
| PPD |  |  |
| Signature |  |  |

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A phase II/III, randomised, observer-blind, placebocontrolled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster $\mathrm{HZ} /$ su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy.

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Detailed Title $\quad$| A phase II/III, randomised, observer-blind, placebo- |
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| controlled, multicentre, clinical trial to assess the |
| immunogenicity and safety of GSK Biologicals' |

## Investigator name

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## Date

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Protocol Amendment 1 Final
eTrack study number and Abbreviated Title

| IND number | BB-IND 13879 |
| :--- | :--- |
| EudraCT number | $2012-002966-11$ |

2012-002966-11
Date of protocol amendment

Amendment 1 Final: 19 November 2012

| Detailed Title | A phase II/III, randomised, observer-blind, placebo- <br> controlled, multicentre, clinical trial to assess the <br> immunogenicity and safety of GSK Biologicals' <br> herpes zoster HZ/su candidate vaccine when <br> administered intramuscularly on a 0 and 1 to 2 <br> months schedule to adults $\geq 18$ years of age with solid <br> tumours receiving chemotherapy |
| :--- | :--- |
| Investigator name | Signature |

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eTrack study number and Abbreviated Title

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IND number
EudraCT number
Date of protocol amendment
Detailed Title

Investigator name

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Date of protocol amendment

## Detailed Title

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## Signature

116427 ZOSTER-028

BB-IND 13879
2012-002966-11
Amendment 1 Final: 19 November 2012
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Date


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116427 (ZOSTER-028)
Protocol Amendment 2 Final

## Protocol Amendment 2 Sponsor Signatory Approval

| eTrack study number and <br> Abbreviated Title | 116427 (ZOSTER-028) |
| :--- | :--- |
| IND number | BB-IND 13879 |
| EudraCT number | $2012-002966-11$ |
| Date of protocol amendment | Amendment 2 Final: 11 August 2014 |
| Detailed Title | A phase II/III, randomised, observer-blind, placebo- <br> controlled, multicentre, clinical trial to assess the <br> immunogenicity and safety of GSK Biologicals' <br> herpes zoster HZ/su candidate vaccine when <br> administered intramuscularly on a 0 and 1 to 2 <br> months schedule to adults $\geq 18$ years of age with solid <br> tumours receiving chemotherapy. |
| Sponsor signatory | Lidia Oostvogels, Project Level Clinical Research <br> and Development Lead, Director, Vaccine Discovery <br> and Development |
| Signature | PPD |

Date


## CONFIDENTIAL

## Protocol Amendment 2 Investigator Agreement

## I agree:

- To conduct the study in compliance with this protocol, any future protocol amendments or protocol administrative changes, with the terms of the clinical trial agreement and with any other study conduct procedures and/or study conduct documents provided by GlaxoSmithKline (GSK) Biologicals.
- To assume responsibility for the proper conduct of the study at this site.
- That I am aware of, and will comply with, 'Good Clinical Practice' (GCP) and all applicable regulatory requirements.
- To ensure that all persons assisting me with the study are adequately informed about the GSK Biologicals' investigational product(s) and other study-related duties and functions as described in the protocol.
- To acquire the reference ranges for laboratory tests performed locally and, if required by local regulations, obtain the laboratory's current certification or Quality Assurance procedure manual.
- To ensure that no clinical samples (including serum samples) are retained onsite or elsewhere without the approval of GSK Biologicals and the express written informed consent of the subject and/or the subject's legally acceptable representative.
- To perform no other biological assays on the clinical samples except those described in the protocol or its amendment(s).
- To co-operate with a representative of GSK Biologicals in the monitoring process of the study and in resolution of queries about the data.
- That I have been informed that certain regulatory authorities require the sponsor to obtain and supply, as necessary, details about the investigator's ownership interest in the sponsor or the investigational product(s), and more generally about his/her financial ties with the sponsor. GSK Biologicals will use and disclose the information solely for the purpose of complying with regulatory requirements.


## Hence I:

- Agree to supply GSK Biologicals with any necessary information regarding ownership interest and financial ties (including those of my spouse and dependent children).
- Agree to promptly update this information if any relevant changes occur during the course of the study and for one year following completion of the study.
- Agree that GSK Biologicals may disclose any information it has about such ownership interests and financial ties to regulatory authorities.
- Agree to provide GSK Biologicals with an updated Curriculum Vitae and other documents required by regulatory agencies for this study.


## CONFIDENTIAL

eTrack study number and Abbreviated Title

## IND number

EudraCT number
Date of protocol amendment Amendment 2 Final: 11 August 2014
Detailed Title
116427 (ZOSTER-028)

BB-IND 13879
2012-002966-11

A phase II/III, randomised, observer-blind, placebo- controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy.

## Investigator name

## Signature



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Date of protocol amendment
Detailed Title

## Investigator name

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## Date

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| E-Track Study Number (if applicable) | 116427 |
| Site ID (if applicable) | NA |


|  | Details |
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| Initial Incident/Issue | The protocol Investigator Agreement(signature page) for Amendment 2 does not contain <br> a checksum. |
| Cause of Incident/Issue | The template which does not contain the checksum was used to obtain PI's signature |
| Consequence(s) of <br> Issue/incident | UnKnown |
| Corrective Action(s) <br> with justification and <br> timeline(s) for <br> completion | At this stage, no corrective action is possible as the documents is already signed and <br> dated by Pl. |
| Outcome of Corrective <br> Action(s) | NA |
| Reference document(s) | NA |
| Additional Information <br> appended to this Note <br> To File | NA |


|  | Full Name and job function | Signature | Date |
| :--- | :--- | :--- | :--- |
| Author | PPD | PPD | 06 sep20.6 |
| Reviewed by (if <br> applicable) |  |  |  |
| Approved by (if <br> applicable) |  |  |  |


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|  | immunogenicity and safety of GSK Biologicals' herpes zoster $\mathrm{HZ} /$ su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy. |

## Investigator name

Signature


Date $\qquad$

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| Investigator name | Dor OP. Purotert |  |
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## Sample Case Report Form

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## GENERAL INSTRUCTIONS

Codes between brackets [ ] are the value encoded in the database.

## ABBREVIATIONS

Abbreviations for medical conditions, clinical events or drug names are to be avoided.

## DATES

Use the following 3-letter abbreviations to indicate months:

| January | = JAN | July | = JUL |
| :---: | :---: | :---: | :---: |
| February | = FEB | August | = AUG |
| March | $=$ MAR | September | = SEP |
| April | = APR | October | = OCT |
| May | = MAY | November | = NOV |
| June | = JUN | December | = DEC |

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## GENERAL INSTRUCTIONS (continued)

## GUIDANCE FOR INITIATING / STARTING A CRF

All subjects who have been approached for a study have to be recorded in the site Screening / Enrolment Log.
For those whom informed consent (IC) was obtained, a unique subject number has to be assigned: an eTrack subject number is to be taken from the range of numbers provided for the centre.

In case of interventional studies (with administration of a medicinal product as described in a research protocol):

- For those who signed an informed consent form (ICF) and who had a GSK treatment (vaccination or medication) and/or an invasive study procedure* to document in the CRF, a CRF must be initiated.
- For those who signed an informed consent form (ICF) but did not have any GSK treatment (vaccination or medication) and/or an invasive study procedure* to document in the CRF, a CRF must not be initiated, unless a SAE must be reported according to protocol requirement.

In case of observational studies and interventional studies without administration of a medicinal product as described in a research protocol, a CRF must be initiated for all subjects who have signed an ICF. For database studies initiation of a CRF is not required.

Subject number must be entered on the CRF cover page and in the header of all CRF pages. Number must be right-aligned.

* Are considered here as invasive study procedures: protocol defined biological samplings, such as blood samplings or biopsies, protocol defined vaccination or other treatment administration;
Are not considered here as invasive study procedures: physical examination, X-ray, collection of medical records such as medical history.

For all subjects participating in the study, the Study Conclusion and the Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information and other sections, if applicable must be completed.

If a subject doesn't participate in the study, neither the Study Conclusion nor the Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information and other sections if applicable have to be completed.


## DEMOGRAPHY

## Date of Birth:

$\qquad$ 11 $\qquad$ |
(Enter only month and year)

| Gender: | ${ }^{[\mathrm{M}]}$ | $\square$ | Male |
| :--- | :--- | :--- | :--- |
|  | $[\mathrm{F}]$ | $\square$ | Female |

Ethnicity:
[1]American Hispanic or Latino ${ }^{[2]} \quad \square$ Not American Hispanic or Latino

Geographic Ancestry: ${ }^{[1]} \quad \square$ African Heritage / African American
[2] $\square$ American Indian or Alaskan Native
[3] $\square$ Asian - Central / South Asian Heritage
[4] $\square$ Asian - East Asian Heritage
[5] $\square$ Asian - Japanese Heritage
[6]Asian - South East Asian Heritage
[7] $\square$Native Hawaiian or Other Pacific Islander
[8]White - Arabic / North African Heritage [9]White - Caucasian / European Heritage [99]Other, please specify: $\qquad$

## SUBJECT STUDY GROUP AND SUB-COHORT

PreChemo: First vaccination at least 10 days before start of chemotherapy $-[3]$ $\qquad$ Part of the CMI [1] $\square$ sub-cohort [4] $\square$ Not part of the CMI sub-cohort[2]OnChemo: First vaccination at start of the first (or second) chemotherapy cycle


## Informed Consent has to be obtained prior to any study procedure

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| 5. GlaxoSmithKline |  |  | 116427 (ZOSTER-028) |  |
|  | Book | Visit | Date of visit | Subject Number |
|  | 1 | PRE-VACCINATION VISIT | \|__|_||__|_||_|__|__| | \|__|__|__|__| |

## INFORMED CONSENT

I certify that Informed Consent has been obtained prior to any study procedure.

[type 4 tests]
Did the subject agree that her/his biological sample(s) may be used
[ N ] No by GSK Biologicals for future research?
$[\mathrm{Y}] \quad \square$ Yes
[NA] $\square$ Not applicable

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116427 (ZOSTER-028)

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 1 | PRE-VACCINATION VISIT |  | \|_1_|_1_|_|| |

## ELIGIBILITY CHECK

Did the subject meet all the entry criteria?
[Y]Yes
$\left.{ }^{[N}\right]$No $\rightarrow$ If No, tick all boxes corresponding to violations of any inclusion/exclusion criteria.

Do not enter the subject into the study if he/she failed any of the inclusion or exclusion criteria below.

## INCLUSION CRITERIA

Tick the boxes corresponding to any of the inclusion criteria the subject failed.
[1] $\square$ Subjects who, in the opinion of the investigator, can and will comply with the requirements of the protocol (e.g., completion of the diary cards, return for follow-up visits, ability to have scheduled contacts to allow evaluation during the study);
[2]Written informed consent obtained from the subject;
[3]A male or female aged 18 years or older at the time of study entry. Refer to Section 11.1 of the protocol for country-specific age of legal consent;
[4]Subject who has been diagnosed with one or more solid tumours (defined as a solid malignancy, i.e., not a blood element malignancy);
[5]Subject who is receiving or will receive a cytotoxic or immunosuppressive chemotherapy (such that the study vaccine can be administered at the latest at the start of the second cycle of chemotherapy).
[6]Life expectancy of greater than one year;
[7]Female subjects of non-childbearing potential may be enrolled in the study;

- Non-childbearing potential is defined as pre-menarche, current tubal ligation, hysterectomy, ovariectomy or post-menopause;
Please refer to the GLOSSARY OF TERMS of the protocol for the definition of menopause.
[8]Female subjects of childbearing potential may be enrolled in the study, if the subject:
- has practiced adequate contraception for 30 days prior to vaccination, and
- has a negative pregnancy test on the day of vaccination, and
- has agreed to continue adequate contraception during the entire treatment period and for 2 months after completion of the vaccination series.
Please refer to the GLOSSARY OF TERMS of the protocol for the definition of adequate contraception.



## ELIGIBILITY CHECK (continued)

## EXCLUSION CRITERIA

Tick the boxes corresponding to any of the exclusion criteria that disqualified the subject from entry.
[9] $\quad \square \quad$ Subjects receiving only newer, more targeted therapies (e.g., trastuzumab) if not taken together with a classical chemotherapy (since these new more targeted therapies are not considered immunosuppressant);
[10]Chronic administration and/or planned administration of systemic glucocorticoids (e.g., prednisone $\geq 20 \mathrm{mg} /$ day, or equivalent for more than 14 consecutive days in total) within one month prior to the first vaccine dose and up to Visit 3 (Month 2). Inhaled, intra-articularly injected and topical steroids are allowed;
[11] $\square$ Previous vaccination against HZ or varicella within 12 months preceding the first dose of study vaccine/ placebo;
[12] $\square \quad$ Planned administration during the study of a HZ vaccine (including an investigational or nonregistered vaccine) other than the study vaccine;
[13] $\square$ Previous chemotherapy course less than one month before first study vaccination;
[14]Occurrence of a varicella or HZ episode by clinical history within the 12 months preceding the firs dose of study vaccine/ placebo;
[15] $\square$ History of allergic disease or reactions likely to be exacerbated by any component of the vaccine or study material and equipment;
[16] $\square \quad$ Administration or planned administration of a live vaccine in the period starting 30 days before the first dose of study vaccine and ending 30 days after the last dose of study vaccine, or, administration or planned administration of a non-replicating vaccine* within 8 days prior to or within 14 days after either dose of study vaccine.
*E.g., inactivated and subunit vaccines, including inactivated and subunit influenza vaccines and pneumococcal conjugate vaccines;
[17]HIV infection by clinical history;
[18]Acute disease and/or fever at the time of vaccination. Acute disease is defined as the presence of a moderate or severe illness with or without fever, but excludes the underlying malignancy, as well as the expected symptoms/signs associated with that disease or its treatment;
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C} / 99.5^{\circ}$ F on oral, axillary or tympanic setti ng , or $\geq 38.0^{\circ} \mathrm{C} / 100.4 \mathrm{~F}$ on rectal setting. The preferred route for recording temperature in this study will be oral.
Subjects with a minor illness (such as mild diarrhoea, mild upper respiratory infection) without fever, may receive the first dose of study vaccine/ placebo at the discretion of the investigator.

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## ELIGIBILITY CHECK (continued)

## EXCLUSION CRITERIA (continued)

Tick the boxes corresponding to any of the exclusion criteria that disqualified the subject from entry.
[19]Pregnant or lactating female;
[20]Female planning to become pregnant or planning to discontinue contraceptive precautions (if of childbearing potential) before Month 3 (i.e., 2 months after the last dose of study vaccine/ placebo).

|  | Book | Visit |  | Subject Number |
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|  | 1 | PRE-VACCINATION VISIT |  | \|__|__|__|__| |

## GENERAL MEDICAL HISTORY / EXAMINATION

Are you aware of any pre-existing conditions, signs or symptoms having started before first study vaccination?
[N] $\square$ No
$[\mathrm{Y}] \square$ Yes $\rightarrow$ Please give diagnosis and tick appropriate Past/Current box

Please record details on the current solid tumor in the subject characteristics section at V1, not here.
Please report medication(s) as specified in the protocol and fill in the medication section.


CRF template version 14 - May 22 2013 - System page 10 - Workbook 1 : with pre-vacc before V1

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HCG URINE PREGNANCY TEST

Has a urine sample been taken? ${ }_{[P R G]}$
[N]No
[Y]Yes $\rightarrow \quad$ Date if different from visit date: $\qquad$ II $\qquad$ || $\qquad$ 1
$\rightarrow \quad$ Pregnancy test result:
[N]Negative [HCG01]
[P]Positive
[NA]Not applicable (female of non childbearing potential or male)

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## VISIT 1 MONTH 0 DOSE 1

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116427 (ZOSTER-028)

|  | Book | Visit | Date of Visit | Subject Number |
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|  | 1 | VISIT 1 - MONTH 0 | \|____||__|__||__| $\mid$ \| $\mid$ | ।___\|_1 |

## SPECIFIC SUBJECT CHARACTERISTICS

## DIAGNOSIS FOR SOLID TUMOUR MALIGNANCY

Please indicate which solid tumour malignancy was diagnosed for the subject?
[1]Lung
[2]Breast
[3]Colorectal
[4]Melanoma
[5]Bladder
[6]Prostate
[7]Pancreas
[8]Other -> please specify: $\qquad$

Please specify date of the diagnosis: $\qquad$ _I $\qquad$ 11 $\qquad$ _

Please specify staging: $\qquad$

## SEROLOGICAL EVIDENCE OF VZV

Has the subject been tested for VZV seropositivity?


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|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 1 | VISIT 1 - MONTH 0 | SPECIFIC SUBJECT <br> CHARACTERISTICS | $1 \ldots 1111111$ |

## SPECIFIC SUBJECT CHARACTERISTICS (Continued)

## PREVIOUS VARICELLA VACCINATION STATUS

Has the subject received any vaccination against varicella more than 12 months before the first dose?
[N] $\square$No
${ }^{[15} \square$ Unknown
$[Y] \square$ Yes $\rightarrow \quad$ Please complete the following table

|  | Vaccine name <br> Trade name is preferred | Route <br> Use codes <br> given below |
| :--- | :--- | :--- |
|  |  | Date of vaccination* |
| For GSK use only |  |  |

Enter approximate date in case the exact date is unknown

## HISTORY OF HZ VACCINATION

Has the subject received any vaccination against HZ more than 12 months before the first dose?


* Enter approximate date in case the exact date is unknown.

| Route codes: | Inhalation | [ IH$]$ | Parenteral | [PE] |
| :---: | :---: | :---: | :---: | :---: |
|  | Intradermal | [iID] | Subcutaneous | [SC] |
|  | Intramuscular | [IM] | Sublingual | [SL] |
|  | Intranasal | $[1 \mathrm{~N}]$ | Transdermal | [TD] |
|  | Intravenous | [IIV] | Other | [OTH] |
|  | Oral | [PO] | Unknown | [UNK] |

CONFIDENTIAL
116427 (ZOSTER-028)

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 1 | VISIT 1 - MONTH 0 | SPECIFIC SUBJECT <br> CHARACTERISTICS | $1 \ldots 1111111$ |

## SPECIFIC SUBJECT CHARACTERISTICS (continued)

HISTORY OF CHEMOTHERAPY, RADIOTHERAPY AND SURGERY
Please encode chemotherapy/radiotherapy or surgery received before study entry, for the solid tumour for which the subject is included in the study.
Note that the chemotherapy (all the cycles given previous to the first administration) should be recorded in the section "Anti-cancer therapy related to the current solid tumour malignancy".

Has the patient received any previous chemotherapy/ radiotherapy or surgery for the solid tumour for which the subject is included in the study?
${ }^{[N]} \square$ No
[Y] $\square$ Yes $\rightarrow$ Please record any subsequent treatment the patient received:

| Type | Specify* | Date of first treatment administration/ surgery | Date of last treatment administration <br> (Not applicable for surgery) |
| :---: | :---: | :---: | :---: |
| I__1 |  | \|_|_|I_|_|_| | I_I_\|I_|_|_| |
| I__1 |  | \|_|_| | \|_1_|1_|_|_| |

*The field 'Specify' is to be completed only for the Types 'Surgery' and 'Other'
(1) Type of therapy
[S] Surgery
[C] Chemotherapy
[R] Radiation
[O] Other

## CONFIDENTIAL



## PERFORMANCE STATUS (ECOG)

Has performance status (ECOG) been assessed?
[Y]Yes $\rightarrow$ Date assessed: $\qquad$ 11 $\qquad$ II |_1_1_1_|
$\rightarrow \quad[0] \square 0 \quad$ Fully active, able to carry on all pre-disease performance without restriction.
[1]1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
[2] $\qquad$ 2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.
[3]3 Capable of only limited selfcare, confined to bed or chair more than $50 \%$ of waking hours.
[4]4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.
${ }_{[\mathrm{N}} \square \mathrm{No}$

Please note that the category " $5=$ dead" is not applicable to this study

[^15]|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 1 | VISIT 1 - MONTH 0 |  | । 1 _ 1 \|__ |

## BLOOD SAMPLE

Has a blood sample been taken for ELISA (approximately 8 mL )? [SER]No
[Y]Yes $\rightarrow$ Date if different from visit date: $\qquad$ 11 $\qquad$ 11 $\qquad$ I

## CMI SAMPLE

## ONLY FOR SUBJECTS IN CMI SUB-COHORT

Has a blood sample been taken for CMI response determination (approximately 30 mL )? [РBMC]
 No

Yes $\rightarrow$ Date if different from visit date $\qquad$ 11 $\qquad$ 11 $\qquad$
$\rightarrow$ Time of sample:

$\rightarrow$ Number of tubes: $\square$

## PREGNANCY TEST

Has a pregnancy test been done? [PRG]
[Y]$\mathrm{Yes} \rightarrow[$ URI]Urine $\quad \rightarrow$ Date if different from visit date: $\qquad$ 11 - 1 II |_1_1_| I

| Pregnancy test result: $\quad$ [N] $\square$ | Negative |  |
| :--- | :--- | :--- |
| [HCG01] |  |  |

SERUM TEST SHOULD BE PERFORMED ONLY IF REQUIRED BY COUNTRY, LOCAL OR ETHICS COMMITTEE REGULATIONS
${ }_{[S E R]} \square$ Serum $\rightarrow$ Date if different from visit date: $\qquad$ || $\qquad$ 11 $\qquad$ , |

Pregnancy test result:
[N]Negative [HCG01]Positive
[N]No
[NA] $\square$Not applicable (female of non childbearing potential or male)


## VACCINE ADMINISTRATION - DOSE 1

Pre-vaccination temperature:
[CE] $\qquad$ |. |__| Celsius
OR
[FA] $\qquad$ I. 1 | Fahrenheit Route: $\qquad$ $\square$ Axillary
[0] $\square$ Oral (preferred)
[R] $\qquad$
[] $\square$ Tympanic

Has Study vaccine or placebo been administered?
[N] $\square$ No $\rightarrow$ Please give reason hereafter.
[Y]Yes $\rightarrow$ Date of administration: $\qquad$ |__ |_1_1_| (if different from visit date)
$\rightarrow$ Administered treatment number: $\qquad$ I
$\rightarrow \quad$ Injection Site/Side/Route:According to protocol: Deltoid -Non dominant - IMDominantNot according to protocol:

| Specify Site: | $[1]$ | $\square$ Deltoid | $[3]$ | $\square$ Thigh |
| :--- | :--- | :--- | :--- | :--- |
| Side: | $[\mathrm{N}]$ | $\square$ Non Dominant | $[\mathrm{D}]$ | $\square$ Dominant |
| Route: | $[\mathrm{IM}]$ | $\square$ Intramuscular | $[\mathrm{SC}]$ | $\square$ Subcutaneous |

$\rightarrow$ if relevant, comment on administration: $\qquad$

## If no vaccination,

$\rightarrow$ Please tick the major reason for non administration
[SAE2] $\square$
Serious Adverse Event and/ or pIMD:
$\rightarrow \quad$ Please complete a SAE Report
$\rightarrow$ Please specify SAE Report No. |___|
[AEX] $\square$Non-Serious Adverse Event: $\rightarrow$ Please complete Non-Serious Adverse Event section
$\rightarrow \quad$ Please specify AE No. $\qquad$ -
[OTH]Other, please specify:
(e.g.: consent withdrawal, Protocol violation, ...)
$\rightarrow$ Please select who made the decision:
[1]Investigator
[S]Subject

## CONFIDENTIAL

gsk


## SOLICITED ADVERSE EVENTS - LOCAL SIGNS/SYMPTOMS

## Study vaccine or placebo injection site

Has the subject experienced any of the following signs/symptoms between Day 0 and Day 6? ${ }^{[N]} \square$ No
[V] $\square$ Yes, please tick No/Yes for each sign/symptom and complete further as necessary.
[U] $\square$ Unknown, no information available
[NA] $\square$ Not applicable, no vaccine administered.

| Local Sign/Symptom | Day 0 | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | After Day 6 |  |  | Medically attended visit |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |  | Ongoing | $\begin{gathered} \text { Max } \\ \text { Intensity/ } \\ \text { size } \\ \hline \end{gathered}$ | Date of last day of sign/symptom |  |
| ```Redness [RE] [N] \(\square\) No \\ [1] \(\square\) Yes \(\rightarrow\) size (mm):``` | I_I | I__1 | 1 | I_I | I_I | 1 | I__1 | $\begin{aligned} & {[\mathrm{N}] \square \mathrm{No}} \\ & {[\mathrm{r}] \square \text { Yes } \rightarrow} \end{aligned}$ | I_I | Tick box if continuing at end of study $\downarrow$ $\qquad$ II $\qquad$ _II $\qquad$ I I $\qquad$ \| or $\square$ | NOHOOERMD $\qquad$ I__ |
| Swelling [SW] [N] No M] Yes $\rightarrow$ size $(\mathrm{mm})$ : | I_1 | I_I | I_I | I_I | I_I | I_1 | I_I | $\begin{aligned} & {[\mathrm{N}] \square \mathrm{No}} \\ & {[\mathrm{r}] \square \text { Yes } \rightarrow} \end{aligned}$ | I_I | Tick box if continuing at end of study $\downarrow$ | NOHOOERMD I_I_\| |
| $\begin{aligned} & \text { Pain }[\mathrm{PA}] \\ & {[\mathrm{N}] \square \mathrm{No}} \\ & {[\mathrm{Y}] \square \mathrm{Yes} \rightarrow \text { intensity }} \end{aligned}$ | 1_1 | 1_1 | 1 | I_I | 1_1 | 1 | 1_1 | $\begin{aligned} & {[\mathrm{N}] \square \mathrm{No}} \\ & {[\mathrm{y}] \square \text { Yes } \rightarrow} \end{aligned}$ | 1 | Tick box if continuing at end of study $\downarrow$ $\qquad$ II $\qquad$ \| $\qquad$ I 1 I or $\square$ | NOHOERMD $\qquad$ I_I - |



If any of these adverse events meets the definition of serious, complete a Serious Adverse Event Report to GSK Biologicals Study Contact for SAE reporting within 24 hours.

## CONFIDENTIAL

gsk


## SOLICITED ADVERSE EVENTS - GENERAL SIGNS/SYMPTOMS

Has the subject experienced any of the following signs/symptoms between Day 0 and Day 6 ?
${ }^{[N]} \square \quad$ No
[Y] $\square$ Yes, please tick No/Yes for each sign/symptom and complete further as necessary
[U] $\square$ Unknown, no information available
Not applicable, no vaccine administered equal to $38.0^{\circ} \mathrm{C} / 100.4$

| $\begin{aligned} & \text { Temperature [TE] } \\ & \geq 37.5^{\circ} / 99.5^{\circ}[\mathrm{A} / \mathrm{O} / \mathrm{T}] \\ & \geq 38.0^{\circ} \mathrm{C} / 100.4^{\mathrm{F}}[\mathrm{R}] \\ & {[\mathrm{N}] \square \mathrm{No}} \\ & {[\mathrm{Y}] \square \text { Yes }} \\ & {[\mathrm{NT}] \square \text { Not Taken }} \end{aligned}$ | Day 0 | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | After Day 6 |  |  | Rel. to inv. Product | Medically attended visit | Tick box if related to the anticancer therapies and/or disease/ tumour |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{gathered} -- \\ \square \\ \begin{array}{c} \square \\ \text { Nat } \\ \text { Taken } \end{array} \\ \hline \end{gathered}$ |  |  | --$\square$$\stackrel{-}{\mathrm{Not}}$ | $\stackrel{-}{\square}$ | $\stackrel{\square}{\square}$ | Ongoing | $\begin{aligned} & \text { Max } \\ & \text { Temp. } \end{aligned}$ | Date of last day of sign/symptom |  |  |  |
|  |  |  |  |  |  |  |  | $\begin{aligned} & {[\mathrm{N}] \square \mathrm{No}} \\ & \mathrm{~K}] \square \mathrm{Yes} \rightarrow \end{aligned}$ |  | Tick box if continuing at end of study $\downarrow$ $1 \quad \\| \quad 1 \quad 1 \quad 11 \quad 1 \quad 1 \quad 1 \quad 1 \text { or } \square$ | $\left[\begin{array}{l} \mathrm{N}] \square \mathrm{No} \\ \mathrm{M}] \\ \mathrm{NO} \end{array}\right.$ | NOHOIERMD $\qquad$ | $\square$ |

```
```

Unit: [CE] }\square\mathrm{ Celsius Route:

```
```

Unit: [CE] }\square\mathrm{ Celsius Route:
[FA] }\square\mathrm{ Fahrenheit
[FA] }\square\mathrm{ Fahrenheit
[\mp@code{[0] }

```
[\mp@code{[0] }
```

```
[T] \square Tympanic
```

```
[T] \square Tympanic
```

```ympanic
```

```
[R] [T] 
```

```
[R] [T] 
```



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CONFIDENTIAL

VISIT 2
MONTH 1
DOSE 2

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | $\mathbf{1}$ | VISIT 2-MONTH 1 |  | 1_1_-_1_-_1_1 |

## CHECK FOR STUDY CONTINUATION

Did the subject return for this visit?Yes $\rightarrow$ Date of visit: $\qquad$ 11 $\qquad$ ||_1_|_|_| $\rightarrow$ Go to next page
[N] $\square$No $\rightarrow$ Please tick only one major reason:
[SAE2] $\square$
Serious Adverse Event and/or pIMD
$\rightarrow$ Please complete a SAE Report
$\rightarrow$ Please specify SAE Report No. I__I_|
$\rightarrow$ Tick box if SAE is fatal:
[AEX]Non-Serious Adverse Event
$\rightarrow$ Please complete Non-Serious Adverse Event section
$\rightarrow$ Please specify AE No. |__I_|
or solicited AE code |__||
[PTV] $\square$
Protocol violation, please specify:

[Cws] $\square$
Consent withdrawal, not due to an adverse event
$\rightarrow$ Please specify the reason (only if the subject has spontaneously explained it):
---------------------------------------------
[MIG]Migrated / moved from the study area
[LFU]Lost to follow-up
[SST] Sponsor study termination
[отн]
Other, please specify: $\qquad$
$\rightarrow$ For serious (except death), non-serious adverse events and Other reasons only:
Please tick who made the decision:Investigator
[s]Subject
$\rightarrow$ Study discontinuation
${ }^{[Y]} \square$ Tick box only if permanent discontinuation, i.e. if the subject definitively withdraws from the study
In this case, terminate the CRF:
Complete Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information, if applicable and Study conclusion.

## CONFIDENTIAL

GlaxoSmithKline
116427 (ZOSTER-028)

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | $\mathbf{1}$ | VISIT 2-MONTH 1 |  | 1_1_-_1_-_1_1 |

## BLOOD SAMPLE

Has a blood sample been taken for ELISA (approximately 8 mL )? [SER]No
[Y]Yes $\rightarrow$ Date if different from visit date: $\qquad$ 11 $\qquad$ 11 $\qquad$ |

## CMI SAMPLE

 ONLY FOR SUBJECTS IN CMI SUB-COHORTHas a blood sample been taken for CMI response determination (approximately 30 mL )? [PBMC]NoYes $\rightarrow$ Date if different from visit date: $\qquad$ | $\qquad$ |______| $\mid$

$$
\rightarrow \text { Time of sample: } \quad \frac{\mid \_1}{\mathrm{hh}}|:|
$$

$\rightarrow$ Number of tubes: $\square$

## PREGNANCY TEST

Has a pregnancy test been done? [PRG]
${ }_{[7]} \square$ Yes $\rightarrow$ [URII $\square$ Urine $\rightarrow$ Date if different from visit date: |___||____||__|__|_|

| Pregnancy test result: | $\quad{ }^{[N]} \square$ | Negative |
| :--- | :--- | :--- |
| [HCG01] | $\square$ | Positive |

SERUM TEST SHOULD BE PERFORMED ONLY IF REQUIRED BY COUNTRY, LOCAL OR ETHICS COMMITTEE REGULATIONS
${ }_{[S E R]} \square$ Serum $\rightarrow$ Date if different from visit date:
II
|_1_1
II |_1_1_1_|
[N]No
[NA]Not applicable (female of non childbearing potential or male)

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 1 | VISIT 2 - DOSE 2 |  | \|__ | 1 |__|__| |



## CONFIDENTIAL

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 1 | visit 2 - MONTH 1 |  | 1_1_1_1_1_1 |

## SOLICITED ADVERSE EVENTS - LOCAL SIGNS/SYMPTOMS

## Study vaccine or placebo injection site

Has the subject experienced any of the following signs/symptoms between Day 0 and Day 6? $[\mathrm{N}] \square$ No
[Y] $\square$ Yes, please tick No/Yes for each sign/symptom and complete further as necessary.
[U] $\square$ Unknown, no information available
[NA] $\square$ Not applicable, no vaccine administered.

| Local Sign/Symptom | Day 0 | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | After Day 6 |  |  | Medically attended visit |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |  | Ongoing | $\begin{gathered} \text { Max } \\ \text { Intensity/ } \\ \text { size } \\ \hline \end{gathered}$ | Date of last day of sign/symptom |  |
| ```Redness [RE] ``` | I_I | I_I | 1 | I_I | I_I | 1 | I_I | $\begin{aligned} & {[\mathrm{N}] \square \mathrm{No}} \\ & {[\mathrm{Y}] \square \mathrm{Yes} \rightarrow} \end{aligned}$ | I_1 | Tick box if continuing at end of study $\downarrow$ $\qquad$ II $\qquad$ _II $\qquad$ I I $\qquad$ \| or $\square$ | NOHOIERMD $\qquad$ I_I 1 |
| Swelling [SW] $[\mathrm{N}] \square \mathrm{No}$ $[\mathrm{Y} \square \mathrm{Yes} \rightarrow$ size $(\mathrm{mm})$ : | I_I | I_I | I_I | I_I | I_1 | I_I | I_I | $\begin{aligned} & {[\mathrm{N}] \square \mathrm{No}} \\ & {[\mathrm{Y}] \square \mathrm{Yes} \rightarrow} \end{aligned}$ | I_I | Tick box if continuing at end of study $\downarrow$ | NOHOIERMD \|_1_| |
| $\begin{aligned} & \text { Pain }[\mathrm{PA}] \\ & {[\mathrm{N}] \square \mathrm{No}} \\ & {[\mathrm{Y}] \square \text { Yes } \rightarrow \text { intensity }} \end{aligned}$ | 1_1 | 1_1 | 1 | 1_1 | 1_1 | 1 | 1_1 | $\begin{aligned} & {[\mathrm{N}] \square \mathrm{No}} \\ & {[\mathrm{Y}] \square \mathrm{Yes} \rightarrow} \end{aligned}$ | 1 | Tick box if continuing at end of study $\downarrow$ $\qquad$ II $\qquad$ \| $\qquad$ I 1 I or $\square$ | NOHOIERMD $\qquad$ I 1 |



If any of these adverse events meets the definition of serious, complete a Serious Adverse Event Report to GSK Biologicals Study Contact for SAE reporting within 24 hours.

## CONFIDENTIAL

gsk


## SOLICITED ADVERSE EVENTS - GENERAL SIGNS/SYMPTOMS

Has the subject experienced any of the following signs/symptoms between Day 0 and Day 6 ?
${ }^{[N]} \square \quad$ No
M] $\square$ Yes, please tick No/Yes for each sign/symptom and complete further as necessary
[U] $\square$ Unknown, no information available
Not applicable, no vaccine administered equal to $38.0^{\circ} \mathrm{C} / 100.4$

| Temperature [TE]$\begin{aligned} & \geq 37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}[\mathrm{~A} / \mathrm{O} / \mathrm{T}] \\ & \geq 38.0^{\circ} \mathrm{C} / 100.4 \mathrm{~F}[\mathrm{R}] \\ & {[\mathrm{N}] \square \mathrm{No}} \\ & {[\mathrm{Y}] \square \text { Yes }} \\ & {[\mathrm{NT}] \square \text { Not Taken }} \end{aligned}$ | Day 0 | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 |  |  | After Day 6 |  |  | Tick box if |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  | $\begin{gathered} -- \\ \square \\ \stackrel{\square}{\text { Not }} \\ \text { Taken } \end{gathered}$ | Ongoing | $\begin{gathered} \text { Max } \\ \text { Temp. } \end{gathered}$ | Date of last day of sign/symptom | Rel. to inv. Product | Medically attended visit | the anticancer therapies and/or disease/ tumour |
|  |  |  |  |  |  |  |  | $\begin{aligned} & {[N] \quad \begin{array}{l} \text { No } \\ (\mathrm{y}) \\ \mathrm{Yeses} \rightarrow \\ \hline \end{array}} \\ & \hline \end{aligned}$ |  | Tick box if continuing at end of study $\downarrow$ II_1_1_11_1_1_1 or | $\begin{array}{r} {[\mathrm{N}) \square} \\ \mathrm{NO} \\ \mathrm{No} \\ \mathrm{Yes} \end{array}$ |  | $\square$ |

```
Unit: [CE] }\square\mathrm{ Celsius Route: [A] }\square\mathrm{ Axillary
    [FA] \square Fahrenheit Route. 
    [R] \square Recta
[T] \square Tympanic
```

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## SOLICITED ADVERSE EVENTS - GENERAL SIGNS/SYMPTOMS (continued)


(*) Gastrointestinal symptoms include nausea, vomiting, diarrhoea and/or abdominal pain
 hours.

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CONFIDENTIAL

VISIT 3 MONTH 2

## CONFIDENTIAL

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | $\mathbf{1}$ | VISIT 3- MONTH 2 |  | \|_1_1_1_1_1 |

## CHECK FOR STUDY CONTINUATION

Did the subject return for this visit?
${ }_{[Y]} \square$ Yes $\rightarrow$ Date of visit: $\qquad$ 11 $\qquad$ || $\qquad$ |
$\rightarrow$ Go to next page
[N] $\square$No $\rightarrow$ Please tick only one major reason:
[SAE2] $\square$ Serious Adverse Event and/or pIMD
$\rightarrow$ Please complete a SAE Report
$\rightarrow$ Please specify SAE Report No. I $\qquad$ I
$\rightarrow$ Tick box if SAE is fatal: $\square$ [AEX]Non-Serious Adverse Event
$\rightarrow$ Please complete Non-Serious Adverse Event section
$\rightarrow$ Please specify AE No. I____| or solicited AE code $\qquad$ 1
[PTV] $\square$Protocol violation, please specify:
 [Cws] $\square$

Consent withdrawal, not due to an adverse event
$\rightarrow$ Please specify the reason (only if the subject has spontaneously explained it):
[MIG]Migrated / moved from the study area
[LFU]Lost to follow-up
[SST]Sponsor study termination [отн]Other, please specify: $\qquad$
$\rightarrow$ For serious (except death), non-serious adverse events and Other reasons only:
Please tick who made the decision:Investigator
[s]Subject
$\rightarrow$ Study discontinuation
$\square$ Tick box only if permanent discontinuation, i.e. if the subject definitively withdraws from the study
In this case, terminate the CRF:
Complete Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information, if applicable and Study conclusion.

| CONFIDENTIAL |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: |
| ClaxoSmithkine |  |  | 116427 (ZOSTER-028) |  |
|  | Book | Visit |  | Subject Number |
|  | 1 | VISIT 3 - MONTH 2 |  | \|__ |

## LABORATORY TESTS

## BLOOD SAMPLE

```
Has a blood sample been taken for ELISA (approximately }8\textrm{mL}\mathrm{ )? [SER]
```

```No
```

```Y Yes \(\rightarrow\) Date if different from visit date:
``` \(\qquad\)
``` ||
``` \(\qquad\)
``` ||
``` \(\qquad\)
``` _
```

CMI SAMPLE ONLY FOR SUBJECTS IN CMI SUB-COHORT

Has a blood sample been taken for CMI response determination (approximately 30 mL )? [PBMC]NoYes $\rightarrow$ Date if different from visit date: $\qquad$ 11 $\qquad$ 11 ! - !
$\rightarrow$ Time of sample:

$\rightarrow \quad$ Number of tubes: $\qquad$

## CONFIDENTIAL

## VISIT 4

## CONFIDENTIAL

116427 (ZOSTER-028)

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 1 | visit 4 |  | \|_1_1_1_1_1._1 |

## If visit 4 coincides with visit 5 , only the visit 5 will be completed

## CHECK FOR STUDY CONTINUATION

Did the subject return for this visit?Yes $\rightarrow$ Date of visit: $\qquad$ || $\qquad$ 11 $\qquad$ I

$$
\rightarrow \text { Go to next page }
$$

[N] $\square$No $\rightarrow$ Please tick only one major reason:
[SAE2] $\square$ Serious Adverse Event and/or pIMD
$\rightarrow$ Please complete a SAE Report
$\rightarrow$ Please specify SAE Report No. I $\qquad$ |
$\rightarrow$ Tick box if SAE is fatal:
[AEX]Non-Serious Adverse Event
$\rightarrow$ Please complete Non-Serious Adverse Event section
$\rightarrow$ Please specify AE No. I___ or solicited AE code |___|
[PTV]
Protocol violation, please specify:
_-_-_-_-_-_-_-_-_-_-_-_-_-_-_ [cws] $\square$

Consent withdrawal, not due to an adverse event
$\rightarrow$ Please specify the reason (only if the subject has spontaneously explained it):
[MIG]Migrated / moved from the study area
[LFU] $\square$ Lost to follow-upSponsor study termination
[VIS5] $\square$ Visit 4 coincides with Visit 5 [отн]Other, please specify: $\qquad$
$\rightarrow$ For serious (except death), non-serious adverse events and Other reasons only:
Please tick who made the decision:Investigator
[s]Subject
$\rightarrow$ Study discontinuation
Only if Visit 4 does NOT coincide with Visit 5
${ }^{[Y]} \square$ Tick box only if permanent discontinuation, i.e. if the subject definitively withdraws from the study In this case, terminate the CRF:
Complete Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information, if applicable and Study conclusion.


## LABORATORY TESTS



CONFIDENTIAL



## CONFIDENTIAL

## CONFIDENTIAL

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 1 | MONTH 9 - PHONE CONTACT |  | 1__1_1 |

If Visit 4 coincides with Phone contact at Month 9, the visit 4 will replace the Month 9 Phone Contact

The subject will be reminded that, after Month 5 phone contact, a phone contact between the subject and the investigator and/or his delegate will take place (except at months that coincide with the subject's scheduled visits) to collect information on any event of interest that may have occurred, including:

- SAEs (Section 7.3 of the study protocol);
- $\quad$ pIMDs (Section 7.1.5.1 of the study protocol);
- intercurrent medical conditions (see Section 6.7 of the study protocol),
- the use of any concomitant medication/product/vaccine/treatment which could impact the immune response or is part of a chemotherapy (Section 6.6.1 of the study protocol);
- or pregnancy (Section 7.3 of the study protocol).

This information will be recorded in the appropriate section of the subject's eCRF.

Has safety information been obtained?$\square$ No $\rightarrow$ $\rightarrow \quad$ Please tick the box if the phone contact month 9 coincides with visit 4$\square$ Yes $\rightarrow$ $\rightarrow \quad$ Date of contact: $\qquad$ 11 $\qquad$ || $\qquad$ _1
$\square$

CONFIDENTIAL

VISIT 5 MONTH 13

## CONFIDENTIAL

GlaxoSmithKline
116427 (ZOSTER-028)

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 1 | VISIT 5-MONTH 13 |  | \|_1_1_1_1_1 |

If visit 4 coincides with visit 5 , only the visit 5 will be completed

## CHECK FOR STUDY CONTINUATION

Did the subject return for this visit?Yes $\rightarrow$ Date of visit: $\mid$ $\qquad$ || $\qquad$ 11 $\qquad$ |

$$
\rightarrow \text { Go to next page }
$$

[N] $\square$No $\rightarrow$ Please tick only one major reason:
[SAE2] $\square$ Serious Adverse Event and/or pIMD
$\rightarrow$ Please complete a SAE Report
$\rightarrow$ Please specify SAE Report No. I $\qquad$ 1
$\rightarrow$ Tick box if SAE is fatal: $\square$
[AEX]Non-Serious Adverse Event
$\rightarrow$ Please complete Non-Serious Adverse Event section
$\rightarrow$ Please specify AE No. |___ | or solicited AE code |___|
[PTV]Protocol violation, please specify:
_-_-_-_-_-_-_-_-_-_-_-_-_-_-_ [CWs] $\square$

Consent withdrawal, not due to an adverse event
$\rightarrow$ Please specify the reason (only if the subject has spontaneously explained it):
[MIG]Migrated / moved from the study area
[LFU]Lost to follow-up
[SST]Sponsor study termination [отн] $\square$Other, please specify: $\qquad$
$\rightarrow$ For serious (except death), non-serious adverse events and Other reasons only:
Please tick who made the decision:Investigator
[s]Subject

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116427 (ZOSTER-028)

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 1 | VISIT 5 - MONTH 13 |  | \|__1_1_1_1_1 |

## LABORATORY TESTS

## BLOOD SAMPLE

Has a blood sample been taken for ELISA (approximately 8 mL )? [SER]No
[Y]Yes $\rightarrow$ Date if different from visit date: $\qquad$ 11 $\qquad$ 11 $\qquad$ I

## CMI SAMPLE <br> ONLY FOR SUBJECTS IN CMI SUB-COHORT

Has a blood sample been taken for CMI response determination (approximately 30 mL )? [PBMC]
[ N$]$ No
[Y]Yes $\rightarrow$ Date if different from visit date: $\qquad$ 11 $\qquad$ |_1_|
$\rightarrow$ Time of sample: $\quad \frac{|\ldots|}{\mathrm{hh}}|\mathrm{l}:| \underline{\mathrm{mm}}$
$\rightarrow$ Number of tubes: $\qquad$

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A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy.

## GlaxoSmithKline Biologicals

Rue de l'Institut 89, B - 1330 Rixensart, Belgium Tel: PPD

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## GENERAL INSTRUCTIONS

Codes between brackets [ ] are the value encoded in the database.

## ABBREVIATIONS

Abbreviations for medical conditions, clinical events or drug names are to be avoided.

## DATES

Use the following 3-letter abbreviations to indicate months:

| January | = JAN | July | = JUL |
| :---: | :---: | :---: | :---: |
| February | = FEB | August | AUG |
| March | $=$ MAR | September | SEP |
| April | = APR | October | OCT |
| May | = MAY | November | NOV |
| June | = JUN | December | DEC |

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## GENERAL INSTRUCTIONS (continued)

## GUIDANCE FOR INITIATING / STARTING A CRF

All subjects who have been approached for a study have to be recorded in the site Screening / Enrolment Log.
For those whom informed consent (IC) was obtained, a unique subject number has to be assigned: an eTrack subject number is to be taken from the range of numbers provided for the centre.

In case of interventional studies (with administration of a medicinal product as described in a research protocol):

- For those who signed an informed consent form (ICF) and who had a GSK treatment (vaccination or medication) and/or an invasive study procedure* to document in the CRF, a CRF must be initiated.
- For those who signed an informed consent form (ICF) but did not have any GSK treatment (vaccination or medication) and/or an invasive study procedure* to document in the CRF, a CRF must not be initiated, unless a SAE must be reported according to protocol requirement.

In case of observational studies and interventional studies without administration of a medicinal product as described in a research protocol, a CRF must be initiated for all subjects who have signed an ICF. For database studies initiation of a CRF is not required.

Subject number must be entered on the CRF cover page and in the header of all CRF pages. Number must be right-aligned.

* Are considered here as invasive study procedures: protocol defined biological samplings, such as blood samplings or biopsies, protocol defined vaccination or other treatment administration;
Are not considered here as invasive study procedures: physical examination, X-ray, collection of medical records such as medical history.

For all subjects participating in the study, the Study Conclusion and the Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information and other sections, if applicable must be completed.

If a subject doesn't participate in the study, neither the Study Conclusion nor the Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information and other sections if applicable have to be completed.


## DEMOGRAPHY

## Date of Birth:

$\qquad$ 11 $\qquad$ |
(Enter only month and year)

| Gender: | ${ }^{[\mathrm{M}]}$ | $\square$ | Male |
| :--- | :--- | :--- | :--- |
|  | $[\mathrm{F}]$ | $\square$ | Female |

Ethnicity:
[1]American Hispanic or Latino ${ }^{[2]} \quad \square$ Not American Hispanic or Latino

Geographic Ancestry: ${ }^{[1]} \quad \square$ African Heritage / African American
[2] $\square$ American Indian or Alaskan Native
[3] $\square$ Asian - Central / South Asian Heritage
[4] $\square$ Asian - East Asian Heritage
[5] $\square$ Asian - Japanese Heritage
[6]Asian - South East Asian Heritage
[7]Native Hawaiian or Other Pacific Islander
[8]White - Arabic / North African Heritage
[9]White - Caucasian / European Heritage [99]Other, please specify: $\qquad$

## SUBJECT STUDY GROUP AND SUB-COHORT

PreChemo: First vaccination at least 10 days before start of chemotherapy $-[3]$ $\qquad$ Part of the CMI sub-cohort[4] $\square$ Not part of the CMI sub-cohort
[2]OnChemo: First vaccination at start of the first (or second) chemotherapy cycle

## CONFIDENTIAL

VISIT 1
MONTH 0
DOSE 1

## Informed Consent has to be obtained prior to any study procedure

| CONFIDENTIAL |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: |
| GlaxoSmithKline |  |  | 116427 (ZOSTER-028) |  |
|  | Book | Visit | Date of visit | Subject Number |
|  | 2 | Visit 1 - Month 0 | ___\||__|_||_1_|_| | \| 1 _ 1 1 1 |

## INFORMED CONSENT

I certify that Informed Consent has been obtained prior to any study procedure.

[type 4 tests]
Did the subject agree that her/his biological sample(s) may be used
[ N ] No by GSK Biologicals for future research?
$[\mathrm{Y}] \quad \square$ Yes
[NA] $\square$ Not applicable

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116427 (ZOSTER-028)

|  | Book | Visit |  | Subject Number |
| :--- | :---: | :---: | :---: | :---: |
|  | 2 | Visit $\mathbf{1}$ - Month 0 |  | \|__________1 |

## ELIGIBILITY CHECK

Did the subject meet all the entry criteria?
[y]Yes
[N]No $\rightarrow$ If No, tick all boxes corresponding to violations of any inclusion/exclusion criteria.

Do not enter the subject into the study if he/she failed any of the inclusion or exclusion criteria below.

## INCLUSION CRITERIA

Tick the boxes corresponding to any of the inclusion criteria the subject failed.
[1] $\square$ Subjects who, in the opinion of the investigator, can and will comply with the requirements of the protocol (e.g., completion of the diary cards, return for follow-up visits, ability to have scheduled contacts to allow evaluation during the study);
[2]Written informed consent obtained from the subject;
[3]A male or female aged 18 years or older at the time of study entry. Refer to Section 11.1 of the protocol for country-specific age of legal consent;
[4]Subject who has been diagnosed with one or more solid tumours (defined as a solid malignancy, i.e., not a blood element malignancy);
[5]Subject who is receiving or will receive a cytotoxic or immunosuppressive chemotherapy (such that the study vaccine can be administered at the latest at the start of the second cycle of chemotherapy).
[6]Life expectancy of greater than one year;
[7]Female subjects of non-childbearing potential may be enrolled in the study;

- Non-childbearing potential is defined as pre-menarche, current tubal ligation, hysterectomy, ovariectomy or post-menopause;
Please refer to the GLOSSARY OF TERMS of the protocol for the definition of menopause.
[8]Female subjects of childbearing potential may be enrolled in the study, if the subject:
- has practiced adequate contraception for 30 days prior to vaccination, and
- has a negative pregnancy test on the day of vaccination, and
- has agreed to continue adequate contraception during the entire treatment period and for 2 months after completion of the vaccination series.
Please refer to the GLOSSARY OF TERMS of the protocol for the definition of adequate contraception.

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | $\mathbf{2}$ | Visit $\mathbf{1}$ - Month 0 |  | \|_1_1_1_1_1 |

## ELIGIBILITY CHECK (continued)

## EXCLUSION CRITERIA

Tick the boxes corresponding to any of the exclusion criteria that disqualified the subject from entry.
[9] $\quad \square \quad$ Subjects receiving only newer, more targeted therapies (e.g., trastuzumab) if not taken together with a classical chemotherapy (since these new more targeted therapies are not considered immunosuppressant);
[10]Chronic administration and/or planned administration of systemic glucocorticoids (e.g., prednisone $\geq 20 \mathrm{mg} /$ day, or equivalent for more than 14 consecutive days in total) within one month prior to the first vaccine dose and up to Visit 3 (Month 2). Inhaled, intra-articularly injected and topical steroids are allowed;
[11] $\square$ Previous vaccination against HZ or varicella within 12 months preceding the first dose of study vaccine/ placebo;
[12] $\square \quad$ Planned administration during the study of a HZ vaccine (including an investigational or nonregistered vaccine) other than the study vaccine;
[13] $\square$ Previous chemotherapy course less than one month before first study vaccination;
[14]Occurrence of a varicella or HZ episode by clinical history within the 12 months preceding the firs dose of study vaccine/ placebo;
[15] $\square$ History of allergic disease or reactions likely to be exacerbated by any component of the vaccine or study material and equipment;
[16] $\square \quad$ Administration or planned administration of a live vaccine in the period starting 30 days before the first dose of study vaccine and ending 30 days after the last dose of study vaccine, or, administration or planned administration of a non-replicating vaccine* within 8 days prior to or within 14 days after either dose of study vaccine.
*E.g., inactivated and subunit vaccines, including inactivated and subunit influenza vaccines and pneumococcal conjugate vaccines;
[17]HIV infection by clinical history;
[18]Acute disease and/or fever at the time of vaccination. Acute disease is defined as the presence of a moderate or severe illness with or without fever, but excludes the underlying malignancy, as well as the expected symptoms/signs associated with that disease or its treatment;
Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C} / 99.5^{\circ}$ F on oral, axillary or tympanic setti ng , or $\geq 38.0^{\circ} \mathrm{C} / 100.4 \mathrm{~F}$ on rectal setting. The preferred route for recording temperature in this study will be oral.
Subjects with a minor illness (such as mild diarrhoea, mild upper respiratory infection) without fever, may receive the first dose of study vaccine/ placebo at the discretion of the investigator.

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| :--- |
| ClaxoSmithkline |
|  |

## ELIGIBILITY CHECK (continued)

## EXCLUSION CRITERIA (continued)

Tick the boxes corresponding to any of the exclusion criteria that disqualified the subject from entry.
[19]Pregnant or lactating female;
[20]Female planning to become pregnant or planning to discontinue contraceptive precautions (if of childbearing potential) before Month 3 (i.e., 2 months after the last dose of study vaccine/ placebo).

| Book | Visit | Subject Number |
| :---: | :---: | :---: |
| 2 | Visit 1 - Month 0 | \|___|_|_|_| |

## GENERAL MEDICAL HISTORY / EXAMINATION

Are you aware of any pre-existing conditions, signs or symptoms having started before first study vaccination?


M $\square$ Yes $\rightarrow$ Please give diagnosis and tick appropriate Past/Current box
Please record details on the current solid tumor in the subject characteristics section at V1, not here.
Please report medication(s) as specified in the protocol and fill in the medication section.


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116427 (ZOSTER-028)

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 2 | VISIT 1 - MONTH 0 |  | \|__1_|__| |

## SPECIFIC SUBJECT CHARACTERISTICS

## DIAGNOSIS FOR SOLID TUMOUR MALIGNANCY

Please indicate which solid tumour malignancy was diagnosed for the subject?
[1]Lung
[2]Breast
[3]Colorectal
[4]Melanoma
[5]Bladder
[6]Prostate
[7]Pancreas
[8]Other -> please specify: $\qquad$

Please specify the date of the diagnosis: $\qquad$ || $\qquad$ || $\qquad$ 1

Please specify staging: $\qquad$

## SEROLOGICAL EVIDENCE OF VZV

Has the subject been tested for VZV seropositivity?
$[\mathrm{Y}] \square$ Yes $\rightarrow \quad[\mathrm{P}] \square$ Positive $[\mathrm{N}] \square$ Negative
$[\mathrm{N}] \square$ No
[U]Unknown

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|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 2 | VISIT 1 - MONTH 0 | SPECIFIC SUBJECT <br> CHARACTERISTICS | 1_1_1_1_1_1 |

## SPECIFIC SUBJECT CHARACTERISTICS (Continued)

## PREVIOUS VARICELLA VACCINATION STATUS

Has the subject received any vaccination against varicella more than 12 months before the first dose?
$\mathrm{N}_{1} \square$ No
[U] $\square$ Unknown
${ }_{[Y]} \square$ Yes $\rightarrow$ Please complete the following table

| Vaccine name Trade name is preferred | Route Use codes given below | Date of vaccination* |
| :---: | :---: | :---: |
|  |  | \|_1_||_1_|_||_1_|_| |
| For GSK use only |  |  |

* Enter approximate date in case the exact date is unknown


## HISTORY OF HZ VACCINATION

Has the subject received any vaccination against HZ more than 12 months before the first dose?
${ }_{[N]} \square$ No
[U] $\square$Unknown
[Y] $\square$ Yes $\rightarrow$ Please complete the following table

|  | Vaccine name <br> Trade name is preferred | Route <br> Use codes <br> given below |
| :--- | :--- | :--- |
| For GSK |  | Date of vaccination* |
|  |  |  |
| For GSK |  |  |

* Enter approximate date in case the exact date is unknown.

Route codes:


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|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 2 | VISIT 1 - MONTH 0 | SPECIFIC SUBJECT <br> CHARACTERISTICS | $1 \ldots 1111111$ |

## SPECIFIC SUBJECT CHARACTERISTICS (continued)

HISTORY OF CHEMOTHERAPY, RADIOTHERAPY AND SURGERY
Please encode chemotherapy/radiotherapy or surgery received before study entry, for the solid tumour for which the subject is included in the study.
Note that the chemotherapy (all the cycles given previous to the first administration) should be recorded in the section "Anti-cancer therapy related to the current solid tumour malignancy".

Has the patient received any previous chemotherapy/ radiotherapy or surgery for the solid tumour for which the subject is included in the study?
${ }^{[N]} \square$ No
[Y] $\square$ Yes $\rightarrow$ Please record any subsequent treatment the patient received:

| Type | Specify* | Date of first treatment administration/ surgery | Date of last treatment administration <br> (Not applicable for surgery) |
| :---: | :---: | :---: | :---: |
| I__1 |  | \|_|_|I_|_|_| | I_I_\|I_|_|_| |
| I__1 |  | \|_|_| | \|_1_|1_|_|_| |

*The field 'Specify' is to be completed only for the Types 'Surgery' and 'Other'
(1) Type of therapy
[S] Surgery
[C] Chemotherapy
[R] Radiation
[O] Other

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|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 2 | VISIT 1 - MONTH 0 |  | 1_1_1_1_1_1 |

## PERFORMANCE STATUS (ECOG)

Has performance status (ECOG) been assessed?Yes $\rightarrow$ Date assessed: $\qquad$ II $\qquad$ 11 $\qquad$ 1_| I $\square 0$ Fully active, able to carry on all pre-disease performance without restriction.
${ }_{\text {11 }} \square$1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
[2]2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than $50 \%$ of waking hours.
[3]3 Capable of only limited selfcare, confined to bed or chair more than $50 \%$ of waking hours.
[4] $\square$ $\qquad$ 4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.
$[\mathrm{N}] \square \mathrm{No}$ Please note that the category " 5 = dead" is not applicable to this study

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|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 2 | VISIT 1 - MONTH 0 |  | \|__|__|__|__| |

## BLOOD SAMPLE

Has a blood sample been taken for ELISA (approximately 8 mL )? [SER]No
[Y]Yes $\rightarrow$ Date if different from visit date: $\qquad$ $1 \mid$ $\qquad$ 11 $\qquad$ |

## CMI SAMPLE

## ONLY FOR SUBJECTS IN CMI SUB-COHORT

Has a blood sample been taken for CMI response determination (approximately 30 mL )? [РBMC]
 No

Yes $\rightarrow$ Date if different from visit date: $\qquad$ 11 $\qquad$ 11 $\qquad$
$\rightarrow$ Time of sample:

$\rightarrow \quad$ Number of tubes: $\square$

## PREGNANCY TEST

Has a pregnancy test been done? [PRG]
[Y]$\mathrm{Yes} \rightarrow[$ URI]Urine $\rightarrow$ Date if different from visit date: $\qquad$ || 1_1 1 11 $\qquad$ I

| Pregnancy test result: | $[\mathrm{N}] \square$ | Negative |
| :--- | :--- | :--- | :--- |
| $[H C G 01]$ |  |  |

## SERUM TEST SHOULD BE PERFORMED ONLY IF REQUIRED BY COUNTRY, LOCAL OR

 ETHICS COMMITTEE REGULATIONS$[S E R] \square$ Serum $\rightarrow$ Date if different from visit date: $\qquad$ || $\qquad$ 11 $\qquad$ |

Pregnancy test result:
[N]Negative [HCG01] $\square$ Positive
[N]No
[NA]Not applicable (female of non childbearing potential or male)


## VACCINE ADMINISTRATION - DOSE 1

Pre-vaccination temperature:
[CE] $\qquad$ |. |__| Celsius
OR
[FA] $\qquad$ I. 1 | Fahrenheit Route: $\qquad$ $\square$ Axillary
[0] $\square$ Oral (preferred)
[R] $\qquad$
[] $\square$ Tympanic

Has Study vaccine or placebo been administered?
[N] $\square$ No $\rightarrow$ Please give reason hereafter.
[Y]Yes $\rightarrow$ Date of administration: $\qquad$ |__ |_1_1_| (if different from visit date)
$\rightarrow$ Administered treatment number: $\qquad$ I
$\rightarrow \quad$ Injection Site/Side/Route:According to protocol: Deltoid -Non dominant - IMDominantNot according to protocol:

| Specify Site: | $[1]$ | $\square$ Deltoid | $[3]$ | $\square$ Thigh |
| :--- | :--- | :--- | :--- | :--- |
| Side: | $[\mathrm{N}]$ | $\square$ Non Dominant | $[\mathrm{D}]$ | $\square$ Dominant |
| Route: | $[\mathrm{IM}]$ | $\square$ Intramuscular | $[\mathrm{SC}]$ | $\square$ Subcutaneous |

$\rightarrow$ if relevant, comment on administration: $\qquad$

## If no vaccination,

$\rightarrow$ Please tick the major reason for non administration


Serious Adverse Event and/ or pIMD:
$\rightarrow$ Please complete a SAE Report
$\rightarrow$ Please specify SAE Report No. |___|
[AEX] $\square$Non-Serious Adverse Event: $\rightarrow$ Please complete Non-Serious Adverse Event section
$\rightarrow \quad$ Please specify AE No. $\qquad$ -
[OTH]Other, please specify:
(e.g.: consent withdrawal, Protocol violation, ...)
$\rightarrow$ Please select who made the decision:
[1]Investigator
[S]Subject

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gsk


## SOLICITED ADVERSE EVENTS - LOCAL SIGNS/SYMPTOMS

## Study vaccine or placebo injection site

Has the subject experienced any of the following signs/symptoms between Day 0 and Day 6 ? [N] $\square$ No
[Y] $\square$ Yes, please tick No/Yes for each sign/symptom and complete further as necessary
[U] $\square$ Unknown, no information available
[NA] $\square \quad$ Not applicable, no vaccine administered

| Local Sign/Symptom | Day 0 | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | After Day 6 |  |  | Medically attended visit |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |  | Ongoing | $\begin{gathered} \text { Max } \\ \text { Intensity/ } \\ \text { size } \\ \hline \end{gathered}$ | Date of last day of sign/symptom |  |
| ```Redness [RE] [N] \(\square\) No \\ [1] \(\square\) Yes \(\rightarrow\) size (mm):``` | I_I | I__1 | 1 | I_I | I_I | 1 | I__1 | $\begin{aligned} & {[\mathrm{N}] \square \mathrm{No}} \\ & {[\mathrm{r}] \square \text { Yes } \rightarrow} \end{aligned}$ | I_I | Tick box if continuing at end of study $\downarrow$ $\qquad$ II $\qquad$ I II $\qquad$ I l or | NOHOOERMD 1_1_\| |
| Swelling [SW] [N] No M] Yes $\rightarrow$ size $(\mathrm{mm})$ : | I_1 | I_I | I_I | I_I | I_I | I_1 | I_I | $\begin{aligned} & {[\mathrm{N}] \square \mathrm{No}} \\ & {[\mathrm{r}] \square \text { Yes } \rightarrow} \end{aligned}$ | I_I | $\qquad$ | NOHOOERMD I_I_\| |
| Pain [PA] $[\mathrm{N}] \square \mathrm{No}$ $[\mathrm{Y}] \square$ Yes $\rightarrow$ intensity | 1_1 | 1_1 | 1 | I_I | 1_1 | 1 | 1_1 | $\begin{aligned} & {[\mathrm{N}] \square \mathrm{No}} \\ & {[\mathrm{y}] \square \text { Yes } \rightarrow} \end{aligned}$ | 1 | Tick box if continuing at end of study $\downarrow$ $\qquad$ II $\qquad$ \| || $\qquad$ I 1 I 1 1 or $\square$ | NOHOERMD $\qquad$ |

```
Intensity:
    0/1/2/3
    (see Adverse Events definitions)
```

```
NO: None
```

NO: None
HO: Hospitalization
HO: Hospitalization
ER. Emergency Ro
ER. Emergency Ro
MD. Medica Peroo

```

If any of these adverse events meets the definition of serious, complete a Serious Adverse Event Report to GSK Biologicals Study Contact for SAE reporting within 24 hours

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gsk


\section*{SOLICITED ADVERSE EVENTS - GENERAL SIGNS/SYMPTOMS}

Has the subject experienced any of the following signs/symptoms between Day 0 and Day 6 ?
\({ }^{[N]} \square \quad\) No
M] \(\square\) Yes, please tick No/Yes for each sign/symptom and complete further as necessary
[U] \(\square\) Unknown, no information available
Not applicable, no vaccine administered equal to \(38.0^{\circ} \mathrm{C} / 100.4\)
\begin{tabular}{|c|c|c|c|c|c|c|c|c|c|c|c|c|c|}
\hline \multirow{3}{*}{\[
\begin{aligned}
& \text { Temperature [TE] } \\
& \geq 37.5^{\circ} / 99.5^{\circ}[\mathrm{A} / \mathrm{O} / \mathrm{T}] \\
& \geq 38.0^{\circ} \mathrm{C} / 100.4^{\mathrm{F}}[\mathrm{R}] \\
& {[\mathrm{N}] \square \mathrm{No}} \\
& {[\mathrm{Y}] \square \text { Yes }} \\
& {[\mathrm{NT}] \square \text { Not Taken }}
\end{aligned}
\]} & Day 0 & Day 1 & Day 2 & Day 3 & Day 4 & Day 5 & Day 6 & \multicolumn{3}{|r|}{After Day 6} & \multirow[b]{2}{*}{Rel. to inv. Product} & \multirow[b]{2}{*}{Medically attended visit} & \multirow[t]{2}{*}{Tick box if related to the anticancer therapies and/or disease/ tumour} \\
\hline & \multirow[b]{2}{*}{} & \multirow[b]{2}{*}{\[
\begin{gathered}
-- \\
\square \\
\begin{array}{c}
\square \\
\text { Nat } \\
\text { Taken }
\end{array} \\
\hline
\end{gathered}
\]} & \multirow[b]{2}{*}{} & \multirow[b]{2}{*}{} & \multirow[b]{2}{*}{--
\(\square\)
\(\stackrel{-}{\mathrm{Not}}\)} & \multirow[b]{2}{*}{\(\stackrel{-}{\square}\)} & \multirow[b]{2}{*}{\[
\stackrel{\square}{\square}
\]} & Ongoing & \[
\begin{aligned}
& \text { Max } \\
& \text { Temp. }
\end{aligned}
\] & Date of last day of sign/symptom & & & \\
\hline & & & & & & & & \[
\begin{aligned}
& {[\mathrm{N}] \square \mathrm{No}} \\
& \mathrm{~K}] \square \mathrm{Yes} \rightarrow
\end{aligned}
\] & & Tick box if continuing at end of study \(\downarrow\)
\[
1 \quad \| \quad 1 \quad 1 \quad 11 \quad 1 \quad 1 \quad 1 \quad 1 \text { or } \square
\] & \[
\left[\begin{array}{l}
\mathrm{N}] \square \mathrm{No} \\
\mathrm{M}] \\
\mathrm{NO}
\end{array}\right.
\] & NOHOIERMD
\(\qquad\) & \(\square\) \\
\hline
\end{tabular}
```

Unit: [CE] }\square\mathrm{ Celsius Route:
[FA] \square Fahrenheit [0] 詯 Oral (preferred)
[\mp@code{[0] }

```
```

\square Rectal
T] }\square\mathrm{ Tympanic

```

CRF template version 14 - May 22 2013-System page 18 - Workbook 2 : with pre-vacc during V1


CRF template version 14 - May 22 2013 - System page 19 - Workbook 2 : with pre-vacc during V1

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VISIT 2
MONTH 1
DOSE 2
\begin{tabular}{|c|c|c|c|c|}
\hline & Book & Visit & & Subject Number \\
\hline & \(\mathbf{2}\) & VISIT 2-MONTH 1 & & 1_1_-_1_-_1_1 \\
\hline
\end{tabular}

\section*{CHECK FOR STUDY CONTINUATION}

Did the subject return for this visit?Yes \(\rightarrow\) Date of visit: \(\qquad\) 11 \(\qquad\) ||_1_|_|_| \(\rightarrow\) Go to next page
[N] \(\square\)No \(\rightarrow\) Please tick only one major reason:
[SAE2] \(\square\)
Serious Adverse Event and/or pIMD
\(\rightarrow\) Please complete a SAE Report
\(\rightarrow\) Please specify SAE Report No. I__I_|
\(\rightarrow\) Tick box if SAE is fatal:
[AEX]Non-Serious Adverse Event
\(\rightarrow\) Please complete Non-Serious Adverse Event section
\(\rightarrow\) Please specify AE No. |__I_|
or solicited AE code |__||
[PTV] \(\square\)
Protocol violation, please specify:

[Cws] \(\square\)
Consent withdrawal, not due to an adverse event
\(\rightarrow\) Please specify the reason (only if the subject has spontaneously explained it):
                ---------------------------------------------
[MIG]Migrated / moved from the study area
[LFU]Lost to follow-up
[SST] Sponsor study termination
[отн]
Other, please specify: \(\qquad\)
\(\rightarrow\) For serious (except death), non-serious adverse events and Other reasons only:
Please tick who made the decision:Investigator
[s]Subject
\(\rightarrow\) Study discontinuation
\({ }^{[Y]} \square\) Tick box only if permanent discontinuation, i.e. if the subject definitively withdraws from the study
In this case, terminate the CRF:
Complete Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information, if applicable and Study conclusion.

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116427 (ZOSTER-028)
\begin{tabular}{|c|c|c|c|c|}
\hline & Book & Visit & & Subject Number \\
\hline & \(\mathbf{2}\) & VISIT 2-MONTH 1 & & 1_1_-_1_-_1_1 \\
\hline
\end{tabular}

\section*{BLOOD SAMPLE}
Has a blood sample been taken for ELISA (approximately 8 mL )? [SER]No
[Y]Yes \(\rightarrow\) Date if different from visit date: \(\qquad\) 11 \(\qquad\) 11 \(\qquad\) |

\section*{CMI SAMPLE} ONLY FOR SUBJECTS IN CMI SUB-COHORT

Has a blood sample been taken for CMI response determination (approximately 30 mL )? \({ }_{\text {[PBMC] }}\)NoYes \(\rightarrow\) Date if different from visit date: \(\qquad\) | \(\qquad\) |______| \(\mid\)
\[
\rightarrow \text { Time of sample: } \quad \frac{\mid \_1}{\mathrm{hh}}-\left|:\left|\frac{1}{\mathrm{~mm}}\right|\right.
\]
\(\rightarrow\) Number of tubes: \(\square\)

\section*{PREGNANCY TEST}

Has a pregnancy test been done? [PRG]
\({ }_{[7]} \square\) Yes \(\rightarrow\) [URII \(\square\) Urine \(\rightarrow\) Date if different from visit date: |___||____||__|__|_|
\begin{tabular}{lll} 
Pregnancy test result: & \(\quad{ }^{[N]} \square\) & Negative \\
[HCG01] & \(\square\) & Positive
\end{tabular}

SERUM TEST SHOULD BE PERFORMED ONLY IF REQUIRED BY COUNTRY, LOCAL OR ETHICS COMMITTEE REGULATIONS
\({ }_{[S E R]} \square\) Serum \(\rightarrow\) Date if different from visit date:
II
|_1_1
II |_1_1_1_|
[N]No
[NA]Not applicable (female of non childbearing potential or male)
\begin{tabular}{|c|c|c|c|c|}
\hline & Book & Visit & & Subject Number \\
\hline & 2 & VISIT 2 - DOSE 2 & & |_1__|_1_1 \\
\hline
\end{tabular}


\section*{CONFIDENTIAL}
gsk


\section*{SOLICITED ADVERSE EVENTS - LOCAL SIGNS/SYMPTOMS}

\section*{Study vaccine or placebo injection site}

Has the subject experienced any of the following signs/symptoms between Day 0 and Day 6 ? [N] \(\square\) No
[Y] \(\square\) Yes, please tick No/Yes for each sign/symptom and complete further as necessary
[U] \(\square\) Unknown, no information available
[NA] \(\square \quad\) Not applicable, no vaccine administered
\begin{tabular}{|c|c|c|c|c|c|c|c|c|c|c|c|}
\hline \multirow[b]{2}{*}{Local Sign/Symptom} & \multirow[b]{2}{*}{Day 0} & \multirow[b]{2}{*}{Day 1} & \multirow[b]{2}{*}{Day 2} & \multirow[b]{2}{*}{Day 3} & \multirow[b]{2}{*}{Day 4} & \multirow[b]{2}{*}{Day 5} & \multirow[b]{2}{*}{Day 6} & \multicolumn{3}{|r|}{After Day 6} & \multirow[b]{2}{*}{Medically attended visit} \\
\hline & & & & & & & & Ongoing & \[
\begin{gathered}
\text { Max } \\
\text { Intensity/ } \\
\text { size } \\
\hline
\end{gathered}
\] & Date of last day of sign/symptom & \\
\hline ```
Redness [RE] 
``` & I_I & I_I & 1 & I__1 & I_I & 1 & I_I & \[
\begin{aligned}
& {[\mathrm{N}] \square \mathrm{No}} \\
& {[\mathrm{Y}] \square \mathrm{Yes} \rightarrow}
\end{aligned}
\] & I_1 & Tick box if continuing at end of study \(\downarrow\)
\(\qquad\) II \(\qquad\) _II \(\qquad\) I I \(\qquad\) | or \(\square\) & NO/HO/ER/MD
\(\qquad\) I__ \\
\hline Swelling [SW]
\([\mathrm{N}] \square \mathrm{No}\)
\([\mathrm{Y} \square \mathrm{Yes} \rightarrow\) size \((\mathrm{mm})\) : & I_I & I_I & I_I & I_I & I_1 & I_I & I_I & \[
\begin{aligned}
& {[\mathrm{N}] \square \mathrm{No}} \\
& {[\mathrm{Y}] \square \mathrm{Yes} \rightarrow}
\end{aligned}
\] & I_I & Tick box if continuing at end of study \(\downarrow\) & NO/HO/ER/MD
\(\qquad\) |_I \\
\hline \[
\begin{aligned}
& \text { Pain }[\mathrm{PA}] \\
& {[\mathrm{N}] \square \mathrm{No}} \\
& {[\mathrm{Y}] \square \text { Yes } \rightarrow \text { intensity }}
\end{aligned}
\] & 1_1 & 1_1 & 1 & I_I & 1_1 & 1 & 1_1 & \[
\begin{aligned}
& {[\mathrm{N}] \square \mathrm{No}} \\
& {[\mathrm{Y}] \square \mathrm{Yes} \rightarrow}
\end{aligned}
\] & 1 & Tick box if continuing at end of study \(\downarrow\)
\(\qquad\) II \(\qquad\) | \(\qquad\) I 1 I or \(\square\) & NOHOERMD
\(\qquad\) \\
\hline
\end{tabular}
```

Intensity:
0/1/2/3
(see Adverse Events definitions)
Medically at
HO: Hospitalization
ER: Emergency Room
MD: Medical Personne

```

If any of these adverse events meets the definition of serious, complete a Serious Adverse Event Report to GSK Biologicals Study Contact for SAE reporting within 24 hours.

\section*{CONFIDENTIAL}
gsk


\section*{SOLICITED ADVERSE EVENTS - GENERAL SIGNS/SYMPTOMS}

Has the subject experienced any of the following signs/symptoms between Day 0 and Day 6 ?
\({ }^{[N]} \square\) No
M] \(\square\) Yes, please tick No/Yes for each sign/symptom and complete further as necessary
[U] \(\square\) Unknown, no information available
Not applicable, no vaccine administered equal to \(38.0^{\circ} \mathrm{C} / 100.4\)
\begin{tabular}{|c|c|c|c|c|c|c|c|c|c|c|c|c|c|}
\hline \multirow{3}{*}{\begin{tabular}{l}
Temperature [TE] \(\geq 37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}[\mathrm{A} / \mathrm{O} / \mathrm{T}]\) \(\geq 38.0^{\circ} \mathrm{C} / 100.4 \mathrm{~F}[\mathrm{R}]\)


No
Yes \\
[NT] \(\square\)

Not Taken
\end{tabular}} & Day 0 & Day 1 & Day 2 & Day 3 & Day 4 & Day 5 & Day 6 & & & After Day 6 & & & \\
\hline & \multirow[b]{2}{*}{} & \multirow[b]{2}{*}{} & \multirow[b]{2}{*}{} & \multirow[b]{2}{*}{} & \multirow[b]{2}{*}{} & \multirow[b]{2}{*}{} & \multirow[b]{2}{*}{--
\(\stackrel{\square}{\text { Not }}\)
Taken} & Ongoing & \[
\begin{aligned}
& \text { Max } \\
& \text { Temp. }
\end{aligned}
\] & Date of last day of sign/symptom & Rel. to inv. Product & Medically attended visit & the anticancer therapies and/or disease/ tumour \\
\hline & & & & & & & & \[
\begin{aligned}
& {[N] \quad \begin{array}{l}
\text { No } \\
(\mathrm{y}) \\
\mathrm{Yeses} \rightarrow \\
\hline
\end{array}} \\
& \hline
\end{aligned}
\] & & Tick box if continuing at end of study \(\downarrow\)
\[
11 \quad 1 \quad 1 \quad 11 \quad 1 \quad 1 \quad 1 \quad \text { or } \square
\] & \[
\begin{gathered}
{[\mathrm{N}]} \\
\mathrm{Y}] \\
\mathrm{No} \\
\mathrm{Yes} \\
\hline
\end{gathered}
\] & NOMOIERMD & \(\square\) \\
\hline
\end{tabular}
```

Unit: [CE] }\square\mathrm{ Celsius Route: [A] }\square\mathrm{ Axillary
[FA] \square Fahrenheit Route.
[R] \square Recta
[T] }\square\mathrm{ Tympanic

```

CRF template version 14 - May 22 2013-System page 25 - Workbook 2 : with pre-vacc during V1


\section*{SOLICITED ADVERSE EVENTS - GENERAL SIGNS/SYMPTOMS (continued)}

(*) Gastrointestinal symptoms include nausea, vomiting, diarrhoea and/or abdominal pain
 hours.

CRF template version 14 - May 22 2013 - System page 26 - Workbook 2 : with pre-vacc during V1

CONFIDENTIAL

VISIT 3 MONTH 2

\section*{CONFIDENTIAL}
\begin{tabular}{|c|c|c|c|c|}
\hline & Book & Visit & & Subject Number \\
\hline & \(\mathbf{2}\) & VISIT 3- MONTH 2 & & |_1_1_1_1_1 \\
\hline
\end{tabular}

\section*{CHECK FOR STUDY CONTINUATION}

Did the subject return for this visit?
\({ }_{[Y]} \square\) Yes \(\rightarrow\) Date of visit: \(\qquad\) 11 \(\qquad\) || \(\qquad\) |
\(\rightarrow\) Go to next page
[N] \(\square\)No \(\rightarrow\) Please tick only one major reason:
[SAE2] \(\square\) Serious Adverse Event and/or pIMD
\(\rightarrow\) Please complete a SAE Report
\(\rightarrow\) Please specify SAE Report No. I \(\qquad\) I
\(\rightarrow\) Tick box if SAE is fatal: \(\square\) [AEX]Non-Serious Adverse Event
\(\rightarrow\) Please complete Non-Serious Adverse Event section
\(\rightarrow\) Please specify AE No. I____| or solicited AE code \(\qquad\) 1
[PTV] \(\square\)Protocol violation, please specify:
 [Cws] \(\square\)

Consent withdrawal, not due to an adverse event
\(\rightarrow\) Please specify the reason (only if the subject has spontaneously explained it):
[MIG]Migrated / moved from the study area
[LFU]Lost to follow-up
[SST]Sponsor study termination [отн]Other, please specify: \(\qquad\)
\(\rightarrow\) For serious (except death), non-serious adverse events and Other reasons only:
Please tick who made the decision:Investigator
[s]Subject
\(\rightarrow\) Study discontinuation
\(\square\) Tick box only if permanent discontinuation, i.e. if the subject definitively withdraws from the study
In this case, terminate the CRF:
Complete Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information, if applicable and Study conclusion.
\begin{tabular}{|c|c|c|c|c|}
\hline \multicolumn{5}{|c|}{CONFIDENTIAL} \\
\hline ClaxoSmithkine & & & \multicolumn{2}{|l|}{116427 (ZOSTER-028)} \\
\hline & Book & Visit & & Subject Number \\
\hline & 2 & VISIT 3 - MONTH 2 & & |__ \\
\hline
\end{tabular}

\section*{LABORATORY TESTS}

\section*{BLOOD SAMPLE}
```

Has a blood sample been taken for ELISA (approximately 8 mL)? [SER]

```
```No
```

```Y Yes \(\rightarrow\) Date if different from visit date:
``` \(\qquad\)
``` ||
``` \(\qquad\)
``` ||
``` \(\qquad\)
``` _
```

CMI SAMPLE ONLY FOR SUBJECTS IN CMI SUB-COHORT

Has a blood sample been taken for CMI response determination (approximately 30 mL )? [PBMC]NoYes $\rightarrow$ Date if different from visit date: $\qquad$ 11 $\qquad$ 11 ! - !
$\rightarrow$ Time of sample:

$\rightarrow \quad$ Number of tubes: $\qquad$

## CONFIDENTIAL

## VISIT 4

## CONFIDENTIAL

116427 (ZOSTER-028)

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | $\mathbf{2}$ | visit 4 |  | \|_1_1_1_1_1 |

## If visit 4 coincides with visit 5 , only the visit 5 will be completed

## CHECK FOR STUDY CONTINUATION

Did the subject return for this visit?Yes $\rightarrow$ Date of visit: $\qquad$ 11 $\qquad$ 11 $\qquad$ -

$$
\rightarrow \text { Go to next page }
$$

[N] $\square$No $\rightarrow$ Please tick only one major reason:
[SAE2] $\square$ Serious Adverse Event and/or pIMD
$\rightarrow$ Please complete a SAE Report
$\rightarrow$ Please specify SAE Report No. I $\qquad$ |
$\rightarrow$ Tick box if SAE is fatal: $\square$
[AEX]Non-Serious Adverse Event
$\rightarrow$ Please complete Non-Serious Adverse Event section
$\rightarrow$ Please specify AE No. I___ or solicited AE code I____|
[PTV]Protocol violation, please specify:
_-_-_-_-_-_-_-_-_-_-_-_-_-_-_-_ [Cws] $\square$

Consent withdrawal, not due to an adverse event
$\rightarrow$ Please specify the reason (only if the subject has spontaneously explained it):
[MIG]Migrated / moved from the study area
[LFU] $\square$ Lost to follow-upSponsor study termination
[VIS5] $\square$ Visit 4 coincides with Visit 5 [отн] $\square$Other, please specify: $\qquad$
$\rightarrow$ For serious (except death), non-serious adverse events and Other reasons only:
Please tick who made the decision:Investigator
[s]Subject
$\rightarrow$ Study discontinuation
Only if Visit 4 does NOT coincide with Visit 5
${ }^{[Y]} \square$ Tick box only if permanent discontinuation, i.e. if the subject definitively withdraws from the study In this case, terminate the CRF:
Complete Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information, if applicable and Study conclusion.

[^16]116427 (ZOSTER-028)

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :--- | :--- |
|  | 2 | VISIT 4 |  | I_1_1_1_1_1 |

## LABORATORY TESTS



Has a blood sample been taken for ELISA (approximately 8 mL )? [SER]No
[Y]Yes $\rightarrow$ Date if different from visit date: $\qquad$ 11 $\qquad$ II $\qquad$

CONFIDENTIAL



## CONFIDENTIAL

## CONFIDENTIAL

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 2 | MONTH 9 - PHONE CONTACT |  | 1__1_1 |

If Visit 4 coincides with Phone contact at Month 9, the visit 4 will replace the Month 9 Phone Contact

The subject will be reminded that, after Month 5 phone contact, a phone contact between the subject and the investigator and/or his delegate will take place (except at months that coincide with the subject's scheduled visits) to collect information on any event of interest that may have occurred, including:

- SAEs (Section 7.3 of the study protocol);
- $\quad$ pIMDs (Section 7.1.5.1 of the study protocol);
- intercurrent medical conditions (see Section 6.7 of the study protocol),
- the use of any concomitant medication/product/vaccine/treatment which could impact the immune response or is part of a chemotherapy (Section 6.6.1 of the study protocol);
- or pregnancy (Section 7.3 of the study protocol).

This information will be recorded in the appropriate section of the subject's eCRF.

Has safety information been obtained?$\square$ No $\rightarrow$ $\rightarrow \quad$ Please tick the box if the phone contact month 9 coincides with visit 4 $\qquad$
[Y]Yes $\rightarrow \quad$ Date of contact: $\qquad$ 11 $\qquad$ || $\qquad$ _1

CONFIDENTIAL

VISIT 5 MONTH 13

## CONFIDENTIAL

GlaxoSmithKline
116427 (ZOSTER-028)

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 2 | VISIT 5-MONTH 13 |  | 1_1_1_1_1_1 |

If visit 4 coincides with visit 5 , only the visit 5 will be completed

## CHECK FOR STUDY CONTINUATION

Did the subject return for this visit?
${ }_{[Y]} \square$Yes $\rightarrow$ Date of visit: $\mid$ $\qquad$ || $\qquad$ 11 $\qquad$ । |
$\rightarrow$ Go to next page
[N]o $\rightarrow$ Please tick only one major reason:
[SAE2] $\square$ Serious Adverse Event and/or pIMD
$\rightarrow$ Please complete a SAE Report
$\rightarrow$ Please specify SAE Report No. I $\qquad$ |
$\rightarrow$ Tick box if SAE is fatal: [AEX]Non-Serious Adverse Event
$\rightarrow$ Please complete Non-Serious Adverse Event section
$\rightarrow$ Please specify AE No. I___| or solicited AE code |___| [PTV]Protocol violation, please specify: [Cws] $\square$

Consent withdrawal, not due to an adverse event
$\rightarrow$ Please specify the reason (only if the subject has spontaneously explained it):
[MIG]Migrated / moved from the study area
[LFU]Lost to follow-up
[SST]Sponsor study termination [OTH] $\square$ Other, please specify: $\qquad$ $\rightarrow$ For serious (except death), non-serious adverse events and Other reasons only: Please tick who made the decision:Investigator
[s]Subject

CONFIDENTIAL

116427 (ZOSTER-028)

|  | Book | Visit |  | Subject Number |
| :---: | :---: | :---: | :---: | :---: |
|  | 2 | VISIT 5 - MONTH 13 |  | \|__1_1_1_1_1 |

## LABORATORY TESTS

## BLOOD SAMPLE

Has a blood sample been taken for ELISA (approximately 8 mL )? [SER]No
[Y]Yes $\rightarrow$ Date if different from visit date: $\qquad$ 11 $\qquad$ 11 $\qquad$ I

## CMI SAMPLE <br> ONLY FOR SUBJECTS IN CMI SUB-COHORT

Has a blood sample been taken for CMI response determination (approximately 30 mL )? [РBMC]
[ N$]$ No
[Y]Yes $\rightarrow$ Date if different from visit date: $\qquad$ 11 $\qquad$ |___1_||
$\rightarrow$ Time of sample: $\quad \frac{|\ldots|}{\mathrm{hh}}|\mathrm{l}:| \underline{\mathrm{mm}}$
$\rightarrow$ Number of tubes: $\qquad$

## CONFIDENTIAL



Diary Cards template version 14 - February 04,2013 - System page:

## CONFIDENTIAL

116427 (ZOSTER-028)
Report Final

## CONFIDENTIAL

## General Instructions

Thank you for your participation in this clinical trial.
During your last study visit, you received a "Diary Card" to fill in every day for a defined period, so that your study doctor or the study staff will know your general health status after the vaccination.
Here below you will find general instructions on how to complete the "Diary Card". There are also other specific instructions relative to each part of the "Diary Card" that you will need to fill in

## INSTRUCTIONS TO COMPLETE THE "DIARY CARD"

- Write clearly, use a pen (never pencil).
- The grey areas are dedicated to the investigator or delegate only. Do not write in these areas.



## CONFIDENTIAL

## HOW TO CORRECT MISTAKES?

- Cross out the mistake with a single line.
- Don't hide the mistake. Don't use correction fluid or don't make inkblots.
- Write the correct response close to the mistaken one
- If the correct response is written outside of the box, circle it and point to it with an arrow towards the box.
- Put your initials near the correction.
- Date the correction


[^17]Please contact your study doctor or the study staff immediately if you have any symptoms that you think are serious.

Diary Cards template version 14 - February 04,2013 - System page: 3

Report Final

## VACCINATION DOSE 1

## CONFIDENTIAL

## Instructions to complete:

Local and general symptoms

- If you experience any other symptoms than those listed in the local symptoms or general symptoms pages, please write these symptoms down in the Adverse Event section.
- If a symptom appears only after day 6, please write this symptom down in the Adverse Event section.


## > HOW TO COMPLETE "AFTER DAY 6"?

- In the columns "After day 6", if the symptom is still ongoing* after day 6, tick "Yes". Otherwise, tick "No".
* Ongoing means:
$\rightarrow$ Intensity is $=1$ or higher or
$\rightarrow$ Oral (in the mouth), axillary (under the armpit), tympanic temperature (in the ear) higher or equal $37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ or
$\rightarrow$ Rectal temperature higher or equal to $38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$
- If Yes
- Please write the worst intensity, the highest temperature or the greatest measure recorded during this follow-up period, after day 6 . And note the date when the symptom has disappeared or tick the box "still ongoing"
- If No, then leave empty the columns "Worst intensity/ greatest size/ highest temperature" and "End Date".


## - BOX "STILL ONGOING" IN COLUMN "END DATE" - WHEN TO TICKIT?

- Tick the box "Still ongoing" if the illness /sign /symptom is still present at the time you return the diary card to the site.



## CONFIDENTIAL

## CONFIDENTIAL

## DID YOU RECEIVE ANY MEDICAL ATTENTION? HOW TO COMPLETE THIS QUESTION?

- Medical attention means hospitalisation, an emergency room visit or a visit to or from medical personnel (medical doctor).
- Tick the box "No" if you did not visit a doctor or go to the hospital or an emergency room for the symptom.
- Tick the box "Yes" if you went to the hospital, an emergency room or if you visited a doctor for the symptom. Keep the type of medical attention (grey column) empty. It will be completed by the study doctor or study staff.



## CONFIDENTIAL

## Instructions to complete:

Local symptoms

## HOW TO COMPLETE THE DAILY VALUE?

- Write down a value for each symptom and each day (measure or intensity). Don't leave any field empty.
- If there is no symptom, please write "0".

| Injection site <br> Swelling $\rightarrow$ size (mm) | mm 2 | mm | mm | mm | mm | mm | m | $\triangle$ № $\square$ Yes $\rightarrow$ | mm | $\square$ | 区 No $\square \mathrm{Yes}$ | HOEPMD |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |

## CONFIDENTIAL

- Redness, swelling and pain may appear around the area where you received the vaccine as shown in this drawing. These are called LOCAL symptoms.
- If similar symptoms appear on another part of your body than this/those shown in the drawing, please report them in the Adverse Event section.


Write down the size of the redness and swelling in millimetres $(\mathrm{mm})$ only. Use the ruler given to you by the site staff.

## - INTENSITY DEFINITIONS

- Redness and swelling: Measure and record the greatest surface diameter in millimetres ( mm ).
- Pain: 0: None

1: Any pain neither interfering with nor preventing normal every day activities.
2: Painful when limb is moved and interferes with every day activities.
3: Significant pain at rest. Prevents normal every day activities.

| $\text { gSk }{ }_{\text {ClaxoSmithkline }} \stackrel{116427}{\text { ZOSTER-028 }}$ | DIARY CARDS <br> Vaccine Dose Number 1 | Subject Number |
| :---: | :---: | :---: |

LOCAL SYMPTOMS
Study vaccine


Diary Cards template version 14 - February 04,2013 - System page: 9

## Instructions to complete:

## General symptoms

## $>$ HOW TO COMPLETE THE DAILY VALUE?

- Write down a value for each symptom and each day (measure or intensity). Don't leave any field empty.
- Write "0" if there is no increase compared to normal


GENERAL SYMPTOMS: TEMPERATURE

- Please use the provided thermometer.
- Take your temperature each day from day of vaccination (day 0 ) until day 6 , and write down the values.
- If you took more than once a day your temperature, then write down the highest one.

Example: if on Day 0

- At 8 am: $37.1^{\circ} \mathrm{C} / 98.8^{\circ} \mathrm{F}$
- At $1 \mathrm{pm}: 37.4^{\circ} \mathrm{C} / 99.3^{\circ} \mathrm{F}$
- At $7 \mathrm{pm}: 37.6^{\circ} \mathrm{C} / 99.7^{\circ} \mathrm{F}$
- Please write down NT (Not Taken) if you did not take your temperature that day.


| gSk116427 <br> ZOSTER-028 | D/ARY CARDS <br> Vaccine Dose Number 1 | Subject Number <br> To be completed by the investigator or delegate |
| :--- | :--- | :--- |

## GENERAL SYMPTOMS

To be completed by the investigator or delegate: Date of vaccination = Day $\mathbf{0}$ :



Diary Cards template version 14 - February 04,2013 - System page: 11

## CONFIDENTIAL

## INTENSITY DEFINITIONS

- Headache: 0 : Normal 1: Easily tolerated 2: interferes with normal activity 3 : prevents normal activity
- Fatigue (feeling tired): 0: Normal 1: Easily tolerated 2: interferes with normal activity 3: prevents normal activity
- Gastrointestinal symptoms (including nausea, vomiting, diarrhoea and/or abdominal pain): 0: Normal 1: Easily tolerated 2: interferes with normal activity 3: prevents normal activity
- Myalgia (muscle aches): 0 : Normal 1: Easily tolerated 2 : interferes with normal activity 3 : prevents normal activity
- Shivering: 0: Normal 1: Easily tolerated 2 : interferes with normal activity 3 : prevents normal activity


## WHEN TO TICK THE BOX 'Tick box if related to the anti-cancer therapies and/or disease/tumour'?

- This is a grey area, so dedicated to the investigator or delegate only. Do not write in these areas
- When the General symptom or the Adverse Event is related to the anti-cancer therapies and/or the disease/tumour, the box should be ticked by the investigator or delegate

| gSk |
| :--- | :--- | :--- |
| GlaxoSmithkine |
| ZOSTER-028 |$\quad$| DIARY CARDS |
| :---: |
| Vaccine Dose Number 1 |$\quad$| Subject Number |
| :---: |

GENERAL SYMPTOMS


Diary Cards template version 14 - February 04,2013 - System page: 13

## Instructions to complete:

## Adverse Events

- If you experience any other symptoms than those listed in the local symptoms or general symptoms pages, please write these symptoms down in this section
- If a symptom appears only after day 6 , please write this symptom down in this section
- If redness, swelling or pain appears on another area than area where you received the vaccine, please report these symptoms in this section.


## INTENSITY DEFINITIONS

- 1: Mild. An adverse event which is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
- 2: Moderate. An adverse event which is sufficiently discomforting to interfere with normal everyday activities.
- 3: Severe. An adverse event which prevents normal, everyday activities. Such an AE would, for example prevent attendance at work and would necessitate the administration of medication or other medical treatment.


## BOX "STILL ONGOING" IN THE COLUMN "END DATE" - WHEN TO TICK IT?

- Tick the box "Still ongoing" if the illness / sign / symptom is still present at the time you return the diary card to the site.


## DID YOU RECEIVE ANY MEDICAL ATTENTION? HOW TO COMPLETE THIS QUESTION?

- Medical attention means hospitalisation, an emergency room visit or a visit to or from medical personnel (medical doctor).
- Tick the box "No" if you did not visit a doctor or go to the hospital or an emergency room for the symptom.
- Tick the box "Yes" if you went to the hospital, an emergency room or if you visited a doctor for the symptom. Keep the type of medical attention (grey column) empty. It will be completed by the study doctor or study staff.

```
Diary Cards template version 14 - February 04, 2013 - System page:14
```

| gSkClaxoSmithkline <br> ZOSTER－028 | DIARY CARDS <br> Vaccine Dose Number 1 | Subject Number <br> To be completed by the investigatoror delegate |
| :--- | :--- | :--- |

ADVERSE EVENTS
Record any adverse event（＝any illness，sign，symptom）other than the local and general symptoms listed on the previous pages，which may have started or any medical condition which may have worsened since the last study vaccination

| IIIness／Sign／Symptom <br> $\square$ if at vaccine injection site $\downarrow$ | Worst Intensity 1／2／3 | Start Date | End Date <br> Tick box if still ongoing $\downarrow$ | Did you receive medical attention？ | Type of medical attention To be completed by the investigator or delegate | Relationship to inv．Product <br> To be completed by the investigator or delegate | Tick box if related to the anti－cancer therapies and／or disease／tumour <br> To be completed by the investigator or delegate |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HOIERMD <br> $\square$ |  | $\square$ |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HOERMD $\square$ | $\begin{aligned} & \square \mathrm{No} \\ & \square \mathrm{Yes} \end{aligned}$ | $\square$ |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HOIERMD | $\begin{aligned} & \square \mathrm{No} \\ & \square \mathrm{Yes} \\ & \hline \end{aligned}$ | $\square$ |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HOIERMD <br> い－ | $\begin{aligned} & \square \mathrm{No} \\ & \square \mathrm{Yes} \\ & \hline \end{aligned}$ | $\square$ |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HOIERMD <br> い」 | $\begin{aligned} & \square \mathrm{No} \\ & \square \mathrm{Yes} \end{aligned}$ | $\square$ |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HOERMD <br> いい |  | $\square$ |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HOERMD <br> いい | $\begin{aligned} & \square \mathrm{No} \\ & \square \mathrm{Yes} \\ & \hline \end{aligned}$ | $\square$ |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HOIERMD <br> いப | $\begin{aligned} & \square \mathrm{No} \\ & \mathrm{Yos} \end{aligned}$ | $\square$ |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | $\begin{aligned} & \text { HOERMD } \\ & \hline 1.1 \end{aligned}$ | $\begin{aligned} & \square \mathrm{No} \\ & \mathrm{Yos} \\ & \hline \end{aligned}$ | $\square$ |

Clarification（s）for Investigator or delegate only：

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CONFIDENTIAL

Report Final

| gSk116427 <br> ZOSTER-028 | D/ARY CARDS <br> Vaccine Dose Number 1 | Subject Number <br> To be completed by the investigator or delegate |
| :--- | :--- | :--- |

## VACCINATION

Record any vaccination received since the last study vaccination

| Vaccination |  | Date of administration |
| :--- | :--- | :--- | Route codes = inhalation $[1 \mathrm{I}]$, intraarticicuar [iR], intraderma

transdermal [TD], vaginal [VA], other [OTH], unknown [UNK]


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## CONFIDENTIAL

## Instructions to complete:

Medication

## DOSE, UNIT AND FREQUENCY

- Write the amount of the medication you took

| Dose, unit and frequency |
| :--- |
| 200 magill 3 times a day |
| 2 coffee spoov 100 mg orice |
| per day |
| 3 supposítories per day |
| Nasal drops 4 tímes per day |

- Most of this information can be found on the label of the medication. You may want to bring the medication to yournext visit with the study doctor or study staff. Then they can help you to fill in the required information.


## BOX "STILL ONGOING"IN THE COLUMN "END DATE"- WHEN TO TICKIT?

- Tick the box "Still ongoing" if the medication is still taken at the time you return the diary card to the site.

| gSk | 116427 <br> ZOSTER-028 | D\|ARY CARDS |
| :--- | :--- | :--- |
| Vaccine Dose Number 1 |  |  |$\quad$| Subject Number |
| :---: |
| To be completed by the investigator or delegate |

## MEDICATION

Record any medication taken at home since the last study vaccination.


Clarification(s) for Investigator or delegate only:

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CONFIDENTIAL

Report Final

| gSkClaxoSmithkline <br> ZOSTER-028 | DIARY CARDS <br> Vaccine Dose Number 1 | Subject Number <br> To be completed by the investigatoror delegate |
| :--- | :--- | :--- |

NOTES
$\square$

INVESTIGATOR'S OR DELEGATE'S SIGNATURE

```
Investigator's or delegate's
signature:
Printed Investigator's or
delegate's name:
\(\square\)
Date: |____|______|________
delegate's name:
```



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## VACCINATION DOSE 2

## CONFIDENTIAL

## Instructions to complete:

Local and general symptoms

- If you experience any other symptoms than those listed in the local symptoms or general symptoms pages, please write these symptoms down in the Adverse Event section.
- If a symptom appears only after day 6, please write this symptom down in the Adverse Event section.


## > HOW TO COMPLETE "AFTER DAY 6"?

- In the columns "After day 6", if the symptom is still ongoing* after day 6, tick "Yes". Otherwise, tick "No".
* Ongoing means:
$\rightarrow$ Intensity is $=1$ or higher or
$\rightarrow$ Oral (in the mouth), axillary (under the armpit), tympanic temperature (in the ear) higher or equal $37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ or
$\rightarrow$ Rectal temperature higher or equal to $38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$
- If Yes
- Please write the worst intensity, the highest temperature or the greatest measure recorded during this follow-up period, after day 6 . And note the date when the symptom has disappeared or tick the box "still ongoing"
- If No, then leave empty the columns "Worst intensity/ greatest size/ highest temperature" and "End Date".


## - BOX "STILL ONGOING" IN COLUMN "END DATE" - WHEN TO TICKIT?

- Tick the box "Still ongoing" if the illness /sign /symptom is still present at the time you return the diary card to the site.



## CONFIDENTIAL

## CONFIDENTIAL

## DID YOU RECEIVE ANY MEDICAL ATTENTION? HOW TO COMPLETE THIS QUESTION?

- Medical attention means hospitalisation, an emergency room visit or a visit to or from medical personnel (medical doctor).
- Tick the box "No" if you did not visit a doctor or go to the hospital or an emergency room for the symptom.
- Tick the box "Yes" if you went to the hospital, an emergency room or if you visited a doctor for the symptom. Keep the type of medical attention (grey column) empty. It will be completed by the study doctor or study staff.



## CONFIDENTIAL

## Instructions to complete:

Local symptoms

## HOW TO COMPLETE THE DAILY VALUE?

- Write down a value for each symptom and each day (measure or intensity). Don't leave any field empty.
- If there is no symptom, please write "0".

| Injection site <br> Swelling $\rightarrow$ size (mm) | mm 2 | mm | mm | mm | mm | mm | m | $\triangle$ № $\square$ Yes $\rightarrow$ | mm | $\square$ | 区 No $\square \mathrm{Yes}$ | HOEPMD |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |

## CONFIDENTIAL

- Redness, swelling and pain may appear around the area where you received the vaccine as shown in this drawing. These are called LOCAL symptoms.
- If similar symptoms appear on another part of your body than this/those shown in the drawing, please report them in the Adverse Event section.


Write down the size of the redness and swelling in millimetres ( mm ) only. Use the ruler given to you by the site staff.

## - INTENSITY DEFINITIONS

- Redness and swelling: Measure and record the greatest surface diameter in millimetres ( mm ).
- Pain: 0: None

1: Any pain neither interfering with nor preventing normal every day activities.
2: Painful when limb is moved and interferes with every day activities.
3: Significant pain at rest. Prevents normal every day activities.

| gSkClaxosmith Kine <br> ZOSTER-028 | D/ARY CARDS <br> Vaccine Dose Number 2 | Subject Number <br> To be completed by the investigator or delegate |
| :--- | :--- | :--- |

## LOCAL SYMPTOMS

Study vaccine


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## Instructions to complete:

## General symptoms

## $>$ HOW TO COMPLETE THE DAILY VALUE?

- Write down a value for each symptom and each day (measure or intensity). Don't leave any field empty.
- Write "0" if there is no increase compared to normal


GENERAL SYMPTOMS: TEMPERATURE

- Please use the provided thermometer.
- Take your temperature each day from day of vaccination (day 0 ) until day 6 , and write down the values.
- If you took more than once a day your temperature, then write down the highest one.

Example: if on Day 0

- At 8 am: $37.1^{\circ} \mathrm{C} / 98.8^{\circ} \mathrm{F}$
- At $1 \mathrm{pm}: 37.4^{\circ} \mathrm{C} / 99.3^{\circ} \mathrm{F}$
- At $7 \mathrm{pm}: 37.6^{\circ} \mathrm{C} / 99.7^{\circ} \mathrm{F}$
- Please write down NT (Not Taken) if you did not take your temperature that day.




## GENERAL SYMPTOMS

## To be completed by the investigator or delegate: Date of vaccination $=$ Day $\mathbf{0}$ :




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## CONFIDENTIAL

## INTENSITY DEFINITIONS

- Headache: 0 : Normal 1: Easily tolerated 2: interferes with normal activity 3 : prevents normal activity
- Fatigue (feeling tired): 0: Normal 1: Easily tolerated 2: interferes with normal activity 3: prevents normal activity
- Gastrointestinal symptoms (including nausea, vomiting, diarrhoea and/or abdominal pain): 0: Normal 1: Easily tolerated 2: interferes with normal activity 3: prevents normal activity
- Myalgia (muscle aches): 0: Normal 1: Easily tolerated 2: interferes with normal activity 3 : prevents normal activity
- Shivering: 0: Normal 1: Easily tolerated 2 : interferes with normal activity 3 : prevents normal activity


## WHEN TO TICK THE BOX 'Tick box if related to the anti-cancer therapies and/or disease/tumour'?

- This is a grey area, so dedicated to the investigator or delegate only. Do not write in these areas.
- When the General symptom or the Adverse Event is related to the anti-cancer therapies and/or the disease/tumour, the box should be ticked by the investigator or delegate

| gSk |
| :--- | :--- | :--- |
| GlaxoSmithkine |
| ZOSTER-028 |$\quad$| DIARY CARDS |
| :---: |
| Vaccine Dose Number 2 |$\quad$| Subject Number |
| :---: |

GENERAL SYMPTOMS


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## Instructions to complete:

## Adverse Events

- If you experience any other symptoms than those listed in the local symptoms or general symptoms pages, please write these symptoms down in this section
- If a symptom appears only after day 6 , please write this symptom down in this section
- If redness, swelling or pain appears on another area than area where you received the vaccine, please report these symptoms in this section.


## INTENSITY DEFINITIONS

- 1: Mild. An adverse event which is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
- 2: Moderate. An adverse event which is sufficiently discomforting to interfere with normal everyday activities.
- 3: Severe. An adverse event which prevents normal, everyday activities. Such an AE would, for example prevent attendance at work and would necessitate the administration of medication or other medical treatment.


## BOX "STILL ONGOING" IN THE COLUMN "END DATE"- WHEN TO TICK IT?

- Tick the box "Still ongoing" if the illness / sign / symptom is still present at the time you return the diary card to the site.


## DID YOU RECEIVE ANY MEDICAL ATTENTION? HOW TO COMPLETE THIS QUESTION?

- Medical attention means hospitalisation, an emergency room visit or a visit to or from medical personnel (medical doctor).
- Tick the box "No" if you did not visit a doctor or go to the hospital or an emergency room for the symptom.
- Tick the box "Yes" if you went to the hospital, an emergency room or if you visited a doctor for the symptom. Keep the type of medical attention (grey column) empty. It will be completed by the study doctor or study staff.

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| gSkClaxoSmithkline <br> ZOSTER－028 | DIARY CARDS <br> Vaccine Dose Number 2 | Subject Number <br> To be completed by the investigatoror delegate |
| :--- | :--- | :--- |

ADVERSE EVENTS
Record any adverse event（＝any illness，sign，symptom）other than the local and general symptoms listed on the previous pages，which may have started or any medical condition which may have worsened since the last study vaccination．

| IIIness／Sign／Symptom <br> $\square$ if at vaccine injection site $\downarrow$ | Worst Intensity 1／2／3 | Start Date | End Date <br> Tick box if still ongoing $\downarrow$ | Did you receive medical attention？ | Type of medica attention To be completed by the investigator or delegate | Relationship to inv．Product <br> To be completed by the investigator or delegate | Tick box if related to the anti－cancer therapies and／or disease／tumour <br> To be completed by the investigator or delegate |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HOIERMD <br> い－ |  | $\square$ |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HOERMD <br> いـ | $\begin{aligned} & \square \mathrm{No} \\ & \square \mathrm{Yes} \end{aligned}$ | $\square$ |
| $\square$ |  |  | $\square$ | $\square$ No $\square$ Yes | HOERMD | $\begin{aligned} & \square \mathrm{No} \\ & \square \mathrm{Yes} \\ & \hline \end{aligned}$ | $\square$ |
| $\square$ |  |  | $\square$ | $\square$ No $\square$ Yes | HOERMD <br> いـ | $\begin{aligned} & \square \mathrm{No} \\ & \square \mathrm{Yes} \\ & \hline \end{aligned}$ | $\square$ |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HO／ERMD <br> い」 | $\begin{aligned} & \square \mathrm{No} \\ & \square \mathrm{Yes} \end{aligned}$ | $\square$ |
| $\square$ |  |  | $\square$ | $\square$ No $\square$ Yes | HOERMD $+$ | $\begin{aligned} & \square \mathrm{No} \\ & \square \mathrm{Yes} \\ & \hline \end{aligned}$ | $\square$ |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HOIERMD $\square$ | $\begin{aligned} & \square \mathrm{No} \\ & \square \mathrm{Yes} \\ & \hline \end{aligned}$ | $\square$ |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HOERMD $\pm$ | $\begin{aligned} & \square \mathrm{No} \\ & \square \mathrm{Yes} \\ & \hline \end{aligned}$ | $\square$ |
| $\square$ |  |  | $\square$ | $\square \mathrm{No}$ $\square \mathrm{Yes}$ | HOIERMD $\pm$ | $\begin{aligned} & \square \mathrm{No} \\ & \square \mathrm{Yes} \\ & \hline \end{aligned}$ | $\square$ |

Clarification（s）for Investigator or delegate only：

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CONFIDENTIAL

Report Final

| gSk116427 <br> ZOSTER-028 | D/ARY CARDS <br> Vaccine Dose Number 2 | Subject Number <br> To be completed by the investigator or delegate |
| :--- | :--- | :--- |

## VACCINATION

Record any vaccination received since the last study vaccination

| Vaccination |  | Date of administration |
| :--- | :--- | :--- | Raute codes = inhalation $[1 \mathrm{I}]$, intraarticular [IRT, intraderma

transdermal [TD], vaginal [VA], other [OTH], unknown [UNK]


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## CONFIDENTIAL

## Instructions to complete:

Medication

## DOSE, UNIT AND FREQUENCY

- Write the amount of the medication you took

| Dose, unit and frequency |
| :--- |
| 200 magill 3 times a day |
| 2 coffee spoov 100 mg orice |
| per day |
| 3 supposítories per day |
| Nasal drops 4 tímes per day |

- Most of this information can be found on the label of the medication. You may want to bring the medication to yournext visit with the study doctor or study staff. Then they can help you to fill in the required information.


## BOX "STILL ONGOING"IN THE COLUMN "END DATE"- WHEN TO TICKIT?

- Tick the box "Still ongoing" if the medication is still taken at the time you return the diary card to the site.

| gSk | 116427 <br> ZOSTER-028 | D\|ARY CARDS |
| :--- | :--- | :--- |
| Vaccine Dose Number 2 |  |  |$\quad$| Subject Number |
| :---: |
| To be completed by the investigator or delegate |

## MEDICATION

Record any medication taken at home since the last study vaccination.


Clarification(s) for Investigator or delegate only:

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CONFIDENTIAL

Report Final

| gSkClaxoSmithkline <br> ZOSTER-028 | DIARY CARDS <br> Vaccine Dose Number 2 | Subject Number <br> To be completed by the investigatoror delegate |
| :--- | :--- | :--- |

NOTES
$\square$

INVESTIGATOR'S OR DELEGATE'S SIGNATURE

```
Investigator's or delegate's
signature:
Printed Investigator's or
delegate's name:
------------------------
Date: |____|__\___| |_______|
```

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## TRAINING APPLICATION

## DEMOGRAPHY

Date of Birth: DEMOG.DOB_RAW
(Enter only month and year)


## SUBJECT STUDY GROUP AND SUB-COHORT



## INFORMED CONSENT

I certify that Informed Consent has been obtained prior to any study procedure.
Informed Consent Date:


Did the subject meet all the entry criteria?
--> tick all boxes corresponding to violations of any inclusion/exclusion criteria.

## ELISHEET.ELIGIBIL

Do not enter the subject into the study if he/she failed any of the inclusion or exclusion criteria below.
INCLUSION Tick the boxes corresponding to any of the inclusion criteria the subject failed.

## CRITERIA

Subjects who, ELIGIBIL.CRIT_NR investigator, can comply with the requirements of the protocol

## ELIGIBIL.CRIT_ANS

Written informed consent obtained from the subject
A male or female, aged 18 years or older (has reached legal consent age) at the time of study entry
Subject who has been diagnosed with one or more solid tumours (defined as a solid malignancy)
Subject who is receiving or will receive a cytotoxic or immunosuppressive chemotherapy
Life expectancy of greater than one year
Female subjects of non-childbearing potential may be enrolled in the study
Female subjects of childbearing potential: contracep 30 days<vac + neg preg test + cont contracep

## EXCLUSION <br> CRITERIA

Tick the boxes corresponding to any of the exclusion criteria that disqualified the subject from entry.
Subjects takinELIGIBIL.CRIT_NR .... ot considered immunosuppressant if not taken with classic chemo

## ELIGIBIL.CRIT_ANS

Chronic administration and/or planned administration of systemic glucocorticoids
Previous vaccination against HZ/varicella within 12 months preceding the 1st dose study vacc/plac
Planned administration during the study of an HZ vaccine other than the study vaccine.
Previous chemotherapy course less than one month before first study vaccination
Occurrence of a varicella\HZ episode within the 12 months preceding the first dose of study vacc
History of allergic disease/reaction exacerbated by any component of the vacc/stdy material, equip
Admin or planned admin of a live vaccine within 30 days before or 30 days after study vaccine doses
HIV infection by clinical history;
Acute disease and/or fever at the time of enrolment
Pregnant or lactating female
Female planning to become pregnant during the treatment period and for two months after

# Are you aware of any pre-existing conditions, signs or symptoms having started before first study vaccination? 

--> Please give diagnosis and tick appropriate Past/Current box
GENHIST.MED_COND
Please record details on the current solid tumor in the subject characteristics section at V1, not here.
Please report medication(s) as specified in the protocol and fill in the medication section.


## HCG URINE PREGNANCY TEST

Has a urine sample been taken?
LABSHEET.SAMPTAKE
(female of non childbearing potential or male)
--> Date if different from visit date:
LABSHEET.SAMPRDAT
--> Pregnancy test result:
LABO_CRF.RAWRES

Did the subject experience any Serious Adverse Event during screening?
(only SAEs related to study participation or to a GSK concurrent medication need to be considered and reported)
--> Please remember to complete a SAE Report
AESHEET.AE_FLAG

Is the subject a screening failure?
(Was the subject withdrawn prior to randomisation or first vaccination?)
--> Please select one major reason:
SCR_CONC.FAIL_FLG
SCR_CONC.FAILREAS
--> Select failing criteria on Eligibility form
--> Please specify the reason (only if the Subject has spontaneously explained it):
--> Please specify: SCR_CONC.FAlL_SP
--> Please complete a SAE Report
$\rightarrow$ Please specify SAE Report No.: SCR_cONC SAE CASE
Note : SAE Report has not to be completed)
--> Tick box if SAE is fatal: SCR_CONC.FATAL
--> Please select who made the decision
--> Except death, please select who made the decision:
SCR_CONC.DECISION

## DIAGNOSIS FOR SOLID TUMOUR MALIGNANCY

Please indicate which solid tumour malignancy was diagnosed for the subject?

| TUM_DIAG.TUM_MAL | please specify: |
| :--- | :--- |
|  | TUM_DIAG.OTH_SPEC |
|  |  |
|  |  |

please specify staging:
TUM_DIAG.STAGING

## SEROLOGICAL EVIDENCE OF VZV

Has the subject been tested for VZV seropositivity?
SERO.TEST_FLG _---> SERO.TEST_RES


|  |  | Vaccine name <br> Trade name is preferred | Route <br> Date of <br> vaccination * |
| :---: | :---: | :---: | :---: |
| HIST_VAC.TRADNAME |  | HIST_VAC.MED_ROUT | HIST_VAC.HIST_DAT |

## HISTORY OF CHEMOTHERAPY, RADIOTHERAPY AND SURGERY

Please encode chemotherapy/radiotherapy or surgery received before study entry, for the solid tumour for which the subject is included in the fiterythat the chemotherapy (all the cycles given previous to the first administration) should be recorded in the section "Anti-cancer therapy related to the current solid tumour malignancy".

Has the patient received any previous chemotherapy/ radiotherapy or
surgery for the solid tumour for which the subject is included in the study?

$\square$

Schedule: With pre-vacc BEFORE V1

## PERFORMANCE STATUS (ECOG)

Has performance status (ECOG) been assessed?
PS_ECOG.PS_YN ${ }^{--->}$Date assessed: PS_ECOG.PS_DATE
PS_ECOG.PS

Please note that the category " 5 = dead" is not applicable to this study

## BLOOD SAMPLE

Has a blood sample been taken for ELISA (approximately 8 mL )?

--> Date if different from visit date:
LABSHEET.RECONCIL

## PREGNANCY TEST

Has a pregnancy test been done?
LABSHEET.SAMPTAKE
SERUM TEST SHOULD BE PERFORMED ONLY IF REOUIRED BY COUNTRY, LOCAL OR ETHICS

--> Pregnancy test result: LABO_CRF.RAWRES


## VACCINE ADMINISTRATION - DOSE 1

| Pre-vaccination temperature: | VS.VSORRES | Route:Vs.vsLoc |  |
| :---: | :---: | :---: | :---: |
|  | vs.vsorresu |  | (preferred) |

Has Study vaccine or placebo been administered?
--> Date of administration: VAC_INFO.VACCRDAT
VACCPROD.V_ADM ${ }_{\text {if }}$ different from visit date)

--> If relevant, comment on administration:

## VACCPROD.VADM_COM

## If no vaccination,

--> Please select the major reason for non administration
VAC_INFO.V_REAS

> --> Please complete a SAE Report
--> Please specify SAE Report No.
--> Please complete Non-Serious Adverse Event section
--> Please specify AE No. VAC_INFO.AE_NB
--> Please specify: VAC_INFO.V_OTH
(e.g.: consent withdrawal, Protocol violation, ...)
--> Please select who made the decision: VAC_INFO.DECISION

Study vaccine or placebo injection site
Has the subject experienced any of the following signs/symptoms between Day 0 and Day $6 ?$
SOLSHEET.SOL_YN please select No/Yes for each sign/symptom and complete further as necessary



Has the subject experienced any of the following signs/symptoms between Day 0 and Day 6 ?

SOLSHEET.SOL_YN please select No/Yes for each sign/symptom and complete further as necessary
Record temperatures if during the solicited period at least one oral/axillary/tympanic measure is above or equal to $37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ or at least one rectal measure is above or equal to $38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$.



## (*) Gastrointestinal symptoms include nausea, vomiting, diarmoea and/or abdominat pain

If any of these adverse events meets the definition of serious, complete a Serious Adverse Event Report to GSK Biologicals Study Contact for SAE reporting within 24 hours.

Did the subject return for this visit?
VIS_INFO.VIS_FLG
-->
--> Go to next screen
--> Please select one major reason:

VIS_INFO.V_REAS
--> Please complete a SAE Report
--> Please specify SAE Report No.
--> Tick box if SAE is fatal: VIS_INFO.FATAL
--> Please complete Non-Serious Adverse Event section
--> Please specify AE No. or solicited AE VIS_INFO.AE_NB VIS_INFO.SYMP_COD
--> Please specify the reason (only if the subject has spontaneously explained it):
Please specify:
VIS_INFO.REAS_COM
--> Except death, please select who made the decision:
--> Please select who made the decision:

## VIS_INFO.DECISION

## --> Study discontinuation

Tick box only if permanent discontinuation, i.e. if the subject definitively withdraws from the study

## VIS_INFO.DISCNT

In this case, terminate the CRF:
Complete Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information, if applicable and Study Conclusion.

## BLOOD SAMPLE

Has a blood sample been taken for ELISA (approximately 8 mL )?

--> Date if different from visit date:
LABSHEET.RECONCIL

## PREGNANCY TEST

Has a pregnancy test been done?
LABSHEET.SAMPTAKE
SERUM TEST SHOULD BE PERFORMED ONLY IF REOUIRED BY COUNTRY, LOCAL OR ETHICS

--> Pregnancy test result: LABO_CRF.RAWRES


## VACCINE ADMINISTRATION - DOSE 2



Has Study vaccine or placebo been administered?
--> Date of administration: VAC_INFO.VACCRDAT
VACCPROD.V_ADM ${ }_{\text {if }}$ different from visit date)

| --> Administered treatment number VACC_TRT.V_TRT |  |
| :---: | :---: |
| --> Please give reason hereafter |  |
|  | - IM |
| --> Protocol administration Site/Side/Route Deltoid | - Non Dominant/ Dominant VACCPROD.P_AP |
|  | Site: VACCPROD.P_APSITE |
| --> Has the vaccine been administered according to the protocol administration site, side, route? |  |
|  | Side: VACCPROD.P_APSIDE |
| Specify site: | Specify |
| Specify side: VACCPROD.P_SIDE | Route: VACCPROD.P_APROUT |
| Specify route: |  |

--> If relevant, comment on administration:

## VACCPROD.VADM_COM

## If no vaccination,

--> Please select the major reason for non administration
VAC_INFO.V_REAS

> --> Please complete a SAE Report
> --> Please specify SAE Report Ngr solicited AE VAC_INFO.SYMP_COD
> --> Please complete Non-Serious Adverse Event section
> --> Please specify AE No.VAC_INFO.AE_NB
> --> Please specify: VAC_INFO.V_OTH
> (e.g.: consent withdrawal, Protocol violation, ...)
--> Please select who made the decision: VAC_INFO.DECISION

Study vaccine or placebo injection site
Has the subject experienced any of the following signs/symptoms between Day 0 and Day $6 ?$
SOLSHEET.SOL_YN please select No/Yes for each sign/symptom and complete further as necessary



Has the subject experienced any of the following signs/symptoms between Day 0 and Day 6 ?

SOLSHEET.SOL_YN please select No/Yes for each sign/symptom and complete further as necessary
Record temperatures if during the solicited period at least one oral/axillary/tympanic measure is above or equal to $37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ or at least one rectal measure is above or equal to $38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$.



## (*) Gastrointestinal symptoms include nausea, vomiting, diarmoea and/or abdominat pain

If any of these adverse events meets the definition of serious, complete a Serious Adverse Event Report to GSK Biologicals Study Contact for SAE reporting within 24 hours.

Did the subject return for this visit?
VIS_INFO.VIS_FLG
-->
--> Go to next screen
--> Please select one major reason:

VIS_INFO.V_REAS
--> Please complete a SAE Report
--> Please specify SAE Report No.
--> Tick box if SAE is fatal: VIS_INFO.FATAL
--> Please complete Non-Serious Adverse Event section
--> Please specify AE No. or solicited AE VIS_INFO.AE_NB VIS_INFO.SYMP_COD
--> Please specify the reason (only if the subject has spontaneously explained it):
Please specify:
VIS_INFO.REAS_COM
--> Except death, please select who made the decision:
--> Please select who made the decision:

## VIS_INFO.DECISION

## --> Study discontinuation

Tick box only if permanent discontinuation, i.e. if the subject definitively withdraws from the study

## VIS_INFO.DISCNT

In this case, terminate the CRF:
Complete Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information, if applicable and Study Conclusion.

## BLOOD SAMPLE

Has a blood sample been taken for ELISA (approximately 8 mL )? LABSHEET.SAMPTAKE

For GSK: Reconciled (CDR only)
LABSHEET.SAMPRDAT
--> Date if different from visit date:

LABSHEET.RECONCIL


## CMI SAMPLE

Has a blood sample been taken for CMI response determination (approximately 30 mL )?

$$
\begin{aligned}
& \text {--> Date if different from visit date: } \\
& \text {--> Time of sample: } \\
& \\
& \text {--> Number of tubes: } \\
& \text { hh }
\end{aligned}
$$

For GSK: Reconciled

$$
\begin{aligned}
& \text { for GSK: Red } \\
& \text { (CDR only) }
\end{aligned}
$$

## If visit 4 coincides with visit 5, only the visit 5 will be completed

Did the subject return for this visit?

```
VIS_INFO.VIS_FLG --> Date of visit: ACTDATES.ACTRDATE
--> Go to next screen
```

--> Please select one major reason:

VIS_INFO.V_REAS
--> Please complete a SAE Report
--> Please specify SAE Report No.
VIS_INFO.SAE_CASE
--> Tick box if SAE is fatal: vIS_INFO.FATAL
--> Please complete Non-Serious Adverse Event section
--> Please specify AE No.
or solicited AE
VIS_INFO.AE_NB
VIS_INFO.SYMP_COD
--> Please specify the reason (only if the subject has spontaneously explained it):
Please specify:
VIS_INFO.REAS_COM
--> Except death, please select who made the decision:
--> Please select who made the decision:

VIS_INFO.DECISION
--> Study discontinuation
Tick box only if permanent discontinuation, i.e. if the subject definitively withdraws from the study
VIS_INFO.DISCNT
In this case, terminate the CRF:
Complete Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information, if applicable and Study Conclusion.

Visit 4 will occur within Months 4 to 13 for a Blood Sampling at the start of the last cycle of chemotherapy (if at least two months after the previous Blood Sampling (Visit 3/Month2))

## If Visit 4 coincides with Phone contact at Month 5, the visit 4 will replace the Month 5 Phone Contact

The subject will be reminded that, after Visit 4, a phone contact between the subject and the investigator and/or his delegate will take place (except at months that coincide with the subject's scheduled visits) to collect information on any event of interest that may have occurred, including:

* SAEs (Section 7.3 of the study protocol);
* pIMDs (Section 7.1.5.1 of the study protocol);
* intercurrent medical conditions (see Section 6.7 of the study protocol),
* the use of any concomitant medication/product/vaccine/treatment which could impact the immune response or is part of a chemotherapy (Section 6.6.1 of the study protocol);
* or pregnancy (Section 7.3 of the study protocol).

This information will be recorded in the appropriate section of the subject's eCRF.
Has safety information been obtained?
--> Date of contact
ACTDATES.ACTRDATE
VIS_INFO.VIS_FLG --> Please tick the box if the phone contact month 5 coincides with visit 4 VIS_INFO.M5_PC_V4

## If Visit 4 coincides with Phone contact at Month 9, the visit 4 will replace the Month 9 Phone Contact

The subject will be reminded that, after Month 5 phone contact, a phone contact between the subject and the investigator and/or his delegate will take place (except at months that coincide with the subject's scheduled visits) to collect information on any event of interest that may have occurred, including:

* SAEs (Section 7.3 of the study protocol);
* pIMDs (Section 7.1.5.1 of the study protocol);
* intercurrent medical conditions (see Section 6.7 of the study protocol),
* the use of any concomitant medication/product/vaccine/treatment which could impact the immune response or is part of a chemotherapy (Section 6.6.1 of the study protocol);
* or pregnancy (Section 7.3 of the study protocol).

This information will be recorded in the appropriate section of the subject's eCRF.
Has safety information been obtained?
--> Date of contact
ACTDATES.ACTRDATE
VIS_INFO.VIS_FLG --> Please tick the box if the phone contact month 9 coincides with visit 4 VIS_INFO.M9_PC_V4

## If visit 4 coincides with visit 5, only the visit 5 will be completed

Did the subject return for this visit?

| VIS_INFO.VIS_FLG |  |
| ---: | :--- |
| $-->$ | Date of visit: |
| ACTDATES.ACTRDATE |  |

--> Please select one major reason:

VIS_INFO.V_REAS
--> Please complete a SAE Report
--> Please specify SAE Report No.
VIS_INFO.SAE_CASE
--> Tick box if SAE is fatal: VIS_INFO.FATAL
--> Please complete Non-Serious Adverse Event section
--> Please specify AE No.
or solicited AE
VIS_INFO.AE_NB
--> Please specify the reason (only if the subject has spontaneously explained it):
Please specify:
VIS_INFO.REAS_COM
--> Except death, please select who made the decision:
--> Please select who made the decision:

VIS_INFO.DECISION

## BLOOD SAMPLE

Has a blood sample been taken for ELISA (approximately 8 mL )? LABSHEET.SAMPTAKE

For GSK: Reconciled (CDR only)
LABSHEET.SAMPRDAT
--> Date if different from visit date:

LABSHEET.RECONCIL


## CMI SAMPLE

Has a blood sample been taken for CMI response determination (approximately 30 mL )?

$$
\begin{aligned}
& \text {--> Date if different from visit date: } \\
& \text {--> Time of sample: } \\
& \\
& \text {--> Number of tubes: } \\
& \text { hh }
\end{aligned}
$$

For GSK: Reconciled

$$
\begin{aligned}
& \text { for GSK: Red } \\
& \text { (CDR only) }
\end{aligned}
$$

## TRAINING APPLICATION

DEMOGRAPHY

Date of Birth: DEMOG.DOB_RAW
(Enter only month and year)


## SUBJECT STUDY GROUP AND SUB-COHORT



## INFORMED CONSENT

I certify that Informed Consent has been obtained prior to any study procedure.
Informed Consent Date:


Did the subject meet all the entry criteria?
--> tick all boxes corresponding to violations of any inclusion/exclusion criteria.
ELISHEET.ELIGIBIL
Do not enter the subject into the study if he/she failed any of the inclusion or exclusion criteria below.
INCLUSION Tick the boxes corresponding to any of the inclusion criteria the subject failed.

## CRITERIA

Subjects who, ELIGIBIL.CRIT_NR investigator, can comply with the requirements of the protocol

## ELIGIBIL.CRIT_ANS

Written informed consent obtained from the subject
A male or female, aged 18 years or older (has reached legal consent age) at the time of study entry
Subject who has been diagnosed with one or more solid tumours (defined as a solid malignancy)
Subject who is receiving or will receive a cytotoxic or immunosuppressive chemotherapy
Life expectancy of greater than one year
Female subjects of non-childbearing potential may be enrolled in the study
Female subjects of childbearing potential: contracep 30 days<vac + neg preg test + cont contracep

## EXCLUSION <br> CRITERIA

Tick the boxes corresponding to any of the exclusion criteria that disqualified the subject from entry.

Subjects takingELIGIBIL.CRIT_NR .... . ot considered immunosuppressant if not taken with classic chemo

## ELIGIBIL.CRIT ANS

Chronic administration and/or planned administration of systemic glucocorticoids
Previous vaccination against HZ/varicella within 12 months preceding the 1st dose study vacc/plac
Planned administration during the study of an HZ vaccine other than the study vaccine.
Previous chemotherapy course less than one month before first study vaccination
Occurrence of a varicella\HZ episode within the 12 months preceding the first dose of study vacc
History of allergic disease/reaction exacerbated by any component of the vacc/stdy material, equip
Admin or planned admin of a live vaccine within 30 days before or 30 days after study vaccine doses
HIV infection by clinical history;
Acute disease and/or fever at the time of enrolment
Pregnant or lactating female
Female planning to become pregnant during the treatment period and for two months after
--> Please give diagnosis and tick appropriate Past/Current box
GENHIST.MED_COND
Please record details on the current solid tumor in the subject characteristics section at V1, not here.
Please report medication(s) as specified in the protocol and fill in the medication section.

| MedDRA SYSTEM ORGAN CLASS | DIAGNOSIS | PAST / |  |
| :---: | :---: | :---: | :---: |
| CIAGNOS.DIAGTERM |  |  |  |

## DIAGNOSIS FOR SOLID TUMOUR MALIGNANCY

Please indicate which solid tumour malignancy was diagnosed for the subject?
TUM_DIAG.TUM_MAL
please specify: TUM_DIAG.OTH_SPEC

Please specify date of diagnosis
TUM_DIAG.DIAG_DAT

Please specify staging:
TUM_DIAG.STAGING

## SEROLOGICAL EVIDENCE OF VZV

Has the subject been tested for VZV seropositivity?
SERO.TEST_FLG _-.--> SERO.TEST_RES



|  |  | Vaccine name <br> Trade name is preferred | Route |
| :---: | :---: | :---: | :---: |
| HIST_VAC.TRADNAME |  | Date of <br> vaccination * |  |
| For GSK - MON: | HIST_VAC.MD_TRANS |  |  |
| For GSK - CDR: | HIST_VAC.GSK_MOD |  |  |
|  |  |  |  |

## HISTORY OF CHEMOTHERAPY, RADIOTHERAPY AND SURGERY

Please encode chemotherapy/radiotherapy or surgery received before study entry, for the solid tumour for which the subject is included in the fiterythat the chemotherapy (all the cycles given previous to the first administration) should be recorded in the section "Anti-cancer therapy related to the current solid tumour malignancy".

Has the patient received any previous chemotherapy/ radiotherapy or
surgery for the solid tumour for which the subject is included in the study?

$\square$

Schedule: With pre-vacc DURING V1

## PERFORMANCE STATUS (ECOG)

Has performance status (ECOG) been assessed?
PS_ECOG.PS_YN ---> Date assessed: PS_ECOG.PS_DATE
PS_ECOG.PS

Please note that the category " 5 = dead" is not applicable to this study

## BLOOD SAMPLE

Has a blood sample been taken for ELISA (approximately 8 mL )?

--> Date if different from visit date:
LABSHEET.RECONCIL

## PREGNANCY TEST

Has a pregnancy test been done?
LABSHEET.SAMPTAKE
SERUM TEST SHOULD BE PERFORMED ONLY IF REOUIRED BY COUNTRY, LOCAL OR ETHICS

--> Pregnancy test result:
LABSHEET.SAMPRDAT
LABO_CRF.RAWRES


## VACCINE ADMINISTRATION - DOSE 1

Pre-vaccination temperature: vs.vsORRES
Has Study vaccine or placebo been administered?
--> Date of administration: VAC_INFO.VACCRDAT
VACCPROD.V_ADM ${ }_{\text {if }}$ different from visit date)

| --> Administered treatment number VACC_TRT.V_TRT |  |
| :---: | :---: |
| --> Please give reason hereafter |  |
|  | - IM |
| --> Protocol administration Site/Side/Route Deltoid | - Non Dominant/ Dominant VACCPROD.P_AP |
|  | Site: VACCPROD.P_APSITE |
| --> Has the vaccine been administered according to the prome | ocol administration site, side, route? |
| Specify site. | Specify Side: VACCPROD.P_APSIDE |
|  | Route: VACCPROD.P APROUT |
| Specify side: VACCPROD.P_SIDE |  |
| Specify route: |  |

--> If relevant, comment on administration:

## VACCPROD.VADM_COM

## If no vaccination,

--> Please select the major reason for non administration
VAC_INFO.V_REAS
--> Please complete a SAE Report
--> Please specify SAE Report No.
--> Please complete Non-Serious Adverse Event section
--> Please specify AE No. VAC_INFO.AE_NB
--> Please specify: VAC_INFO.V_OTH
(e.g.: consent withdrawal, Protocol violation, ...)
--> Please select who made the decision: VAC_INFO.DECISION

Study vaccine or placebo injection site
Has the subject experienced any of the following signs/symptoms between Day 0 and Day $6 ?$
SOLSHEET.SOL_YN please select No/Yes for each sign/symptom and complete further as necessary



Has the subject experienced any of the following signs/symptoms between Day 0 and Day 6 ?

SOLSHEET.SOL_YN please select No/Yes for each sign/symptom and complete further as necessary
Record temperatures if during the solicited period at least one oral/axillary/tympanic measure is above or equal to $37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ or at least one rectal measure is above or equal to $38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$.



If any of these adverse events meets the definition of serious, complete a Serious Adverse Event Report to GSK Biologicals Study Contact for SAE reporting within 24 hours.

Did the subject return for this visit?
VIS_INFO.VIS_FLG
-->
-->
--> Please select one major reason:

VIS_INFO.V_REAS
--> Please complete a SAE Report
--> Please specify SAE Report No.
--> Tick box if SAE is fatal: VIS_INFO.FATAL
--> Please complete Non-Serious Adverse Event section
--> Please specify AE No. or solicited AE VIS_INFO.AE_NB VIS_INFO.SYMP_COD
--> Please specify the reason (only if the subject has spontaneously explained it):
Please specify:
VIS_INFO.REAS_COM
--> Except death, please select who made the decision:
--> Please select who made the decision:

## VIS_INFO.DECISION

## --> Study discontinuation

Tick box only if permanent discontinuation, i.e. if the subject definitively withdraws from the study

## VIS_INFO.DISCNT

In this case, terminate the CRF:
Complete Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information, if applicable and Study Conclusion.

## BLOOD SAMPLE

Has a blood sample been taken for ELISA (approximately 8 mL )?

--> Date if different from visit date:
LABSHEET.RECONCIL

## PREGNANCY TEST

Has a pregnancy test been done?
LABSHEET.SAMPTAKE
SERUM TEST SHOULD BE PERFORMED ONLY IF REOUIRED BY COUNTRY, LOCAL OR ETHICS

--> Pregnancy test result:
LABSHEET.SAMPRDAT
LABO_CRF.RAWRES


## VACCINE ADMINISTRATION - DOSE 2

| Pre-vaccination temperature: | vs.vsorres | Route:vs.vsLoc | (preferred) |
| :---: | :---: | :---: | :---: |

Has Study vaccine or placebo been administered?
--> Date of administration: VAC_INFO.VACCRDAT
VACCPROD.V_ADM ${ }_{\text {if }}$ different from visit date)

--> If relevant, comment on administration:

## VACCPROD.VADM_COM

## If no vaccination,

--> Please select the major reason for non administration
VAC_INFO.V_REAS

> --> Please complete a SAE Report
> --> Please specify SAE Report Nor solicited AE VAC_INFO.SYMP_COD
> --> Please complete Non-Serious Adverse Event section
> --> Please specify AE No.VAC_INFO.AE_NB
> --> Please specify: VAC_INFO.v_OTH
> (e.g.: consent withdrawal, Protocol violation, ...)
--> Please select who made the decision: VAC_INFO.DECISION

Study vaccine or placebo injection site
Has the subject experienced any of the following signs/symptoms between Day 0 and Day $6 ?$
SOLSHEET.SOL_YN please select No/Yes for each sign/symptom and complete further as necessary



Has the subject experienced any of the following signs/symptoms between Day 0 and Day 6 ?

SOLSHEET.SOL_YN please select No/Yes for each sign/symptom and complete further as necessary
Record temperatures if during the solicited period at least one oral/axillary/tympanic measure is above or equal to $37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ or at least one rectal measure is above or equal to $38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$.



If any of these adverse events meets the definition of serious, complete a Serious Adverse Event Report to GSK Biologicals Study Contact for SAE reporting within 24 hours.

Did the subject return for this visit?
VIS_INFO.VIS_FLG
-->
-->
--> Please select one major reason:

VIS_INFO.V_REAS
--> Please complete a SAE Report
--> Please specify SAE Report No.
--> Tick box if SAE is fatal: VIS_INFO.FATAL
--> Please complete Non-Serious Adverse Event section
--> Please specify AE No. or solicited AE VIS_INFO.AE_NB VIS_INFO.SYMP_COD
--> Please specify the reason (only if the subject has spontaneously explained it):
Please specify:
VIS_INFO.REAS_COM
--> Except death, please select who made the decision:
--> Please select who made the decision:

## VIS_INFO.DECISION

## --> Study discontinuation

Tick box only if permanent discontinuation, i.e. if the subject definitively withdraws from the study

## VIS_INFO.DISCNT

In this case, terminate the CRF:
Complete Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information, if applicable and Study Conclusion.

## BLOOD SAMPLE

Has a blood sample been taken for ELISA (approximately 8 mL )? LABSHEET.SAMPTAKE

For GSK: Reconciled (CDR only)
LABSHEET.SAMPRDAT
--> Date if different from visit date:

LABSHEET.RECONCIL


## CMI SAMPLE

Has a blood sample been taken for CMI response determination (approximately 30 mL )?

$$
\begin{aligned}
& \text {--> Date if different from visit date: } \\
& \text {--> Time of sample: } \\
& \\
& \text {--> Number of tubes: } \\
& \text { hh }
\end{aligned}
$$

For GSK: Reconciled

$$
\begin{aligned}
& \text { for GSK: Red } \\
& \text { (CDR only) }
\end{aligned}
$$

## If visit 4 coincides with visit 5, only the visit 5 will be completed

Did the subject return for this visit?

```
VIS_INFO.VIS_FLG --> Date of visit: ACTDATES.ACTRDATE
--> Go to next screen
```

--> Please select one major reason:

VIS_INFO.V_REAS
--> Please complete a SAE Report
--> Please specify SAE Report No.
VIS_INFO.SAE_CASE
--> Tick box if SAE is fatal: vIS_INFO.FATAL
--> Please complete Non-Serious Adverse Event section
--> Please specify AE No.
VIS_INFO.AE_NB
--> Please specify the reason (only if the subject has spontaneously explained it):
Please specify:

> VIS_INFO.REAS_COM
--> Except death, please select who made the decision:
--> Please select who made the decision:

VIS_INFO.DECISION
--> Study discontinuation
Tick box only if permanent discontinuation, i.e. if the subject definitively withdraws from the study
VIS_INFO.DISCNT
In this case, terminate the CRF:
Complete Medication, Concomitant Vaccination, (S)AE sections, Pregnancy Information, if applicable and Study Conclusion.

Visit 4 will occur within Months 4 to 13 for a Blood Sampling at the start of the last cycle of chemotherapy (if at least two months after the previous Blood Sampling (Visit 3/Month2))

## If Visit 4 coincides with Phone contact at Month 5, the visit 4 will replace the Month 5 Phone Contact

The subject will be reminded that, after Visit 4, a phone contact between the subject and the investigator and/or his delegate will take place (except at months that coincide with the subject's scheduled visits) to collect information on any event of interest that may have occurred, including:

* SAEs (Section 7.3 of the study protocol);
* pIMDs (Section 7.1.5.1 of the study protocol);
* intercurrent medical conditions (see Section 6.7 of the study protocol),
* the use of any concomitant medication/product/vaccine/treatment which could impact the immune response or is part of a chemotherapy (Section 6.6.1 of the study protocol);
* or pregnancy (Section 7.3 of the study protocol).

This information will be recorded in the appropriate section of the subject's eCRF.
Has safety information been obtained?
--> Date of contact
ACTDATES.ACTRDATE
VIS_INFO.VIS_FLG --> Please tick the box if the phone contact month 5 coincides with visit 4 VIS_INFO.M5_PC_V4

## If Visit 4 coincides with Phone contact at Month 9, the visit 4 will replace the Month 9 Phone Contact

The subject will be reminded that, after Month 5 phone contact, a phone contact between the subject and the investigator and/or his delegate will take place (except at months that coincide with the subject's scheduled visits) to collect information on any event of interest that may have occurred, including:

* SAEs (Section 7.3 of the study protocol);
* pIMDs (Section 7.1.5.1 of the study protocol);
* intercurrent medical conditions (see Section 6.7 of the study protocol),
* the use of any concomitant medication/product/vaccine/treatment which could impact the immune response or is part of a chemotherapy (Section 6.6.1 of the study protocol);
* or pregnancy (Section 7.3 of the study protocol).

This information will be recorded in the appropriate section of the subject's eCRF.
Has safety information been obtained?
--> Date of contact
ACTDATES.ACTRDATE
VIS_INFO.VIS_FLG --> Please tick the box if the phone contact month 9 coincides with visit 4 VIS_INFO.M9_PC_V4

## If visit 4 coincides with visit 5, only the visit 5 will be completed

Did the subject return for this visit?

| VIS_INFO.VIS_FLG |  |
| ---: | :--- |
| $-->$ | Date of visit: |
| ACTDATES.ACTRDATE |  |

--> Please select one major reason:

VIS_INFO.V_REAS
--> Please complete a SAE Report
--> Please specify SAE Report No.
VIS_INFO.SAE_CASE
--> Tick box if SAE is fatal: vIS_INFO.FATAL
--> Please complete Non-Serious Adverse Event section
--> Please specify AE No.
or solicited AE
VIS_INFO.AE_NB
--> Please specify the reason (only if the subject has spontaneously explained it):
Please specify:
VIS_INFO.REAS_COM
--> Except death, please select who made the decision:
--> Please select who made the decision:

VIS_INFO.DECISION

## BLOOD SAMPLE

Has a blood sample been taken for ELISA (approximately 8 mL )? LABSHEET.SAMPTAKE

For GSK: Reconciled (CDR only)
LABSHEET.SAMPRDAT
--> Date if different from visit date:

LABSHEET.RECONCIL


## CMI SAMPLE

Has a blood sample been taken for CMI response determination (approximately 30 mL )?

$$
\begin{aligned}
& \text {--> Date if different from visit date: } \\
& \text {--> Time of sample: } \\
& \\
& \text {--> Number of tubes: } \\
& \text { hh }
\end{aligned}
$$

For GSK: Reconciled

$$
\begin{aligned}
& \text { for GSK: Red } \\
& \text { (CDR only) }
\end{aligned}
$$



Have any vaccines required to be reported as per protocol other than the study vaccine(s) been administered?

CVSHEET.CV_-FLAG Please complete the following table


Have any vaccines required to be reported as per protocol other than the study vaccine(s) been administered?

CVSHEET.CV_-FLAG Please complete the following table


In case of SAE, please note the following: medications recorded in the SAE Report must not be reported again here.
The chemotherapy should be recorded in the specific section, NOT here
Have any medications that are required to be reported per protocol been administered?
--> Please complete the following table


In case of SAE, please note the following: medications recorded in the SAE Report must not be reported again here.
The chemotherapy should be recorded in the specific section, NOT here
Have any medications that are required to be reported per protocol been administered?
--> Please complete the following table


Please report serious adverse events only in the Serious Adverse Event Report, not here

## Please report potential immune mediated diseases (pIMDs) using the SAE Report, not here

Have any non-serious adverse events that are required to be reported per protocol occurred?
AESHEET.AE_FLAG ${ }^{-->}$please complete the following table


Please report serious adverse events only in the Serious Adverse Event Report, not here

## Please report potential immune mediated diseases (pIMDs) using the SAE Report, not here

Have any non-serious adverse events that are required to be reported per protocol occurred?
AESHEET.AE_FLAG ${ }^{-->}$please complete the following table


## ANTI-CANCER THERAPY(IES) RELATED TO THE CURRENT SOLID TUMOUR MALIGNANCY

Please encode all chemotherapy, radiotherapy and immunotherapy cycles for the solid tumour for which the subject is included in the study.

Has the patient received any anti-cancer therapy(ies) for the solid tumour for which he/she is included?


## ANTI-CANCER THERAPY(IES) RELATED TO THE CURRENT SOLID TUMOUR MALIGNANCY

Please encode all chemotherapy, radiotherapy and immunotherapy cycles for the solid tumour for which the subject is included in the study.

Has the patient received any anti-cancer therapy(ies) for the solid tumour for which he/she is included?


## Relevant medical / family history Pregnancy report number: 10Р_HIST.PREG_NB

This report should be completed according to the protocol reporting requirements. (Report pregnancy of subject's partner only when specified in the protocol)

Who is this report being completed for? §OP_HIST.PARTNER
Mother's date of birth: OP_HIST.MDOBDTC (Enter only month and year)

Date of last menstrual period: OP_HIST.LMPDTC Estimated date of delivery: OP_HIST.ESTDLDTC
Was the mother using a method of contraception? Specify: OP_HIST.CONTMET
Type of conception: OP_HIST.CONC_TP
Relevant laboratory tests and procedures (e.g. ultrasound, amniocentesis and chorionic villi sampling including dates of tests and procedures): OP_HIST.LAB_YN
OP_HIST.LAB_DET

| Previous pregnancies? | OP_HIST.PRPRG YN |  |
| :---: | :---: | :---: |
|  | Type of pregnancy | Number |
|  | OP_PRPRG.PRG_TP | OP_PRPRG.PRG_CNT |



| Medical condition | Start date | Ongoing at time |
| :---: | :---: | :---: |
| End date |  |  |
| PREGNANCY REPORT (Part 1/3) |  | 26/02/2014 15:13:10 <br> e-N@ble - Parameters 3.5.1 |

## of pregnancy

OP_RMC.RMC_DESC
For GSK - SAF: OP_RMC.RMC_MOD

OP_RMC.RMCSDTC OP_RMC.RMC_ONG

Any additional factors in mother, father or family that may have an impact on the outcome of the pregnancy (including habitual exposure such as alcohol / substance abuse, chronic illnesses, familial birth defect / genetic / chromosomal disorders and medication use)?
For familv historv. specify who is concerned (uncle, grand-father,...)
OP HIST.AD FACT

OP_HIST.COMMENTS

Was the subject withdrawn from the study as a result of this pregnancy? OP_HIST.WITHDRAW

## Schedule: Sections

## Drug exposure

Investigational product(s) / Study vaccine(s):

| Visit | Vacc. Date | Vacc. <br> Adm. | Not Adm. | No info | Treatment nb | Dose nb | Time Ons | Un |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| OP_STDVA.ACT_DESC | OP_STDVA.DATE_VAC |  |  |  | OP_STDVA.TREAT |  | OP_ST | vaL |  |
|  |  |  |  |  | OP_STDVA.P_DOSE |  |  | OP_STDVA.TTO_UNIT |  |

Enter below ALL medications (e.g. prescription, OTC, etc.) and non-investigational vaccines taken by the mother 60 days before or during pregnancy
Non-investigational product(s): OP_DRGEX.MED_YN


GlaxoSmithKline

## Schedule:



## Pregnancy Status

If any of the outcomes / associated events fulfil the criteria of a SAE, complete a SAE report.

| Pregnancy outcome: $\quad$OP_OUTC.PROUTCOM |  |
| :--- | :--- |
|  | * This outcome must be recorded as an SAE |

Method used for delivery: OP_OUTC.DELIVMET

## Foetal / neonatal information

Number of neonates:

$$
\text { Gestational weeks at birth / miscarriage / termination: } \quad \text { weeks }
$$

OP_OUTC.WKCNT

|  | Infant's gender: <br> OP_NNINF.SEX | Length: <br> OP_NNINF.HEIGHT_U |  | Weight: | Apgar score (0-10): |  | R_3 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |  |
|  |  |  |  | P_NNINF.WEIGHT_U | OP_NNINF.APGAR_1 | OP_NNINF.APG |  |
|  |  |  | OP_NNINF.HEIGHT | T OP_NNI | GHT -OP_NNINF | R_2 |  |

OP_OUTC.DETAILS

Administrative comments: Enter below any comments not related to the clinical description of the event: technical issue, reason for mistake, late reporting,...

## Serious Adverse Event (SAE) detaidsse enter 1 SAE/Diagnosis per event field

* These fields must be completed to save the screen



## Serious Adverse Event (Part 2/6)

## Seriousness Specify reason(s) for considering this event as SAE, tick all that

 For 'Non-Serious pIMD', no seriousness criteria must be ticked```
    Results in death --> Autopsy performed --> Summarise findings in narrative
OC_CRIT.DEATH
    Is life threatening
OC_CRIT.LIFE_THR
Requires hospitalisation or prolongation of hospitalisation --> Provide admission and discharge date(s) in narrative OC_CRIT.REQ_HOSP
Results in disability / incapacity (substantial / permanent) OC_CRIT.DIS_INC
Congenital anomaly / birth defect in the offspring OC_CRIT.C_ANOMAL
Other --> Specify in narrative OC_CRIT.CL_SIGN
```

Is the SAE linked to a 'Pregnancy episode'?

Does the report involve parent or child? OC_DEMOG.PREG_STATUS OC_DEMOG.PC_INDIC

## For SAFETY Team ONLY

Date of Birth:

OC_DEMOG.BIRTH_DT
Country:

OC_SAFAD.COUNTRY

Date of first onset:
Relationship:
OC_DEMOG.F_ONS_DT

OC_DEMOG.RELATION

| Visit | Vacc. Date | Vacc. Adm. | Not Adm. | No info | Treatment nb | Dose nb |  | Unit | Sae dose link? |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| OC_STDVA.ACT_DESC | OC_STDVA.DATE_VAC |  |  |  | OC_STDVA.TREATM |  | OC_STDVA.TTO_VAL |  | OC_STDVA.S |
|  |  |  |  |  | OC_STDVA.P_DOSE |  |  | OC_STDVA.TTO_UNIT |  |

Relevant medication(s): any medication that may help explain the SAE, may have caused the SAE or was used to treat the SAE


Vaccination(s): ONLY vaccination other than investigational which may have caused the SAE

|  |  |  | Route | Vaccination date | Therapy code |
| :---: | :---: | :---: | :---: | :---: | :---: |
| oc_cmvac.tradname | cmvac.manufact |  | OC_CMVAC.MED_ROUT | oc_CMVAC.medsrdat | oc_CMVAC.th_Code |
| TTO since last dose: | oc_cmvac.tto_vac oc_cmvac.t | OC_CMVAC.GSk_MOD | SAF: | OC_CMVAC.TH_MOD |  |

## Subject's relevant medical condition(s) / risk factor(s)?

any past or current medical disorder, allergy, surgery that may be RELEVANT to the SAE.
Relevant additional details, family or social history should be described in narrative.
OC_MDFLG.RMC_FLG


## Relevant diagnostic result(s)elevant tests: those done to diagnose or confirm the SAE or rule out other diagnoses.

OC_LABSH.LAB_YFirst attempt to enter the Test name using the drop down menu from the grid. For tests not found in the grid, record the
Test entered in grid information in the free text section. If NONE of the tests can be found in the grid, enter 'No test found' in the field hereafter


## General narrative comments Do NOT enter all in CAPS

Please provide a clear (this narrative will be provided to regulatory authorities) and brief chronological description (with dates) of the clinical course of the event including:

- Associated signs and symptoms
- Clinical evolution (hospitalisation, outcome, description of sequelae if any, autopsy results, etc.)
- Non-drug treatment such as surgery
- Other information useful for the medical assessment of the case (e.g. reason for diagnosis if not obvious or if diagnosis changed)
- Relevant additional risk factors including family or social history (negative sentence can also be helpful)
- Possible cause(s) of the event
- Rationale for relationship when SAE is possibly related to study product, concomitant product or study procedure


Administrative comments: Enter below any comments not related to the clinical description of the event: technical issue, reason for mistake, late reporting, etc...

## For safety team ONLY

Oceans Id: OC_SAFAD.OCEAN_IDDE Case Id: OC_SAFAD.CASE_REF

## PHYSICIAN REVIEW

## Reviewer Name:

Review Status:

## Last upload date:

 Last Responsible Person: Request Upload:OC_SAFAD.LSTULOAD
OC_SAFAD.LST_RESP
Case type: OC_SAFAD.CASE_TYP

## Case type

OC_SAFAD.REQDLOAD

Last review date:
Comment:

## Patient Status

MDRVIS.PID_STAT

## Treatment and follow-up phase

Medical review performed up to visit: (Tick all the visits that were medically reviewed. Do not tick a visit if the visit was blank, i.e. do not tick if CRF study continuation question is neither Yes, nor No)

```
MDRVIS.PRE_Y nation visit
MDRVIS.V1_Y (Month 0-admin 1)
MDRVIS.V2_Y (Month 1-admin 2)
MDRVIS.V3_Y (Month 2)
MDRVIS.V4_Y 'Months 4 to 13 (Month 6)
    MDRVIS.V4_PC5 h 5 coincides with visit 4
    MDRVIS.V4_PC9 h 9 coincides with visit 4
MDRVIS.PC5_Y ; phone contact (Month 5)
MDRVIS.PC9_Y I phone contact (Month 9)
MDRVIS.V5_Y (Month 13)
    MDRVIS.V4_V5 des with visit 5
MDRVIS.STCONC_Y iclusion
    MDRVIS.REVREAD r CRDL review: activity:
```

MDRVIS.MDR_ACT

MDRVIS.MDRNAME
MDRVIS.OTHMDR

MDRVIS.LSTREVDT

```
MDR comment(s)/finding(s)
```


## MDRVIS.MCOMREV



CRDL review comments
CDMREW.CCOMREV

MDR_ELIM.PROVIOYN<br>I protocol deviations observed for this patient amongst the criteria listed below:<br>(Tick all that apply)

Add a row by applicable criteria

$\qquad$

## List of investigators, IEC/IRB and distribution of subjects

| Investigator | Sub-Investigator | Center no. | Description of Research Facility, Hospital/ Institution, and Address | Name of IEC/IRB Committee, Address | Numb er of Subje cts | \% of Subje cts* |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Canada |  |  |  |  |  |  |
| Diaconescu, Razvan | Chamakhi, Ines <br> Gaudet, Guylaine <br> Lesperance, Bernard <br> Moquin, Jean-Pierre <br> Rousseau, Julie <br> Roy, Josee-Anne <br> Tosikyan, Axel <br> Whittom, Renaud | PPD | Hopital du Sacre-Coeur de Montreal, J3040, 5400 Boulevard Gouin West, Montreal, Québec, H4J 1C5, Canada | Hospital du Sacre-Creur de Montreal, 5400 boul. Gouin Ouest, Montreal (Quebec) H4J IC5 | 3 | 1.1 |
| Li, Jing | Bin, James Disperati, Patricia Shao, Richard | PPD | Toronto East General Hospital, Oncology Clinical Trials, 825 Coxwell Avenue, Toronto, Ontario, Canada, M4C 3E7 | Ontario Cancer Research Ethics Board, MaRS Centre, South Tower, Suite 800, 101 College Street, Toronto, Ontario, Canada, M5G 0A3 | 2 | 0.8 |
| McNeil, Shelly | Halperin, Scott Langley, Joanne Mailman, Tim | -PPD | IWK Health Centre, CTRC, Goldbloom Pavilion, 4th Floor, 5850 / 5980 University Avenue, Halifax, Nova Scotia, Canada, B3K 6R8 | Capital Health Research Ethics Board, Centre for Clinical Research, Room 118, 5790 University Avenue, Halifax, Nova Scotia, Canada B3H IV7 <br> IWK Health Centre Research, 5850/5980 University Avenue, PO Box 9700, Halifax, Nova Scotia B3K6R8, Canada. | 1 | 0.4 |

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| Investigator | Sub-Investigator | Center no. | Description of Research Facility, Hospital/ Institution, and Address | Name of IEC/IRB Committee, Address | Numb er of Subje cts | $\begin{aligned} & \text { \% of } \\ & \text { Subje } \\ & \text { cts* }^{*} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Czech Republic |  |  |  |  |  |  |
| Stahalova, Vladimira | Betlachova, Lucie | PPD | FN Bulovka, Ustav radiacni onkologie, Na Truhlarce 100, Praha 8, Czech Republic, 18000 | Ethics Committee, University Hospital Hradec Kralove, Sokolska 581, 50005 Hradec Kralove | 5 | 1.9 |
| France |  |  |  |  |  |  |
| Blay, Jean-Yves | Bachelot, Thomas Cassier, Philippe Heudel, PierreEtienne <br> Pérol, Maurice Ray-Coquard, Isabelle | PPD | CRLCC Léon Bérard, Département Cancérologie Médicale, 28 rue Laennec, Lyon Cedex 08, France, 69373 | Comite de Protection des Personnes SUD-EST IV, Centre Leon Berard, 28 rue Laennec, 69373 LYON CEDEX 08 | 1 | 0.4 |
| Legouffe, Eric | Chapelle, Angelique | PPD | Centre ONCOGARD, Institut de Cancérologie du Gard, Rue du Professeur Henri Pujol, Nîmes cedex 9, France, 30029 | Comite de Protection des Personnes SUD-EST IV, Centre Leon Berard, 28 rue Laennec, 69373 LYON CEDEX 08 | 2 | 0.8 |
| Maurina, Tristan | Adotevi, Olivier <br> Dobi, Erion <br> Montcuquet, Philippe <br> Pivot, Xavier <br> Villanueva, Cristian | -PPD | CHU de Besançon - Hôpital Jean Minjoz, Service d'Oncologie, 3, boulevard Alexandre Fleming, Besançon cedex, France, 25030 | Comite de Protection des Personnes SUD-EST IV, Centre Leon Berard, 28 rue Laennec, 69373 LYON CEDEX 08 | 4 | 1.5 |

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| Investigator | Sub-Investigator | Center no. | Description of Research Facility, Hospital/ Institution, and Address | Name of IEC/IRB Committee, Address | Numb er of Subje cts | \% of Subje cts* |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Moisy, Nancy | Di Rito, Alessia D'Onofrio, Ida | PPD | Centre Médical de Forcilles, Service ORL, Ferolles-Attilly, France, 77150 | Comite de Protection des Personnes SUD-EST IV, Centre Leon Berard, 28 rue Laennec, 69373 LYON CEDEX 08 | 13 | 4.9 |
| Korea, Republic of |  |  |  |  |  |  |
| Im, Seock Ah |  | PPD | Seoul National University Hospital, Department of Internal Medicine, 101 Daehangro, Jongno-gu, Seoul, Korea, Republic of, 110-744 | Seoul National University College of Medicine/Seoul National University Hospital IRB, 101, Daehak-ro Jongnogu, Seoul, 110-744, Korea | 8 | 3.0 |
| Jung, Kyung-Hae |  | PPD | Asan Medical Center, 388-1 pungnap-dong, songpa-gu, Seoul, Korea, Republic of, 138736 | Asan Medical centre Institutional Review Board, 88, 43-gil, Olympic-ro, Songpa-gu, Seoul 138-736 | 17 | 6.4 |
| Kim, Yeul Hong |  | PPD | Korea University Anam Hospital, 126-1, Anam-Dong 5-ga, Sungbuk-Ku, Seoul, Korea, Republic of, 136-705 | Korea University Anam Hospital Institutional Review Board, 73 Inchon-ro, Seongbuk-gu, Seoul, Korea, Republic of, 02841 | 10 | 3.8 |

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| Investigator | Sub-Investigator | Center no. | Description of Research Facility, Hospital/ Institution, and Address | Name of IEC/IRB <br> Committee, Address | Numb er of Subje cts | $\%$ of Subje cts* |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Spain |  |  |  |  |  |  |
| Delgado Mingorance, Ignacio | Blanco Campanario, Esperanza <br> Gómez-Ulla Astray, Jacobo Jaraquemada Peláez, Teresa Mediano Rambla, María Dolores Puerto Picas, Jose Maria Rodríguez Mowbray, José Ramón | PPD | Hospital Infanta Cristina, Unidad De Cuidados Intensivos, Avenida de Elvas S/N, Badajoz, Spain, 6080 | Comité de Investigación, Hospital Infanta Cristina, Avda. de Elvas, s/n. C.P. 06080 Badajoz, SPAIN | 36 | 13.5 |
| García Foncillas, Jesús | Arranz Cozar, Juan Luis <br> Carames Sánchez, Cristina <br> Casado Echarren, Victoria <br> del Campo, Teresa <br> Deschamps, Ambar <br> Hernández Guerrero, <br> Tatiana <br> Rubio Romero, <br> Gustavo <br> Villamor Mielgo, José <br> Miguel | PPD | Fundación Jiménez Díaz, Av. Reyes Católicos, 2, Madrid, Spain, 28040 | Comité de Investigación, Fundacion Jimenez Diaz, Avda. Reyes Católicos, 22840, Madrid, SPAIN | 2 | 0.8 |

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| Investigator | Sub-Investigator | Center no. | Description of Research Facility, Hospital/ Institution, and Address | Name of IEC/IRB Committee, Address | Numb er of Subje cts | \% of Subje cts* |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Gómez Raposo, César | Casado Saenz, Enrique Zambrana Tevar, Francisco | PPD | Hospital Infanta Sofia, Paseo de Europa 34, San Sebastian de los Reyes, Spain, 28702 | Comité de Investigación, Hospital Infanta Sofía, Secretaría Técnica del Hospital la Paz, $\mathrm{P}^{0}$ de la Castellana 261, Escuela de enfermería planta 4, despacho 424, 28064, Madrid | 6 | 2.3 |
| Grande Pulido, Enrique | Alcalde Pampliega, <br> Rebeca <br> Díaz-Agero Pérez, <br> Cristina <br> Ferreiro Monteagudo, <br> Reyes <br> Garrido López, Pilar <br> Guillén Ponce, <br> Carmen <br> Longo Muñoz, <br> Federico <br> López Fresneña, <br> Nieves <br> Lopez Miranda, <br> Elena <br> Martínez Jáñez, <br> Noelia <br> Pachón Olmos, <br> Vanessa <br> Pita López, María | PPD | Hospital Ramón y Cajal, Ctra.de Colmenar Viejo km.9,1, Madrid, Spain, 28034 | Comité de Investigación, Hospital Ramón y Cajal, Ctra de Colmenar Viejo, Km 9,100. Puerta -2 Dcha, 28034, Madrid, SPAIN | 14 | 5.3 |


| Investigator | Sub-Investigator | Center no. | Description of Research Facility, Hospital/ Institution, and Address | Name of IEC/IRB Committee, Address | Numb er of Subje cts | \% of Subje cts* |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | José <br> Robustillo Rodela, <br> Ana <br> Rodríguez Garrote, Mercedes <br> Vaz Salgado, $\mathrm{M}^{a}$ Angeles |  |  |  |  |  |
| López Martín, José Antonio | Adeva Alfonso, Jorge <br> Calvo Ferrándiz, <br> Aitana <br> Robles Díaz, Luis | PPD | Hospital Doce de Octubre, Ctra. de Andalucía Km. 5,4, Madrid, Spain, 28041 | Comité de Investigación, Hospital 12 de Octubre, Centro Ambulatorio, bloque D, planta 6á, Avda. De Córdoba s/n, 28041, Madrid | 3 | 1.1 |
| Marrupe González, David | García Adrián, Silvia Méndez Ureña, Miguel Quibén Pereira, rosa | PPD | Hospital de Móstoles, Río Jucar, $\mathrm{s} / \mathrm{n}$, Móstoles (Madrid), Spain, 28460 | Comité de Investigación, Hospital Universitario de Móstoles, Unidad de asesoria jurídica, $2^{\text {a }}$ planta, C/ Río Júcar, s/n, 28935, Móstoles, Madrid, SPAIN | 10 | 3.8 |
| Martín Jiménez, Miguel | Álvarez Álvarez, <br> Rosa <br> Arranz Arija, Jose <br> Angel <br> Blanco Codesido, <br> Montserrat <br> Escobar Alvarez, <br> Yolanda <br> García Alfonso, Pilar | PPD | Hospital Gregorio Marañón, C/ Dr. Esquerdo, 46, Madrid, Spain, 28007 | Comité de Investigación, Hospital General Universatario, Gregorio Marañon C/Maiquez, $\mathrm{n}^{\circ} 7$, planta baja, Pabellón de Investigación, 28009, Madrid | 8 | 3.0 |

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| Investigator | Sub-Investigator | Center no. | Description of Research <br> Facility, Hospital/ Institution, <br> and Address | Name of IEC/IRB <br> Committee, Address | Numb <br> er of <br> Subje <br> cts |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | García Gómez, <br> Ramón <br> González del Val <br> Subje <br> cts* |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  | Subirats, Ricardo <br> Jerez Gilarranz, <br> Yolanda <br> López López, Cristina <br> López-Tarruella <br> Cobo, Sara <br> Márquez Rodas, lván <br> Muñoz Martín, <br> Andrés <br> Palomero Plaza, <br> Maria Isabel <br> Rodríguez Pérez, <br> Paz <br> Sabín Domínguez, <br> Pilar |  |  |  |  |  |

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| Investigator | Sub-Investigator | Center no. | Description of Research Facility, Hospital/ Institution, and Address | Name of IEC/IRB Committee, Address | Numb <br> er of <br> Subje cts | \% of Subje cts* |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Gutiérrez Sanz, <br> Lourdes <br> Méndez García, <br> Miriam <br> Núñez Martín, Rafael <br> Palka Gotlowska, <br> Magda <br> Pérez Calleja, David <br> Provencio, Mariano <br> Rubio Martínez, <br> Judith <br> Ruiz Casado, Ana <br> Sánchez Ruiz, <br> Antonio |  |  |  |  |  |
| Puente Vázquez, Javier | Alfonso Sansegundo, Rosario Gonzalez Larriba, Jose Luis Moreno Antón, Fernando | PPD | Clínico San Carlos, Servicio de Oncología, C/ Dr. Martín Lagos, s/n, Madrid, Spain, 28040 | Comité de Investigación, Hospital Clinico San Carlos, Ciudad Universitaria, C/Doctor Martín Lagos $\mathrm{s} / \mathrm{n}$, Planta 1, Puerta G. Ala Norte | 10 | 3.8 |
| Rodríguez Moreno, Juan Francisco | Álvarez Gallego, Rafael Calvo Aller, Emiliano Calvo Plaza, Isabel Cubillo Gracián, Antonio Fernández Abad, | PPD | Centro Oncológico Integral Clara Campal, C/ Oña, 10, Madrid, Spain, 28050 | Comité de Investigación, Centro Oncológico Integral Clara Campal, Hospital Universitario de Madrid, Monteprincipe 25, 28660 Boadilla, Madrid | 18 | 6.8 |

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| Investigator | Sub-Investigator | Center no. | Description of Research Facility, Hospital/ Institution, and Address | Name of IEC/IRB Committee, Address | Numb er of Subje cts | \% of Subje cts* |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Maria <br> Garcia Estevez, <br> Laura <br> García-Donas, Jesús <br> Rodríguez Pascual, <br> Jesús <br> Romero Laorden, Nuria |  |  |  |  |  |
| Rubio Viqueira, Belen Díaz Pedroche, Carmen (FPI) | Aguilar Romo, Eva <br> María <br> Gajate Bureau, Pablo <br> González Cortijo, <br> Lucía <br> González González, <br> Federico <br> Hornedo Muguiro, <br> Javier <br> Pérez Carrión, <br> Ramón | PPD | Hospital Quirón Madrid, c/ Diego de Velázquez, 1, Pozuelo de Alarcón/Madrid, Spain, 28223 | Comité de Investigación Quirón Madrid, Hospital Universitario Quirón Madrid, Servicio de Oncología Médica, c/ Diego de Velázquez 1, planta -1, 28223 Pozuelo de Alarcón, Madrid, Hospital Universitario Puerta de Hierro, C/ Joaquín Rodrigo 2, 28222, Majadahonda, Madrid, SPAIN | 17 | 6.4 |
| Ruiz Camps, María Isabel | Biosca Gómez de Tejada, Mercedes Campins Martí, Magda Martínez Gómez, Xavier Uriona Tuma, Sonia María | PPD | Hospital Vall d' Hebrón, Passeig de la Vall d'Hebrón, 119, Barcelona, Spain, 8035 | Comité de Investigación, Hospital Vall d’Hebrón, 119129, Edificio Institut de Recerca, Planta 3 ${ }^{\text {a }}$, 08035, Barcelona, SPAIN | 8 | 3.0 |


| Investigator | Sub-Investigator | Center no. | Description of Research Facility, Hospital/ Institution, and Address | Name of IEC/IRB Committee, Address | Numb er of Subje cts | \% of Subje cts* |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| United Kingdom |  |  |  |  |  |  |
| Farrugia, David | Benstead, Kim <br> Reed, Nick <br> Shepherd, Stephen | PPD | Cheltenham General Hospital, Sandford Road, Cheltenham, Gloucestershire, United Kingdom, GL53 7AN | NHS, Health Research Authority, NRES Committee London - South East, HRA, Ground Floor, Skipton House, 80 London Road, London, United Kingdom, SE16LH NHS, Health Research Authority, NRES Committee London - South East, Bristol Research Ethics Committee Centre, Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT | 5 | 1.9 |
| Forrest, Jenny | Bliss, Peter <br> Ford, Victoria <br> Napier, Mark <br> Nassar, Ayman <br> Scatchard, Kate <br> Sheehan, Denise <br> Srinivasan, Rajaguru | PPD | Royal Devon \& Exeter Hospital, Oncology Clinical Trials, Room S142, Cherrybrook, Barrack Road, Exeter, United Kingdom, EX2 5DW | NHS, Health Research Authority, NRES Committee London - South East, HRA, Ground Floor, Skipton House, 80 London Road, London, United Kingdom, SE16LH NHS, Health Research Authority, NRES Committee London - South East, Bristol Research Ethics Committee Centre, Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT | 3 | 1.1 |

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116427 (ZOSTER-028)

| Investigator | Sub-Investigator | Center no. | Description of Research Facility, Hospital/ Institution, and Address | Name of IEC/IRB <br> Committee, Address | Numb er of Subje cts | \% of Subje cts* |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Kristeleit, Hartmut | Ahmad, Shahreen <br> Maisey, Nick <br> Pintus, Elias <br> Tsoukalas, Nikolaos | PPD | The Queen Elizabeth Hospital, Stadium Road, Woolwich, London, United Kingdom, SE18 4QH | NHS, Health Research Authority, NRES Committee London - South East, HRA, Ground Floor, Skipton House, 80 London Road, London, United Kingdom, SE16LH NHS, Health Research Authority, NRES Committee London - South East, Bristol Research Ethics Committee Centre, Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT | 5 | 1.9 |
| Last, Kim | Belvedere, Ornella Chan, Samuel Mekki, Rasheid | PPD | York Hospital, Wigginton Road, York, United Kingdom, YO31 8HE | NHS, Health Research Authority, NRES Committee London - South East, HRA, Ground Floor, Skipton House, 80 London Road, London, United Kingdom, SE16LH NHS, Health Research Authority, NRES Committee London - South East, Bristol Research Ethics Committee Centre, Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT | 4 | 1.5 |

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116427 (ZOSTER-028)
$\left.\begin{array}{|l|l|l|l|l|l|l|}\hline \text { Investigator } & \text { Sub-Investigator } & \text { Center no. } & \begin{array}{l}\text { Description of Research } \\ \text { Facility, Hospital/ Institution, } \\ \text { and Address }\end{array} & \begin{array}{l}\text { Name of IEC/IRB } \\ \text { Committee, Address }\end{array} & \begin{array}{l}\text { Numb } \\ \text { er of } \\ \text { Subje } \\ \text { cts }\end{array} \\ \hline \text { Lowndes, Sarah of } \\ \text { Subje } \\ \text { cts* }\end{array}\right\}$

[^18]
## Representative written information for patient and sample consent forms

## CONFIDENTIAL

## Instructions for Local ICF development

The LOC should ensure that all local legal regulatory requirements are satisfied before finalizing the Local ICF. It is strongly recommended to align the content of the Local ICF with the content of the Model ICF and this template.

When developing a Local ICF, all changes to the content that affect the meaning of the Model ICF should be justified and documented locally. Any black bold text in the final Model ICF is GSK Biologicals' mandatory wording and should be retained, any alterations or additions to this text must be communicated to the central team prior to the finalization of the local ICF.

Refer to Appendix B Best Practices document for the development of the Local ICF.
Note: In the final Local ICF all text should be in the same format i.e. any bold text must be in normal font and red hidden text must not be retained.

Refer to INS_51928, SOP_54823, GUI_51905 and GUI-BIO-CLIN-0014 for more information.
(Delete the instructions above from the Final Local ICF).

## INFORMED CONSENT FORM

Study Identification: ZOSTER-028 (116427)

## Study Title: An observer-bind study to evaluate immunogenicity and safety of GSK Biologicals' Herpes Zoster vaccine GSK1437173A in adults $\geq 18$ years of age with solid tumours receiving chemotherapy

Model ICF Version Number: 01 (replace with Version of Local ICF)
Date: 07/SEP/2012 (replace with Date of Local ICF)
Company Name: GlaxoSmithKline (GSK) Biologicals S.A.
Subject/Patient Identification: Insert subject/patient ID here What is consent?

Consent means agreeing to take part in this research study. You can decide if you want to take part in this study or not. Please take time to read the following information and ask the study doctor or study staff if you have any questions. They will explain the study fully to you. You can talk in confidence with family, friends and your doctor to help you make a decision. You must sign the Consent pages at the end of this form if you decide to join this study. You will receive a copy of this form.

## Why is this study being done?

This study is to test how well a new vaccine works to protect against shingles. The vaccine will be tested in people who received chemotherapy for solid tumours. You will soon get such a treatment or have just gotten the first cycle of chemotherapy. Therefore, we invite you to join this research study.

Shingles is a disease caused by a virus. The same virus causes chickenpox. You can get chickenpox when you are a child. After that, the virus stays in the body but is asleep. You can get shingles when the virus wakes up.

If your immunity (resistance to disease) decreases, the risk of getting shingles increases. This can happen from a disease or some treatments (such as chemotherapy). A decreased immunity could also impact the way you are responding to a vaccine.

Shingles most often occurs on the chest or back. But it can occur anywhere on the body such as the face or on an arm or leg. The first sign of shingles is often pain, tingling, itching or burning. The first sign is mostly on only one side of your body. This pain can even be caused by air blowing on the skin. Clothes rubbing against the skin or hot or cold temperatures can also cause pain. Within a few days, a rash appears in the same place. The rash may begin as red spots, but blisters soon form. This typical rash is mostly painful and may be itchy. Some people with shingles also have fever, muscle aches and headaches. After the rash has healed, sometimes people can still feel pain in the same place. This is called post-herpetic neuralgia, or PHN and can last for months or even years.

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The new vaccine against shingles that GlaxoSmithKline (GSK) Biologicals is testing in people is not yet approved. The doctors cannot yet prescribe it to the public. It is being studied first. That is why we call it a study vaccine. One part of the study vaccine is recognised by the part of the body that makes defense responses. The study vaccine is made from only a part of the shingles virus. So there is no risk that the study vaccine itself will cause shingles or chicken pox. It is thought that the body's defense response to the study vaccine will protect you from getting shingles. A substance known as adjuvant is part of the study vaccine to help make a better response. This study will look at your body's defense responses during your course of chemotherapy. For this, we will need to collect blood samples before and after vaccination.

If you decide to take part in this study, you will be enrolled into 1 of 2 treatment groups. Both groups will get 2 shots ( 1 to 2 months apart). Both shots will either be the active study vaccine or a solution without active ingredients called placebo.

In both groups you can receive the first vaccination either at least 10 days before chemotherapy or on the first day of the first (or second) chemotherapy cycle.

## How is GSK involved?

GSK is a company that studies and makes vaccines, medicines and other health products. GSK planned and organized this study. GSK pays the study doctor and the institution to run this study.

GSK will be the owner of the study results. GSK plans to use these to get patents, sell the vaccine in the future or make profits in other ways. You will not be paid for any part of this.

The information and materials we give you about this study are confidential and belong to GSK. We ask that you keep it private. You can share this information with your doctor, family or friends when discussing about your participation in this study and your healthcare.

## Who can join this study?

You can only be in this study if:
a. You are aged 18 years or older [Please update in accordance with the age of legal consent in your country] when you join the study. You can follow the study procedures;
b. You will be receiving chemotherapy for solid tumours and have not had more than two cycles of chemotherapy;
c. You have not had chickenpox or shingles in the year before you get the first shot of the study vaccine or placebo;
d. You did not get a vaccine against chickenpox or shingles in the year before;
e. You did not get in the past and are not planning to get certain medication, vaccines or therapy. Your study doctor will explain this;

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f. If you are a woman, you must not be pregnant or nursing a baby;
g. If you are a woman and can get pregnant, for a certain time you must agree to use contraception. This time is from 30 days before your first injection. It lasts until 2 months after your second injection.

The study doctor will also check some other aspects before you can join this study.
You can ask your study doctor for more details.

## What does this study involve?

About 200 people will take part in this study. When we have enough people taking part in this study, we will not include or invite any more. It is possible that you will be screened, but not vaccinated, even if you meet all criteria.

The study will be done in different countries worldwide.
If you agree to take part then you will receive either the study vaccine or the placebo. A computer will be used to put you into one of these 2 treatment groups (study vaccine or placebo). You have an equal chance of being in either group. Neither you nor the study doctor can choose a group. Neither you nor the study doctor, or other study staff, will know which treatment group you are in. You will find out what group you are in after the whole study is finished. The study doctor can also tell you in case of a medical emergency.

A computer will also decide if you should start your vaccination (study vaccine or placebo) at least 10 days before the start of chemotherapy or on the first day of the first (or second) chemotherapy cycle.

A total of 6 office visits planned for the study. There is a visit some time before the day of the first vaccination (called the Pre-vaccination visit). This visit is followed by 5 study visits (Visits 1 to 5) and 2 phone contacts (Month 5 and Month 9).

The procedures during the study visits are listed below. They are also summarized in Appendix A.

If you agree to take part in this study, it is important that you follow all the study procedures explained below.

- The Pre-vaccination visit will occur up to about 30 days before Visit 1 and can occur on the same day as Visit 1.
- The study staff will explain the study to you. They will ask you questions about your health and medications that you are taking. This is needed to see if you can take part in this study.
- You will be asked to read and sign this Informed Consent Form (ICF).
- If you are a woman, you will have a urine pregnancy test at the Pre-vaccination visit.
- Visit 1 will be scheduled in relation to your first chemotherapy cycle.

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- Visit 1 will occur at most 1 month before, to as few as, 10 days before the start of your first chemotherapy cycle; or at the first day of your first or second chemotherapy cycle (allowing a 1 day window before or after).
- You will reconfirm if you agree to join [If required by local regulations].
- The study staff will ask you if any changes occurred with respect to your health since the Pre-vaccination visit to confirm that you can take part in the study.
- If needed, the study doctor will check you (called a physical exam) to make sure you are healthy enough to be in the study.
- If you are a woman, we will collect a urine sample for a pregnancy test before vaccination. [Local, if applicable: If a serum pregnancy test is required at your site (e.g., due to requirement of EC/IRB) prior to vaccination at Visits 1 and 2, insert "blood" instead of "urine", and add the appropriate blood sample volume].
- At Visit 1 and all the following visits you will have a blood sampling (*see below) to test your response to the study vaccine.
- At Visit 1 you will get the first injection of either the study vaccine or placebo in the arm. You will have to wait at the study office for at least 30 minutes. This is so the study staff can make sure you are well enough to leave.
- You will receive a safety diary card on the day of each vaccination, for you to fill out at home, and return at your next visit ( $* *$ see below) .
- You should contact the study doctor or the study staff immediately if you get any symptoms that you feel may be serious at any time during the study.
- Visit 2 will occur 1 to 2 months after Visit 1.
- The study staff will ask you if any changes occurred with respect to your health since Visit 1.
- You will return the safety diary card you received at Visit 1 and you will receive a second diary card to write down safety information and information regarding any medication/vaccination taken for the next 30 days ( $* *$ see below).
- If you are a woman, we will collect a urine sample for a pregnancy test before vaccination. [Local, if applicable: If a serum pregnancy test is required at your site (e.g., due to requirement of EC/IRB) prior to vaccination at Visits 1 and 2, insert "blood" instead of "urine", and add the appropriate blood sample volume].
- You will have a blood sampling (*see below) to test your response to the study vaccine.
- At Visit 2 you will receive the second injection of either the study vaccine or placebo in the arm. You will have to wait at the study office for at least 30 minutes. This is so the study staff can make sure you are well enough to leave.
- Visit 3 will occur 1 month after Visit 2.
- The study staff will ask you if any changes occurred with respect to your health since Visit 2.

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- You will return the safety diary card you filled out since the last vaccination (**see below).
- You will have a blood sampling (*see below) to test your response to the study vaccine.
- A Month 5 Phone Contact will happen about 2 months after Visit 3 (***see below), and the study office will contact you by a phone call.
- You will be asked about certain changes in your medical condition and medications.
- Visit 4, is a conditional visit and may occur within Months 4 to 13 ( ${ }^{* * *}$ see below) at the start of your last cycle of chemotherapy (if at least two months after the previous Visit 3).
- Thus, the timing of this particular visit will be variable depending on your chemotherapy schedule and on when you started vaccination in relation to your chemotherapy.
- You will have a blood sampling (*see below) to test your response to the study vaccine.
- A Month 9 Phone Contact will happen about 4 months after the Month 5 Phone Contact ( $* * *$ see below), and the study office will contact you by a phone call.
- You will be asked about certain changes in your medical condition and medications.
- Should Visit 4 occur around Month 9, it will replace the Month 9 Phone Contact.
- Visit 5 will be about 12 months after the second vaccination.
- You will have a blood sampling (*see below) to test your response to the study vaccine.
- You will be in the study for at least 14 months and will be told at that time your participation in the study has ended.

At each Visit and during the Phone Contacts, the study staff will ask about your health, any medicines you took since your previous visit and for how long you took them, as well as if you have received any other vaccination.

At any time during the study, you should contact the study doctor or the study staff immediately should you get any symptoms that you feel may be serious.
*Before the first and second injections at Visit 1 and Visit 2, and at all subsequent visits, about one and a half teaspoonfuls ( $\sim 8 \mathrm{~mL}$ ) of blood will be taken from you. This will be used to test your body's immune response. For some subjects, about one ounce ( $\sim 30 \mathrm{~mL}$ ) of blood will also be taken (at Visits 1, 2, 3 and 5). This is for a different kind of immune test. The study staff will inform you if you are part of this sub-group.
**You will receive a safety diary card on the day of each vaccination. The study staff will explain to you how to complete the safety diary card. The card must be returned to the study office at your next visit. Completion of the safety diary card involves writing:

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- On the day of each vaccination and the following 6 days: write down your temperature, any pain, redness or swelling at the injection site and any medical consultation you had.
- On the day of each vaccination and the following 29 days: write down any other unusual things you experience, any medical consultation you had (outside the regular chemotherapy cycles), and any medication or vaccination you may have taken (outside the regular chemotherapy cycles).
***Should Visit 4 coincide with Month 5 or Month 9, it will replace the Month 5 or the Month 9 Phone Contact, respectively. The study staff will inform you accordingly.

You will receive a card with study contact information. Keep this card with you at all times during the study. Show this card to the medical staff if you need emergency care during the study. The medical staff can then contact your study doctor if needed to ask about the vaccine or product you received.

You will be asked at the end of the study if we can contact you for future related studies. If you agree to be contacted, it does not mean that you have to take part in future related studies. If you do not want to be contacted, we would like to know why. We will record your answer.

## What about pregnancy and breastfeeding?

It is not known if the vaccine used in this study may have an effect on the unborn baby. You will not be able to join this study if you are pregnant or nursing a baby.

If you are a woman who can get pregnant, you will need to use birth control. This will be from 30 days before the first shot, until 2 months after the second shot. The study doctor will tell you about birth control methods that can be used during this study.

You will have a urine pregnancy test at the Pre-vaccination visit and before each vaccination at Visits 1 and 2. [Local, if applicable: If a serum pregnancy test is required at your site (e.g., due to requirement of $\mathrm{EC} / \mathrm{IRB}$ ) prior to vaccination at Visits 1 and 2; insert: "blood" instead of "urine"; and delete: "at the Prevaccination visit and"] The pregnancy test must be negative in order for you to receive the study vaccine.

Tell the study doctor if you are pregnant. If you get pregnant during the study, you may not receive any more vaccine but may remain in the study for follow-up.

## What will happen to samples taken in this study?

As part of the study, you will be asked to give samples of your blood. Your blood samples may be sent to GSK or other laboratories working with GSK including those outside [insert name of country] to:

- measure how your body reacts to the study vaccine.
- ensure the quality of the tests we use for the study vaccine and/or disease(s)


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- improve tests and develop new tests linked to the study vaccine and/or disease(s). These tests will never include testing related to your genes’ hereditary characteristics.
- improve tests and develop new tests linked to the study vaccine and/or disease(s). These tests will never include testing related to your genes' hereditary characteristics. GSK will always ask in advance approval for this research to an independent ethics committee or review board;
- Urine samples will be collected from women for pregnancy testing at the Prevaccination Visit and before each vaccination at Visits 1 and 2. [Local, if applicable: If a serum pregnancy test is required at your site (e.g., due to requirement of $\mathrm{EC} / \mathrm{IRB}$ ) prior to vaccination at Visits 1 and 2, insert "Blood" instead of "Urine", and delete "at the Pre-vaccination Visit and"].

Samples will not be labeled with information that directly identifies you but will be given a code so that it does not directly identify you.

Your samples will be kept for a maximum of 20 years from the end of the study. Any sample remaining at that time will be destroyed.

## Optional tests on your samples:

If you agree, your sample(s) may also be used for future research. GSK will always ask approval for this research to an independent ethics committee or independent review board.

You can choose not to allow these optional tests and still be in the study.

## What side effects or risks can you expect in this study?

The shingles vaccine used in this study has been tested previously in clinical research studies.

We have results from about a thousand people. They all received the active study vaccine. Most of these people (95\%) were 50 years or older. The vaccine has mostly been well tolerated. The most common side effects were at the site of injection. Side effects at the site of the injection included pain, redness, and swelling. They occurred in more than 1 in 10 people (more than $10 \%$ ) who got the vaccine. In fact, more than $50 \%$ of people who got the study vaccine had pain at the injection site. These symptoms were usually mild and resolved within a few days. Other side effects seen in more than $10 \%$ of people who got the vaccine included tiredness, muscle pain, headache, fever and symptoms such as nausea, vomiting, diarrhea and/or abdominal pain. The side effect of shivering was less likely. It occurred in about 1 to $10 \%$ of people who got the vaccine. These symptoms were also usually mild and resolved within a few days.

The shingles vaccine may cause some side effects that are not known at the present time. However, should any new findings (including findings from other studies or in animals) regarding any risks involved with the study vaccine be discovered during the course of the research, you will be notified immediately.

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Unexpected side-effects, like serious allergic reactions, to the vaccine may occur. All the medical equipment to help you in such a case will be available.

When you give blood you may feel faint, or have mild pain, bruising, irritation or redness where the blood is taken. These reactions usually last only a short time.

There may be possible risks to a pregnant woman, embryo, foetus or nursing infant. Such risks are not known at this time. Therefore, you will not be allowed to enter this study if you are pregnant or breastfeeding. You should also not plan a pregnancy or breastfeed before 2 months after you have received the second vaccine dose.

The side effects that you may report in this study will be shared with experts on shingles. The experts will make any recommendations to ensure the safety of the people participating to the study.

Many adults and children have received vaccines that contain a substance known as an "adjuvant". These adjuvants are similar to what is in the vaccine that you may get in this study. Rarely, some of these people have developed illnesses, sometimes serious, called autoimmune diseases, where their immune system harms their own body. These illnesses have also developed in people who have not received these vaccines. We do not know if the study vaccine(s) can actually cause autoimmune diseases. GSK therefore follows this question closely.

## What benefits can you expect in this study?

Taking part in this study may not have a direct benefit for you.
If you get the placebo, there is no expected benefit.
If you get the study vaccine, we do not know yet if it will protect you against shingles.
The study vaccine, study tests, and follow-up by the study doctor will be free of charge. You do not need to pay for these.

Information from this study will help us learn more about shingles vaccines.

## Are there other products or treatment?

Shingles can be treated with:

- Antiviral medication;
- Medication to treat the pain when you have shingles.

There is no approved vaccine available to prevent shingles in people who have received chemotherapy to treat solid tumours.

This section should be completed locally using the most current information regarding the treatments/ vaccines/ products that are available in the country and their important potential benefits and risks. State if there are no alternate treatments.

## Do you have to stay in the study?

You may choose to leave the study at any time, without giving a reason. If you do give a reason, then it may be recorded. Your choice will not change the medical care you receive outside of this study.

We will share with you any new information that may change your choice to stay in the study. We will share this information with you as soon as possible.

Tell the study doctor if you no longer want to take part.
GSK may choose to stop the study or the study doctor may choose to stop your participation in the study at any time. We will then tell you why.

We may ask you to leave the study if:

- Test results show that this study is not right for you;
- You do not follow instructions for treatment or follow-up visits;
- You decide that you want to become pregnant or plan to discontinue contraceptive precautions before 2 months after you received the second vaccination;
- The study doctor thinks it is in your best interest to stop, e.g., if you have specific health problems.


## What happens if you leave the study?

Check local regulations and seek local legal advice for the use of data after subject withdrawal. If any changes are made to this section in the Local ICF compared to the Model ICF, in response to a request from any source, these should be discussed with the central study team and GSK Biologicals ICF taskforce for alignment prior to the finalization of the local ICF, so that the impact for database collection can be taken into account.

No more information about you will be collected after you leave the study. All the information and samples collected before you left the study will still be used.

If the doctor becomes aware of any relevant safety information about you after you left the study, this will be collected.

We may also contact you later for information. This is to help us better understand the safety profile of the vaccine.

## What about your personal and medical information?

If changes are made to this text it needs to be checked with the local Legal team that this is aligned with local rules and regulations.

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It is very important to us that information about you stays private and safe. GSK will protect your information according to the law.
When you sign this consent form you agree that we can use information about you as follows.

1. Information about you may be checked by GSK and others, like agencies that approve and monitor studies. This is to make sure that the study is being run properly.
2. Besides that, only the staff at this study site can use information that can be linked to you. Such information is your name and address. The information can only be used for the purpose of the study.
3. Study information will be labeled with a code number (for example, PPD It will not include your name or address. The study doctor has the link between your name and the code number.
4. The link between your name and the code number will not be shared. Only the code number and coded information will be sent to GSK.
5. GSK will use your coded information for research only.
6. GSK may:

- keep it electronically. GSK may analyze it by computer to find out what the study is telling us.
- share it with agencies that approve new vaccines and medicines.
- share it with people who check that the study is done properly. Such people are the for instance the ethics committee.
- combine it with results from other studies to learn more about the vaccine and shingles. This may help us to assess the risks and benefits of GSK (or other) vaccines or medicines. Or it may help to better understand the disease.
- publish study results in medical journals, for meetings and on the internet for other researchers to use.
- share coded information with other companies, organizations or universities to carry out research..
Data about you collected during the trial may be moved to, stored and used in the country where you live. These data may also be moved to, stored and used in another country where GSK or those working with GSK have offices.

Use of this information may take place in countries with lower data protection rules than the country you live in. If your data is moved to another country, it will still be treated as stated in this ICF. GSK will ensure this.

Information about this study will appear on the GSK Clinical Study Register http://www.gsk-clinicalstudyregister.com/. This information may also appear in clinical trial registries in countries where this study is done.

If you withdraw your consent for us to use information about you, you can no longer stay in the study.

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At any time, you may ask to see your personal information. You may ask to correct it if needed. Please contact the person responsible for your rights in this study. This contact information is given in this consent form.

In some cases, we may not be able to share your study information with you. This could be anytime during the study. But the study doctor will share any important medical information.

## What happens if you get hurt while taking part in this study?

[Please add appropriate local compensation for injury terms.]
Compensation for injury language to be used for GSK sponsored studies in the UK (and in countries which have no special local requirements)

If you are hurt by a vaccine / product or a clinical procedure that you would not have been given outside this study, you will be compensated. Your study doctor can give you information about the compensation guidelines for this kind of hurt.

Signing this consent form does not change any legal rights you may have.

## GSK sponsored studies in Other Regions

[The participating countries should complete if there are local compensation for injury requirements.]

## Will you be paid for being in the study?

[This section should be completed locally.]
You will not be paid for taking part in this study. OR
We will reimburse you for the cost of travelling to your study visits. You may receive up to [amount] for travel / per visit.

## Do you have to pay anything to be in the study?

[Information related to this section is added at a regional or country level when it is appropriate for a study and/or is required by local practice)]

## Who should you contact if you have questions?

Person to contact for any questions: name, address, telephone number.
Person to contact about your rights: name, address, telephone number.
Person to contact in case of injury: name, address, telephone number.

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## Consent statement

I,
(Printed name of Subject)

- confirm that I have read the written information (or have had the information read to me) for study 116427 (ZOSTER-028) ICF version 01, 07 SEP 2012 ( 15 pages) (to be updated locally), and the study procedures have been explained to me by study staff during the consent process for this study.
- confirm that I have had the chance to ask questions about this study and I am satisfied with the answers and explanations that have been given.
- understand that I give access to data about me to authorised persons described in this information sheet.
- I know what will happen to my blood/tissue samples.
- understand that by signing this form any of my identifiable medical information given to someone that is not a health care provider is not protected by the US federal privacy rules called the HIPAA Privacy Regulations. [For US sites only]
- have been given time and opportunity to consider taking part in this study.

Tick as appropriate (this decision will not affect your ability to enter the study):
I agree that my family doctor will be told that I am taking part in the study.


## Tick as appropriate:

I agree that my biological samples may be used for future research. GSK will always ask approval for this research to an independent ethics committee or independent review board. I understand that if I select "No", I can still take part in the study.


Subject ID $\qquad$
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[Note: If more than one page, the subsequent page must contain the subject's name.]
*Printed name of subject

I agree to take part in this study.
Signature of subject
Date day/month/ year
Thumbprint of subject* $\qquad$
Date: day/ month/ year

* In case the subject is unable to write.

Printed name of person conducting consent

Signature of person
conducting consent Date: day/ month/ year

I confirm that I am independent of the study, that I attended the informed consent process and that I have read the written information for the study.
**Printed name of Witness

Signature of Witness

> Date: day/month/ year
** Witness is only required if the subject is unable to read.

## YOU MAY HAVE HAD A PRE-VACCINATION VISIT AND YOU MAY HAVE SIGNED THE ICF MORE THAN 30 DAYS AGO. IN THIS CASE, YOU NEED TO CONFIRM CONSENT BEFORE VISIT 1.

Signature of subject


* In case the subject is unable to write.

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## Appendix A Summary of activities during the study

The table shows what will happen at each study visit for all participants in the study.

| Visit number and time point | What will happen at this visit |
| :---: | :---: |
| Pre-vaccination visit (up to 30 days before Visit 1 and can be on the same day as Visit 1) | 1. The study doctor or staff will explain the study. <br> 2. If you agree to join, you will sign the consent form. <br> 3. You will answer medical questions to see if you can join the study. <br> 4. Women who may get pregnant will have a urinary pregnancy test. |
| Visit 1 at Day 0/Month 0 (visit of your first vaccination) | 1. You will reconfirm if you agree to join [If required by local regulations]. <br> 2. The study staff will ask you if any changes occurred with respect to your health. since the Pre-vaccination visit to confirm that you can take part in the study <br> 3. You will answer questions about your Health in the past. <br> 4. If needed, the study doctor will check you (called a physical exam) to make sure you are healthy enough to be in the study. <br> 5. You will get a urine test for pregnancy (only if you are a woman who can get pregnant) ['serum test', in case a serum pregnancy test is required in your site (e.g., due to requirement of EC/IRB)]. <br> 6. The study doctor or staff will take your temperature. <br> 7. The study staff will take a blood sample* for baseline that can be used to compare with immune responses after you receive the study vaccine or placebo. <br> 8. You will receive the first injection of the study vaccine or placebo. <br> 9. You must wait for 30 minutes in the study office to make sure there are no serious reactions before you leave the study office. <br> 10. You will receive a safety diary card to write down: <br> - Your temperature, any pain, redness or swelling at the injection site and any medical consultation you had from the day of vaccination and the next 6 days, <br> - If you were not scheduled to have the vaccination during your chemotherapy cycle, you will write down if you experience tiredness, headache, muscle ache or gastrointestinal symptoms (nausea, vomiting, diarrhea or stomach ache) or shivering from the day of vaccination and the next 6 days, <br> - Any other unusual things you experience, any medical consultation you had, and any medication or vaccination you may have taken from the day of vaccination and the next 29 days. |
| Visit 2 at Month 1 ( 1 to 2 months after Visit 1) | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. <br> 4. You will get a urine test for pregnancy (only if you are a woman who can get pregnant) [Local: If a serum pregnancy test is required at your site (e.g., due to requirement of EC/IRB) prior to vaccination at Visits 1 and 2, insert "blood" instead of "urine"]. <br> 5. The study doctor or staff will take your temperature. <br> 6. The study staff will take a blood sample* for measurement of immune responses. <br> 7. You will receive the second injection. <br> 8. You must wait for 30 minutes in the study office to make sure there are no serious reactions before you leave the study office. <br> 9. You will return the safety diary card you received at Visit 1 and you will receive a second diary card to write down safety information and information regarding any medication/vaccination taken for 30 days. |

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| Visit number and time point | What will happen at this visit |
| :---: | :---: |
| Visit 3 at Month 2 (1 month after Visit 2) | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. <br> 4. The study staff will take a blood sample* for measurement of immune responses. <br> 5. You will return the safety diary card you received at Visit 2. |
| Phone Contact at Month 5** | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. |
| Visit 4 between Month 4 and Month $13^{* *}$ | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. <br> 4. The study staff will take a blood sample* for measurement of immune responses. |
| Phone Contact at Month 9** | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. |
| Visit 5 <br> (12 months after Visit 2) | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. <br> 4. The study staff will take a blood sample* for measurement of immune responses. <br> 5. You will be informed that your participation in the study has ended. <br> 6. The study staff will ask you if you would be willing to participate to a follow-up study. |

* Before the first and second injections at Visit 1 and Visit 2, and at all subsequent visits, about one and a half teaspoonfuls ( $\sim 8 \mathrm{~mL}$ ) of blood will be taken. For a sub-group of subjects, about an ounce ( $\sim 30 \mathrm{~mL}$ ) of blood will also be taken (at Visits 1, 2, 3 and 5).
** Should Visit 4 coincide with Month 5 or Month 9, it will replace the Month 5 or the Month 9 Phone Contact, respectively. The study staff will inform you accordingly.


## Best Practices Document for the Development of the Local ICF

 Delete the following Appendix in the Final local ICF.
## Appendix B GlaxoSmithKline Biologicals Best Practices Document for the Development of the Local ICF

## Introduction

The local informed consent form (ICF) is created based on the GSK Biologicals internally approved model ICF and is adapted according to country or local requirements.

The model ICF is the recommended content and structure which contains all ICH and GSK required elements and is aligned with the study protocol.

The content of the local ICF should be aligned with the Model ICF and any local specifications and regulations included.

The local GSK approved version should be submitted for ethical/regulatory approval and should be presented to the subject/patient and/or their legally acceptable representative.

It is essential that the version of the local ICF is accurately tracked, with a unique version number, date and reference to the model ICF on which it is based, to ensure that the correct version of the ICF is used and can be identified if needed.

It is strongly recommended to have a final local ICF, back-translated in English, available in the Investigator's study file to ensure site readiness in case of audits and/or inspections.

## Objective

These best practices are intended to give adequate support and to ensure consistency while developing the local ICF from the model ICF.

It is a tool to know what changes are not permitted and what changes can be justified and/or are required per local regulations and site specific information.

The development of the accurate and complete local ICF is a local responsibility and alignment with the model ICF is essential to study conduct.

Any changes made to the local ICF from the model ICF must be documented at local level.

## Human Sample Management

The collection of human tissue samples, the intended use, and secondary use, if retained, and how the subject's confidentiality would be maintained for the retained samples, must be reported in the ICF.

The content of this section must be fully aligned with the Use of Human Samples form. This form allows the central project team to track the actual testing at GSK (or laboratories used for GSK-sponsored studies) with the individual subject's consent and

Best Practices Document for the Development of the Local ICF local regulations. To avoid ethical and legal implications and invalidating the study data, any changes made to this section must be discussed with the central project team and GSK Biologicals' central ICF taskforce for alignment prior to the finalization of the local ICF.

## Subject/patient data after withdrawal

The retention of samples collected and data recorded before withdrawal and the continued collection of safety information after withdrawal must be reported in the ICF. Check local regulations and seek local legal advice for the use of data after subject/patient withdrawal. If any changes are made to this section in response to a request from any source, these changes must be discussed with the central project team and GSK Biologicals' central ICF taskforce for alignment prior to the finalization of the local ICF, so that the impact for database collection and sample destruction can be taken into account

## Type of changes

Changes to the local ICF can be classified into 3 categories:

## 'Not permitted' changes

BOLD BLACK mandatory text in the model ICF should not be changed.

## 'Required' changes

Required changes must be made in the local ICF to add country-specific or centerspecific information. (Indicated as BOLD RED text in the model ICF e.g. investigator details).

## 'Justified' changes

Justified changes may be necessary in some countries to comply with local requirements / regulations or to comply with a specific template e.g. country specific compensation guidance text.

In addition, some text can be clarified / simplified, provided the meaning remains the same as in the model ICF and does not contradict or change the intended meaning of the model ICF.

Changes that require a specific rationale or justification, that may be necessary in specific situations e.g. storage duration of samples, or changes required by the relevant Ethics Committees, can also be justified.

## Best Practices per ICF Section

This table describes the type of changes (not permitted, required or justified) for each ICF section of the local ICF compared to the model ICF.

| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| Study Identification |  |  |
| Check if study identification is identical to Model ICF. | Not permitted | The study identification and study number allows us to link the document to the study protocol, the corresponding IRB/IEC approvals, all relevant study documentation and ensures that the subject/patient is linked to the correct study. |
| Study Title |  |  |
| Check if study title is identical to Model ICF. | Not permitted | The study title allows us to link the document to the study protocol, the corresponding IRB/IEC approvals, all relevant study documentation and ensures that the subject/patient is linked to the correct study. |
| ICF Version Number and Date |  |  |
| Update with version and date of Local ICF and check if reference to the Model ICF version and date is included. Specify country and subset if applicable. | Required | It is mandatory to include an ICF version number, the date of the final version, the page number and the total number of pages (for the Local and Model ICF). <br> Each ICF type has to be uniquely identified and must include a reference to the source. The version of the local ICF allows us to link the ICF to the corresponding approval documents. If the version is omitted in the local ICF, the subject may not receive the most up to date ICF and thus may not receive the complete information required to make an informed consent. |
| Company Name |  |  |
| Check if company name is GlaxoSmithKline (GSK) Biologicals S.A. or the local GSK affiliate if this is required by local regulations. | Justified | A change to this section is permitted if it is justified by local regulations. <br> For some countries, the local GSK affiliate should be indicated as Company Name. |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| Subject/Patient Identification |  |  |
| Check whether there is space foreseen to insert the subject ID. | Required | The subject/patient ID should be mentioned on the ICF to be able to link the subject/patient ID with the corresponding source documents and RDE entries. |
| Header |  |  |
| Check if study identification in header is identical to Model ICF. | Not permitted | The study identification and study number allows us to link the document to the study protocol, the corresponding IRB/IEC approvals, all relevant study documentation and ensures that the subject/patient is linked to the correct study. |
| Footer |  |  |
| Indicate version of Local ICF and check if reference to the Model ICF version is included. Specify country and subset if applicable. | Required | It is mandatory to include an ICF version number, the date of the final version, the page number and the total number of pages (for the Local and Model ICF). <br> Each ICF type has to be uniquely identified and must include a reference to the source. The version of the local ICF allows us to link the ICF to the corresponding approval documents. <br> If the version is omitted in the local ICF, the subject/patient may not receive the most up to date ICF and thus may not receive the complete information required to make an informed consent. |
| What is consent? |  |  |
| Explain the consent process and check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | Freely given and written informed consent must be obtained from each subject/patient/LAR prior to study participation. Informed consent involves an education and information exchange that takes place between the researcher and the potential subject/patient. How the process of consenting looks like, needs to be explained in the |

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\hline \multicolumn{1}{|c|}{ ICF section } \& \multicolumn{1}{|c|}{| Type of |
| :--- |
| changes |} \& \multicolumn{1}{c|}{ Rationale/Impact }

\end{tabular}

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| Type of section <br> changes |


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| ICF section Type of <br> changes <br> Check if the QA (Quality <br> Assurance) on tests related to <br> the study vaccine/ disease <br> (type 2 testing) is reported in <br> the Local ICF. Not permitted |
| QA testing will be done at all times, <br> assuming it is allowed as per <br> individual subject's/patient's <br> consent. If QA testing is not <br> mentioned in the ICF, there is a risk <br> that GSK will be unable to perform <br> the protocol tests and therefore this <br> type of testing cannot be omitted. |
| Check local regulations <br> regarding tests related to the <br> product/disease under study <br> (type 3a and 3b testing). <br> [If there are concerns <br> regarding this text then this <br> should be discussed with the <br> central team and GSK <br> Biologicals' central ICF <br> taskforce for alignment prior to <br> the finalization of the local <br> ICF] |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| Check Local regulations regarding storage duration. Check if the wording "for a maximum of 20 years" is not changed into "for 20 years". [If there are concerns regarding this text then this should be discussed with the central project team and GSK Biologicals' central ICF taskforce for alignment prior to the finalization of the local ICF] | Justified | It is necessary to put a defined storage period in the ICF. As a standard, GSK proposes to store samples for "for a maximum of" 20 years. Attention should be paid to the used wording "for a maximum of" 20 years. This wording allows GSK to cover different situations (e.g. to keep samples for maximum 20 years, to destroy samples when GSK no longer wants to store them or no longer is interested in testing, when physical integrity of some type of samples does not permit such long storage, etc). <br> Any changes to this section should be captured in the UHSF. This will allow the laboratory to take the appropriate measures for sample storage, "for a maximum of 20 " years or as defined in the ICF and documented in the UHSF section called "other". |
| Check local regulations regarding future research. [If there are concerns regarding this text then this should be discussed with the central project team and GSK Biologicals' central ICF taskforce for alignment prior to the finalization of the local ICF] | Justified | A change to this section is justified, since depending on local regulations, this type of testing is allowed or not. However, the wording of the text itself, should not be changed and nothing should be added! We capture this info in the CRF/eCRF by the mean of the UHSF, which contains standard wording so if the wording in the ICF is changed, this will not be matching with the UHSF. This form allows the central project team to track the actual testing at GSK (or laboratories used for GSKsponsored studies) with the individual subject's/patient's consent and local regulations. If this text is changed, there is a risk to use human samples outside the |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
|  |  | subject‘s consent. <br> This has major ethical and legal implications and can lead to a loss of company reputation, lack of confidence, invalid study data, etc.... |
| What side effects or risks can you expect in the study? |  |  |
| Check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | The content of this section is required by ICH-GCP. The reasonably foreseeable risks or inconveniences to the subject should be mentioned in the ICF. If any of this information is omitted in the local ICF, the subject may not receive the complete information required to make an informed consent. Text can be simplified if necessary. <br> Refer to the GSK Position Paper on 'Communication of Individual Immunological Assay Results to Study Sites' for additional information. |
| Check if the text on autoimmune diseases (applicable if product/vaccine contains an adjuvant) is identical to the Model ICF. | Not permitted | The text on autoimmune diseases has been approved by GSK upper management following feedback from Authorities. The AID wording should remain consistent in all projects and countries. There is a reputational risk associated to the fact that GSK might seem to be sharing different information with Subjects/Patients/Externally on AID. |
| Check if the text on Rotarix, if applicable, is identical to the Model ICF. | Not permitted | This text has been approved by GSK upper management following feedback from Authorities. |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| What benefits can you expect in the study? |  |  |
| Check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | The content of this section is required by ICH-GCP. The reasonably expected benefits or indirect benefits or if there is no direct clinical benefit for the subjects/patients must be included in the local ICF. Text can be simplified if necessary |
| Are there other products or treatment? |  |  |
| Check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | It is an ICH-GCP requirement to provide to the subject information on alternative procedures or treatment that may be available and their important potential benefits and risks. <br> Omitting any of this information would be violating the rights of the subject/patient to freely participate to the study and would be putting the company reputation at risk. Text can be simplified if necessary. |
| Add currently available local alternatives, if applicable. | Required | This information must be added locally to the ICF using the most current information regarding the treatments that are available in the country. |
| Do you have to stay in the study? |  |  |
| Explain voluntary participation and check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | The content of this section is required by ICH-GCP. <br> Omitting any of this information would be violating the rights of the subject/patient to freely participate to the study and would be putting the company reputation at risk. Text can be simplified if necessary. |
| What happens if you leave the study? |  |  |
| Check if the text on the use of data after subject/patient withdrawal is identical to the | Justified | The bold text in this section has been approved by Medical Governance. Changes to this |


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| Type of <br> changes |
| Model ICF. <br> [Check local regulations and <br> seek local legal advice] <br> [If the text needs to be changed <br> it should be discussed with the <br> central project team and GSK <br> Biologicals' central ICF <br> taskforce for alignment prior to <br> the finalization of the local |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| Will you be paid for being in the study? |  |  |
| Information related to this section is added at a regional or country level. | Required | The content of this section is required by ICH-GCP and must be included in the ICF so that the subject/patient is well informed before consenting to participation. The anticipated prorated payment or other financial benefit, if any, to the subject for participating in the study should be mentioned in the ICF. <br> Explain if expenses incurred by subjects for clinical visits made because of their participation in the study will be reimbursed or not. |
| Do you have to pay anything to be in the study? |  |  |
| This section is optional. Information related to this section is added at a regional or country level when it is appropriate for a study and/or is required by local practice. | Justified | If appropriate for a study, include here information on cost/expenses that subject/patient will have to bear for taking part in the study i.e., whether the subject/patient or the subject's/patient's insurance will be charged for any study item or procedure. According to ICH-GCP, the anticipated expenses, if any, to the subject/patient for participating in the study should be mentioned. |
| Who should you contact if you have questions? |  |  |
| Add local contact details. | Required | The content of this section is required by ICH-GCP. The subject/patient must have a contact person for further information regarding the study, his rights and who to contact in the event of trialrelated injury. |
| Consent statement |  |  |
| Check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | The consent statement should be aligned with ICH-GCP requirements. Omitting any of the information can have legal |


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| Best Practices Document for the Development of the Local ICF |
| Type of <br> changes |

## References

SOP_54823, Development and implementation of Informed Consent for clinical studies.
GUI_51905, Guidance for Informed Consent documents.
GUI-BIO-CLIN-0014, Guidance for the development of Informed Consent-related documents.

GSK's Position Paper on Communication of Individual Immunological Assay Results To Study Sites.

GSK's Clarification Paper on Handling Data after Subject withdrawal.
GSK's Clarification Paper on Future Use of Biospecimens

## CONFIDENTIAL

## Instructions for Local ICF development

The LOC should ensure that all local legal regulatory requirements are satisfied before finalizing the Local ICF. It is strongly recommended to align the content of the Local ICF with the content of the Model ICF and this template.

When developing a Local ICF, all changes to the content that affect the meaning of the Model ICF should be justified and documented locally. Any black bold text in the final Model ICF is GSK Biologicals' mandatory wording and should be retained, any alterations or additions to this text must be communicated to the central team prior to the finalization of the local ICF.

Refer to Appendix B Best Practices document for the development of the Local ICF.
Note: In the final Local ICF all text should be in the same format i.e. any bold text must be in normal font and red hidden text must not be retained.

Refer to INS_51928, SOP_54823, GUI_51905 and GUI-BIO-CLIN-0014 for more information.
(Delete the instructions above from the Final Local ICF).

## INFORMED CONSENT FORM

Study Identification: ZOSTER-028 (116427)

## Study Title: An observer-bind study to evaluate immunogenicity and safety of GSK Biologicals' Herpes Zoster vaccine GSK1437173A in adults $\geq 18$ years of age with solid tumours receiving chemotherapy <br> Model ICF Version Number: 02 (replace with Version of Local ICF) <br> Date: 02/OCT/2012 (replace with Date of Local ICF) <br> Company Name: GlaxoSmithKline (GSK) Biologicals S.A. <br> Subject/Patient Identification: Insert subject/patient ID here What is consent?

Consent means agreeing to take part in this research study. You can decide if you want to take part in this study or not. Please take time to read the following information and ask the study doctor or study staff if you have any questions. They will explain the study fully to you. You can talk in confidence with family, friends and your doctor to help you make a decision. You must sign the Consent pages at the end of this form if you decide to join this study. You will receive a copy of this form.

## Why is this study being done?

This study is to test how well a new vaccine works to protect against shingles. The vaccine will be tested in people who received chemotherapy for solid tumours. You will soon get such a treatment or have just gotten the first cycle of chemotherapy. Therefore, we invite you to join this research study.

Shingles is a disease caused by a virus. The same virus causes chickenpox. You can get chickenpox when you are a child. After that, the virus stays in the body but is asleep. You can get shingles when the virus wakes up.

If your immunity (resistance to disease) decreases, the risk of getting shingles increases. This can happen from a disease or some treatments (such as chemotherapy). A decreased immunity could also impact the way you are responding to a vaccine.

Shingles most often occurs on the chest or back. But it can occur anywhere on the body such as the face or on an arm or leg. The first sign of shingles is often pain, tingling, itching or burning. The first sign is mostly on only one side of your body. This pain can even be caused by air blowing on the skin. Clothes rubbing against the skin or hot or cold temperatures can also cause pain. Within a few days, a rash appears in the same place. The rash may begin as red spots, but blisters soon form. This typical rash is mostly painful and may be itchy. Some people with shingles also have fever, muscle aches and headaches. After the rash has healed, sometimes people can still feel pain in the same place. This is called post-herpetic neuralgia, or PHN and can last for months or even years.

## Informed Consent Form

## CONFIDENTIAL

Study Identification ZOSTER-028 (116427)
The new vaccine against shingles that GlaxoSmithKline (GSK) Biologicals is testing in people is not yet approved. The doctors cannot yet prescribe it to the public. It is being studied first. That is why we call it a study vaccine. One part of the study vaccine is recognised by the part of the body that makes defense responses. The study vaccine is made from only a part of the shingles virus. So there is no risk that the study vaccine itself will cause shingles or chicken pox. It is thought that the body's defense response to the study vaccine will protect you from getting shingles. A substance known as adjuvant is part of the study vaccine to help make a better response. This study will look at your body's defense responses during your course of chemotherapy. For this, we will need to collect blood samples before and after vaccination.

If you decide to take part in this study, you will be enrolled into 1 of 2 treatment groups. Both groups will get 2 shots ( 1 to 2 months apart). Both shots will either be the active study vaccine or a solution without active ingredients called placebo.

In both groups you can receive the first vaccination either at least 10 days before chemotherapy or on the first day of the first (or second) chemotherapy cycle.

## How is GSK involved?

GSK is a company that studies and makes vaccines, medicines and other health products. GSK planned and organized this study. GSK pays the study doctor and the institution to run this study.

GSK will be the owner of the study results. GSK plans to use these to get patents, sell the vaccine in the future or make profits in other ways. You will not be paid for any part of this.

The information and materials we give you about this study are confidential and belong to GSK. We ask that you keep it private. You can share this information with your doctor, family or friends when discussing about your participation in this study and your healthcare.

## Who can join this study?

You can only be in this study if:
a. You are aged 18 years or older [Please update in accordance with the age of legal consent in your country] when you join the study. You can follow the study procedures;
b. You will be receiving chemotherapy for solid tumours and have not had more than two cycles of chemotherapy;
c. You have not had chickenpox or shingles in the year before you get the first shot of the study vaccine or placebo;
d. You did not get a vaccine against chickenpox or shingles in the year before;
e. You did not get in the past and are not planning to get certain medication, vaccines or therapy. Your study doctor will explain this;

Informed Consent Form

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Study Identification ZOSTER-028 (116427)
f. If you are a woman, you must not be pregnant or nursing a baby;
g. If you are a woman and can get pregnant, for a certain time you must agree to use contraception. This time is from 30 days before your first injection. It lasts until 2 months after your second injection.

The study doctor will also check some other aspects before you can join this study.
You can ask your study doctor for more details.

## What does this study involve?

About 200 people will take part in this study. When we have enough people taking part in this study, we will not include or invite any more. It is possible that you will be screened, but not vaccinated, even if you meet all criteria.

The study will be done in different countries worldwide.
If you agree to take part then you will receive either the study vaccine or the placebo. A computer will be used to put you into one of these 2 treatment groups (study vaccine or placebo). You have an equal chance of being in either group. Neither you nor the study doctor can choose a group. Neither you nor the study doctor, or other study staff, will know which treatment group you are in. You will find out what group you are in after the whole study is finished. The study doctor can also tell you in case of a medical emergency.

A computer will also decide if you should start your vaccination (study vaccine or placebo) at least 10 days before the start of chemotherapy or on the first day of the first (or second) chemotherapy cycle.

A total of 6 office visits planned for the study. There is a visit some time before the day of the first vaccination (called the Pre-vaccination visit). This visit is followed by 5 study visits (Visits 1 to 5) and 2 phone contacts (Month 5 and Month 9).

The procedures during the study visits are listed below. They are also summarized in Appendix A.

If you agree to take part in this study, it is important that you follow all the study procedures explained below.

- The Pre-vaccination visit will occur up to about 30 days before Visit 1 and can occur on the same day as Visit 1.
- The study staff will explain the study to you. They will ask you questions about your health and medications that you are taking. This is needed to see if you can take part in this study.
- You will be asked to read and sign this Informed Consent Form (ICF).
- If you are a woman, you will have a urine pregnancy test at the Pre-vaccination visit.


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- Visit 1 will be scheduled in relation to your first chemotherapy cycle.
- Visit 1 will occur at most 1 month before, to as few as, 10 days before the start of your first chemotherapy cycle; or at the first day of your first or second chemotherapy cycle (allowing a 1 day window before or after).
- You will reconfirm if you agree to join [If required by local regulations].
- The study staff will ask you if any changes occurred with respect to your health since the Pre-vaccination visit to confirm that you can take part in the study.
- If needed, the study doctor will check you (called a physical exam) to make sure you are healthy enough to be in the study.
- If you are a woman, we will collect a urine sample for a pregnancy test before vaccination. [Local, if applicable: If a serum pregnancy test is required at your site (e.g., due to requirement of EC/IRB) prior to vaccination at Visits 1 and 2, insert "blood" instead of "urine", and add the appropriate blood sample volume].
- At Visit 1 and all the following visits you will have a blood sampling (*see below) to test your response to the study vaccine.
- At Visit 1 you will get the first injection of either the study vaccine or placebo in the arm. You will have to wait at the study office for at least 30 minutes. This is so the study staff can make sure you are well enough to leave.
- You will receive a safety diary card on the day of each vaccination, for you to fill out at home, and return at your next visit ( $* *$ see below).
- You should contact the study doctor or the study staff immediately if you get any symptoms that you feel may be serious at any time during the study.
- Visit 2 will occur 1 to 2 months after Visit 1.
- The study staff will ask you if any changes occurred with respect to your health since Visit 1.
- You will return the safety diary card you received at Visit 1 and you will receive a second diary card to write down safety information and information regarding any medication/vaccination taken for the next 30 days ( ${ }^{*}$ see below).
- If you are a woman, we will collect a urine sample for a pregnancy test before vaccination. [Local, if applicable: If a serum pregnancy test is required at your site (e.g., due to requirement of EC/IRB) prior to vaccination at Visits 1 and 2, insert "blood" instead of "urine", and add the appropriate blood sample volume].
- You will have a blood sampling (*see below) to test your response to the study vaccine.
- At Visit 2 you will receive the second injection of either the study vaccine or placebo in the arm. You will have to wait at the study office for at least 30 minutes. This is so the study staff can make sure you are well enough to leave.

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- Visit 3 will occur 1 month after Visit 2.
- The study staff will ask you if any changes occurred with respect to your health since Visit 2.
- You will return the safety diary card you filled out since the last vaccination (**see below).
- You will have a blood sampling (*see below) to test your response to the study vaccine.
- A Month 5 Phone Contact will happen about 2 months after Visit 3 ( ${ }^{* * *}$ see below), and the study office will contact you by a phone call.
- You will be asked about certain changes in your medical condition and medications.
- Visit 4, is a conditional visit and may occur within Months 4 to 13 ( $*^{* *}$ see below) at the start of your last cycle of chemotherapy (if at least two months after the previous Visit 3).
- Thus, the timing of this particular visit will be variable depending on your chemotherapy schedule and on when you started vaccination in relation to your chemotherapy.
- You will have a blood sampling (*see below) to test your response to the study vaccine.
- A Month 9 Phone Contact will happen about 4 months after the Month 5 Phone Contact $(* * *$ see below), and the study office will contact you by a phone call.
- You will be asked about certain changes in your medical condition and medications.
- Should Visit 4 occur around Month 9, it will replace the Month 9 Phone Contact.
- Visit 5 will be about 12 months after the second vaccination.
- You will have a blood sampling (*see below) to test your response to the study vaccine.
- You will be in the study for at least 14 months and will be told at that time your participation in the study has ended.

At each Visit and during the Phone Contacts, the study staff will ask about your health, any medicines you took since your previous visit and for how long you took them, as well as if you have received any other vaccination.

At any time during the study, you should contact the study doctor or the study staff immediately should you get any symptoms that you feel may be serious.
*Before the first and second injections at Visit 1 and Visit 2, and at all subsequent visits, about one and a half teaspoonfuls $(\sim 8 \mathrm{~mL})$ of blood will be taken from you. This will be used to test your body's immune response. For some subjects, about one ounce ( $\sim 30 \mathrm{~mL}$ ) of blood will also be taken (at Visits 1, 2, 3 and 5). This is for a different kind of immune test. The study staff will inform you if you are part of this sub-group.

CONFIDENTIAL
Study Identification ZOSTER-028 (116427)
**You will receive a safety diary card on the day of each vaccination. The study staff will explain to you how to complete the safety diary card. The card must be returned to the study office at your next visit. Completion of the safety diary card involves writing:

- On the day of each vaccination and the following 6 days: write down your temperature, any pain, redness or swelling at the injection site and any medical consultation you had.
- On the day of each vaccination and the following 29 days: write down any other unusual things you experience, any medical consultation you had (outside the regular chemotherapy cycles), and any medication or vaccination you may have taken (outside the regular chemotherapy cycles).
***Should Visit 4 coincide with Month 5 or Month 9, it will replace the Month 5 or the Month 9 Phone Contact, respectively. The study staff will inform you accordingly.
[Include the following statement if material about shingles is provided.] The study doctor will give you material with pictures and information on the signs and symptoms of shingles.

You will receive a card with study contact information. Keep this card with you at all times during the study. Show this card to the medical staff if you need emergency care during the study. The medical staff can then contact your study doctor if needed to ask about the vaccine or product you received.

You will be asked at the end of the study if we can contact you for future related studies. If you agree to be contacted, it does not mean that you have to take part in future related studies. If you do not want to be contacted, we would like to know why. We will record your answer.

## What about pregnancy and breastfeeding?

It is not known if the vaccine used in this study may have an effect on the unborn baby. You will not be able to join this study if you are pregnant or nursing a baby.

If you are a woman who can get pregnant, you will need to use birth control. This will be from 30 days before the first shot, until 2 months after the second shot. The study doctor will tell you about birth control methods that can be used during this study.

You will have a urine pregnancy test at the Pre-vaccination visit and before each vaccination at Visits 1 and 2. [Local, if applicable: If a serum pregnancy test is required at your site (e.g., due to requirement of EC/IRB) prior to vaccination at Visits 1 and 2; insert: "blood" instead of "urine"; and delete: "at the Prevaccination visit and"] The pregnancy test must be negative in order for you to receive the study vaccine.

Tell the study doctor if you are pregnant. If you get pregnant during the study, you may not receive any more vaccine but may remain in the study for follow-up.

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## What will happen to samples taken in this study?

As part of the study, you will be asked to give samples of your blood. Your blood samples may be sent to GSK or other laboratories working with GSK including those outside [insert name of country] to:

- measure how your body reacts to the study vaccine.
- ensure the quality of the tests we use for the study vaccine and/or disease(s)
- improve tests and develop new tests linked to the study vaccine and/or disease(s). These tests will never include testing related to your genes' hereditary characteristics.
- Urine samples will be collected from women for pregnancy testing at the Prevaccination Visit and before each vaccination at Visits 1 and 2. [Local, if applicable: If a serum pregnancy test is required at your site (e.g., due to requirement of $\mathrm{EC} / \mathrm{IRB}$ ) prior to vaccination at Visits 1 and 2, insert "Blood" instead of "Urine", and delete "at the Pre-vaccination Visit and"].

Your samples will be given a code so that it does not directly identify you.
Your samples will be kept for a maximum of 20 years from the end of the study. Any sample remaining at that time will be destroyed.

## Optional tests on your samples:

If you agree, your sample(s) may also be used for future research. GSK will always ask approval for this research to an independent ethics committee or independent review board.

You can choose not to allow these optional tests and still be in the study.

## What side effects or risks can you expect in this study?

The shingles vaccine used in this study has been tested previously in clinical research studies.

We have results from about a thousand people. They all received the active study vaccine. Most of these people ( $95 \%$ ) were 50 years or older. The vaccine has mostly been well tolerated. The most common side effects were at the site of injection. Side effects at the site of the injection included pain, redness, and swelling. They occurred in more than 1 in 10 people (more than $10 \%$ ) who got the vaccine. In fact, more than $50 \%$ of people who got the study vaccine had pain at the injection site. These symptoms were usually mild and resolved within a few days. Other side effects seen in more than $10 \%$ of people who got the vaccine included tiredness, muscle pain, headache, fever and symptoms such as nausea, vomiting, diarrhea and/or abdominal pain. The side effect of shivering was less likely. It occurred in about 1 to $10 \%$ of people who got the vaccine. These symptoms were also usually mild and resolved within a few days.

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The shingles vaccine may cause some side effects that are not known at the present time. However, should any new findings (including findings from other studies or in animals) regarding any risks involved with the study vaccine be discovered during the course of the research, you will be notified immediately.

Unexpected side-effects, like serious allergic reactions, to the vaccine may occur. All the medical equipment to help you in such a case will be available.

When you give blood you may feel faint, or have mild pain, bruising, irritation or redness where the blood is taken. These reactions usually last only a short time.

There may be possible risks to a pregnant woman, embryo, foetus or nursing infant. Such risks are not known at this time. Therefore, you will not be allowed to enter this study if you are pregnant or breastfeeding. You should also not plan a pregnancy or breastfeed before 2 months after you have received the second vaccine dose.

The side effects that you may report in this study will be shared with experts on shingles. The experts will make any recommendations to ensure the safety of the people participating to the study.

Many adults and children have received vaccines that contain a substance known as an "adjuvant". These adjuvants are similar to what is in the vaccine that you may get in this study. Rarely, some of these people have developed illnesses, sometimes serious, called autoimmune diseases, where their immune system harms their own body. These illnesses have also developed in people who have not received these vaccines. We do not know if the study vaccine(s) can actually cause autoimmune diseases. GSK therefore follows this question closely.

## What benefits can you expect in this study?

Taking part in this study may not have a direct benefit for you.
If you get the placebo, there is no expected benefit.
If you get the study vaccine, we do not know yet if it will protect you against shingles.
The study vaccine, study tests, and follow-up by the study doctor will be free of charge. You do not need to pay for these.

Information from this study will help us learn more about shingles vaccines.

## Are there other products or treatment?

Shingles can be treated with:

- Antiviral medication;
- Medication to treat the pain when you have shingles.

There is no approved vaccine available to prevent shingles in people who have received chemotherapy to treat solid tumours.

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Study Identification ZOSTER-028 (116427)
This section should be completed locally using the most current information regarding the treatments/ vaccines/ products that are available in the country and their important potential benefits and risks. State if there are no alternate treatments.

## Do you have to stay in the study?

You may choose to leave the study at any time, without giving a reason. If you do give a reason, then it may be recorded. Your choice will not change the medical care you receive outside of this study.

We will share with you any new information that may change your choice to stay in the study. We will share this information with you as soon as possible.

Tell the study doctor if you no longer want to take part.
GSK may choose to stop the study or the study doctor may choose to stop your participation in the study at any time. We will then tell you why.

We may ask you to leave the study if:

- Test results show that this study is not right for you;
- You do not follow instructions for treatment or follow-up visits;
- You decide that you want to become pregnant or plan to discontinue contraceptive precautions before 2 months after you received the second vaccination;
- The study doctor thinks it is in your best interest to stop, e.g., if you have specific health problems.


## What happens if you leave the study?

Check local regulations and seek local legal advice for the use of data after subject withdrawal. If any changes are made to this section in the Local ICF compared to the Model ICF, in response to a request from any source, these should be discussed with the central study team and GSK Biologicals ICF taskforce for alignment prior to the finalization of the local ICF, so that the impact for database collection can be taken into account.

No more information about you will be collected after you leave the study. All the information and samples collected before you left the study will still be used.

If the doctor becomes aware of any relevant safety information about you after you left the study, this will be collected.

## We may also contact you later for information. This is to help us better understand the safety profile of the vaccine.

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## What about your personal and medical information?

If changes are made to this text it needs to be checked with the local Legal team that this is aligned with local rules and regulations.

It is very important that your personal and medical information stay confidential and secure. Your personal and medical information will be protected in accordance with current law.

When you sign this consent form you agree that your personal and medical information can be used as described here.

- Your personal and medical information may be checked by GSK and others (like agencies that approve and monitor studies). This is to make sure that the study is being run properly.
- Besides that, only the researchers at this study site can use information that identifies you (such as name and address) and only for the purpose of the study.
- Your information collected during the study will be labeled with a code number (for example, PPD It will not include your name or address. The study doctor will have the link between your name and the code number.
- The link between your name and the code number will not be shared. Only the code number and coded information will be sent to GSK.
- GSK will use your coded information for research only, including research looking at improving the quality and efficiency in conducting clinical research trials in general.
- GSK may:
- keep it electronically, and analyse it by computer to find out what the study is telling us. This may be done by GSK or a third party, in which case GSK will ensure that the third party is required to keep your data secure.
- share it with regulatory agencies that approve new vaccines and medicines,
- share it with people who check that the study is done properly (like the independent ethics committee or review boards),
- combine it with results from other studies to learn more about the vaccine and this disease and related conditions. This may help us to assess the risks and benefits of GSK (or other) vaccines or medicines, or to improve disease understanding,
- publish study results in medical journals, for meetings and on the internet for other researchers to use. Your name will not appear in any publication.
- share coded information with other companies, organisations or universities to carry out research, including research looking at improving the quality and efficiency in conducting clinical research trials in general.

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Personal and medical data collected during the trial may be moved to, stored and used in the country where you live or another country where GSK or those working with GSK work.

Use of this information may take place in countries with lower data protection rules than the country where you live. GSK will make sure that if your data are moved to another country, it will still be treated as stated in this Informed Consent Form.

A description of this clinical trial will be available on the GSK Clinical Study Register http://www.gsk-clinicalstudyregister.com/ and may also appear in clinical trial registries in countries in which the clinical study is conducted.

If you withdraw your consent for us to use your personal information you will no longer be able to continue in the study.

At any time, you may ask to see your personal information and correct it if necessary.
In some circumstances you may not be able to access your study information while the study is ongoing. However the study doctor will share any important medical information if it is relevant to your health during the course of the study.

## What happens if you get hurt while taking part in this study?

[Please add appropriate local compensation for injury terms.]
Compensation for injury language to be used for GSK sponsored studies in the UK (and in countries which have no special local requirements)

If you are hurt by a vaccine / product or a clinical procedure that you would not have been given outside this study, you will be compensated. Your study doctor can give you information about the compensation guidelines for this kind of hurt.

## GSK sponsored studies in Other Regions

[The participating countries should complete if there are local compensation for injury requirements.]

## Will you be paid for being in the study?

[This section should be completed locally.]
You will not be paid for taking part in this study. OR
We will reimburse you for the cost of travelling to your study visits. You may receive up to [amount] for travel / per visit.

## Do you have to pay anything to be in the study?

[Information related to this section is added at a regional or country level when it is appropriate for a study and/or is required by local practice)]

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Study Identification ZOSTER-028 (116427)
Who should you contact if you have questions?
Person to contact for any questions: name, address, telephone number.

Person to contact about your rights: name, address, telephone number.
Person to contact in case of injury: name, address, telephone number.
$\qquad$
CONFIDENTIAL
Study Identification ZOSTER-028 (116427)

## Consent statement

I,
(Printed name of Subject)

- confirm that I have read the written information (or have had the information read to me) for study 116427 (ZOSTER-028) ICF Version 02, 02 OCT 2012 ( 16 pages) (to be updated locally), and the study procedures have been explained to me by study staff during the consent process for this study.
- confirm that I have had the chance to ask questions about this study and I am satisfied with the answers and explanations that have been given.
- understand that I give access to data about me to authorised persons described in this information sheet.
- I know what will happen to my blood/tissue samples.
- have been given time and opportunity to consider taking part in this study.

Tick as appropriate (this decision will not affect your ability to enter the study):
I agree that my family doctor will be told that I am taking part in the study.
[Note: Not applicable if investigator is family doctor or if there is no family doctor.]
$\square$
Yes $\square$
No

## Tick as appropriate:

I agree that my biological samples may be used for future research. GSK will always ask approval for this research to an independent ethics committee or independent review board. I understand that if I select "No", I can still take part in the study.


Subject ID $\qquad$
CONFIDENTIAL
Study Identification ZOSTER-028 (116427)
[Note: If more than one page, the subsequent page must contain the subject's name.]
*Printed name of subject

I agree to take part in this study.
Signature of subject
Date day/month/ year
Thumbprint of subject*
Date: day/month/year

* In case the subject is unable to write.

Printed name of person conducting consent

Signature of person conducting consent
$\qquad$
Date: day/month/ year

I confirm that I am independent of the study, that I attended the informed consent process and that I have read the written information for the study.
**Printed name of Witness

Signature of Witness
Date: day/month/ year
** Witness is only required if the subject is unable to read.

## YOU MAY HAVE HAD A PRE-VACCINATION VISIT AND YOU MAY HAVE SIGNED THE ICF MORE THAN 30 DAYS AGO. IN THIS CASE, YOU NEED TO CONFIRM CONSENT BEFORE VISIT 1.

Signature of subject
Date: day/month/ year
Thumbprint of subject*
Date: day/month/ year

* In case the subject is unable to write.

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## Appendix A Summary of activities during the study

The table shows what will happen at each study visit for all participants in the study.

| Visit number and time point | What will happen at this visit |
| :---: | :---: |
| Pre-vaccination visit (up to 30 days before Visit 1 and can be on the same day as Visit 1) | 1. The study doctor or staff will explain the study. <br> 2. If you agree to join, you will sign the consent form. <br> 3. You will answer medical questions to see if you can join the study. <br> 4. Women who may get pregnant will have a urinary pregnancy test. |
| Visit 1 at Day 0/Month 0 (visit of your first vaccination) | 1. You will reconfirm if you agree to join [If required by local regulations]. <br> 2. The study staff will ask you if any changes occurred with respect to your health. since the Pre-vaccination visit to confirm that you can take part in the study <br> 3. You will answer questions about your Health in the past. <br> 4. If needed, the study doctor will check you (called a physical exam) to make sure you are healthy enough to be in the study. <br> 5. You will get a urine test for pregnancy (only if you are a woman who can get pregnant) ['serum test', in case a serum pregnancy test is required in your site (e.g., due to requirement of EC/IRB)]. <br> 6. The study doctor or staff will take your temperature. <br> 7. The study staff will take a blood sample* for baseline that can be used to compare with immune responses after you receive the study vaccine or placebo. <br> 8. You will receive the first injection of the study vaccine or placebo. <br> 9. You must wait for 30 minutes in the study office to make sure there are no serious reactions before you leave the study office. <br> 10. You will receive a safety diary card to write down: <br> - Your temperature, any pain, redness or swelling at the injection site and any medical consultation you had from the day of vaccination and the next 6 days, <br> - If you were not scheduled to have the vaccination during your chemotherapy cycle, you will write down if you experience tiredness, headache, muscle ache or gastrointestinal symptoms (nausea, vomiting, diarrhea or stomach ache) or shivering from the day of vaccination and the next 6 days, <br> - Any other unusual things you experience, any medical consultation you had, and any medication or vaccination you may have taken from the day of vaccination and the next 29 days. |
| Visit 2 at Month 1 (1 to 2 months after Visit 1) | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. <br> 4. You will get a urine test for pregnancy (only if you are a woman who can get pregnant) [Local: If a serum pregnancy test is required at your site (e.g., due to requirement of EC/IRB) prior to vaccination at Visits 1 and 2, insert "blood" instead of "urine"]. <br> 5. The study doctor or staff will take your temperature. <br> 6. The study staff will take a blood sample* for measurement of immune responses. <br> 7. You will receive the second injection. <br> 8. You must wait for 30 minutes in the study office to make sure there are no serious reactions before you leave the study office. <br> 9. You will return the safety diary card you received at Visit 1 and you will receive a second diary card to write down safety information and information regarding any medication/vaccination taken for 30 days. |

Indicate version: i.e. Local (specify country and subset if applicable) ICF Version Number NN, Dated: DD/MMM/YYYY, based on Model ICF Version Number 02, Dated: 02/OCT/2012

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| Visit number and time point | What will happen at this visit |
| :---: | :---: |
| Visit 3 at Month 2 (1 month after Visit 2) | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. <br> 4. The study staff will take a blood sample* for measurement of immune responses. <br> 5. You will return the safety diary card you received at Visit 2. |
| Phone Contact at Month 5** | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. |
| Visit 4 between Month 4 and Month $13^{* *}$ | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. <br> 4. The study staff will take a blood sample* for measurement of immune responses. |
| Phone Contact at Month 9** | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. |
| Visit 5 <br> (12 months after Visit 2) | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. <br> 4. The study staff will take a blood sample ${ }^{*}$ for measurement of immune responses. <br> 5. You will be informed that your participation in the study has ended. <br> 6. The study staff will ask you if you would be willing to participate to a follow-up study. |

* Before the first and second injections at Visit 1 and Visit 2, and at all subsequent visits, about one and a half teaspoonfuls ( $\sim 8 \mathrm{~mL}$ ) of blood will be taken. For a sub-group of subjects, about an ounce ( $\sim 30 \mathrm{~mL}$ ) of blood will also be taken (at Visits 1, 2, 3 and 5).
** Should Visit 4 coincide with Month 5 or Month 9 , it will replace the Month 5 or the Month 9 Phone Contact, respectively. The study staff will inform you accordingly.


## Best Practices Document for the Development of the Local ICF

 Delete the following Appendix in the Final local ICF.
## Appendix B GlaxoSmithKline Biologicals Best Practices Document for the Development of the Local ICF

## Introduction

The local informed consent form (ICF) is created based on the GSK Biologicals internally approved model ICF and is adapted according to country or local requirements.

The model ICF is the recommended content and structure which contains all ICH and GSK required elements and is aligned with the study protocol.

The content of the local ICF should be aligned with the Model ICF and any local specifications and regulations included.

The local GSK approved version should be submitted for ethical/regulatory approval and should be presented to the subject/patient and/or their legally acceptable representative.

It is essential that the version of the local ICF is accurately tracked, with a unique version number, date and reference to the model ICF on which it is based, to ensure that the correct version of the ICF is used and can be identified if needed.

It is strongly recommended to have a final local ICF, back-translated in English, available in the Investigator's study file to ensure site readiness in case of audits and/or inspections.

## Objective

These best practices are intended to give adequate support and to ensure consistency while developing the local ICF from the model ICF.

It is a tool to know what changes are not permitted and what changes can be justified and/or are required per local regulations and site specific information.

The development of the accurate and complete local ICF is a local responsibility and alignment with the model ICF is essential to study conduct.

Any changes made to the local ICF from the model ICF must be documented at local level.

## Human Sample Management

The collection of human tissue samples, the intended use, and secondary use, if retained, and how the subject's confidentiality would be maintained for the retained samples, must be reported in the ICF.

The content of this section must be fully aligned with the Use of Human Samples form. This form allows the central project team to track the actual testing at GSK (or laboratories used for GSK-sponsored studies) with the individual subject's consent and

Best Practices Document for the Development of the Local ICF local regulations. To avoid ethical and legal implications and invalidating the study data, any changes made to this section must be discussed with the central project team and GSK Biologicals' central ICF taskforce for alignment prior to the finalization of the local ICF.

## Subject/patient data after withdrawal

The retention of samples collected and data recorded before withdrawal and the continued collection of safety information after withdrawal must be reported in the ICF. Check local regulations and seek local legal advice for the use of data after subject/patient withdrawal. If any changes are made to this section in response to a request from any source, these changes must be discussed with the central project team and GSK Biologicals' central ICF taskforce for alignment prior to the finalization of the local ICF, so that the impact for database collection and sample destruction can be taken into account

## Type of changes

Changes to the local ICF can be classified into 3 categories:

## 'Not permitted' changes

BOLD BLACK mandatory text in the model ICF should not be changed.

## 'Required' changes

Required changes must be made in the local ICF to add country-specific or centerspecific information. (Indicated as BOLD RED text in the model ICF e.g. investigator details).

## ‘Justified’ changes

Justified changes may be necessary in some countries to comply with local requirements / regulations or to comply with a specific template e.g. country specific compensation guidance text.

In addition, some text can be clarified / simplified, provided the meaning remains the same as in the model ICF and does not contradict or change the intended meaning of the model ICF.

Changes that require a specific rationale or justification, that may be necessary in specific situations e.g. storage duration of samples, or changes required by the relevant Ethics Committees, can also be justified.

## Best Practices per ICF Section

This table describes the type of changes (not permitted, required or justified) for each ICF section of the local ICF compared to the model ICF.

| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| Study Identification |  |  |
| Check if study identification is identical to Model ICF. | Not permitted | The study identification and study number allows us to link the document to the study protocol, the corresponding IRB/IEC approvals, all relevant study documentation and ensures that the subject/patient is linked to the correct study. |
| Study Title |  |  |
| Check if study title is identical to Model ICF. | Not permitted | The study title allows us to link the document to the study protocol, the corresponding IRB/IEC approvals, all relevant study documentation and ensures that the subject/patient is linked to the correct study. |
| ICF Version Number and Date |  |  |
| Update with version and date of Local ICF and check if reference to the Model ICF version and date is included. Specify country and subset if applicable. | Required | It is mandatory to include an ICF version number, the date of the final version, the page number and the total number of pages (for the Local and Model ICF). <br> Each ICF type has to be uniquely identified and must include a reference to the source. The version of the local ICF allows us to link the ICF to the corresponding approval documents. If the version is omitted in the local ICF, the subject may not receive the most up to date ICF and thus may not receive the complete information required to make an informed consent. |
| Company Name |  |  |
| Check if company name is GlaxoSmithKline (GSK) Biologicals S.A. or the local GSK affiliate if this is required by local regulations. | Justified | A change to this section is permitted if it is justified by local regulations. <br> For some countries, the local GSK affiliate should be indicated as Company Name. |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| Subject/Patient Identification |  |  |
| Check whether there is space foreseen to insert the subject ID. | Required | The subject/patient ID should be mentioned on the ICF to be able to link the subject/patient ID with the corresponding source documents and RDE entries. |
| Header |  |  |
| Check if study identification in header is identical to Model ICF. | Not permitted | The study identification and study number allows us to link the document to the study protocol, the corresponding IRB/IEC approvals, all relevant study documentation and ensures that the subject/patient is linked to the correct study. |
| Footer |  |  |
| Indicate version of Local ICF and check if reference to the Model ICF version is included. Specify country and subset if applicable. | Required | It is mandatory to include an ICF version number, the date of the final version, the page number and the total number of pages (for the Local and Model ICF). <br> Each ICF type has to be uniquely identified and must include a reference to the source. The version of the local ICF allows us to link the ICF to the corresponding approval documents. <br> If the version is omitted in the local ICF, the subject/patient may not receive the most up to date ICF and thus may not receive the complete information required to make an informed consent. |
| What is consent? |  |  |
| Explain the consent process and check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | Freely given and written informed consent must be obtained from each subject/patient/LAR prior to study participation. Informed consent involves an education and information exchange that takes place between the researcher and the potential subject/patient. How the process of consenting looks like, needs to be explained in the |

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\hline \multicolumn{1}{|c|}{ ICF section } \& \multicolumn{1}{|c|}{| Type of |
| :--- |
| changes |} \& \multicolumn{1}{c|}{ Rationale/Impact }

\end{tabular}

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| GlaxoSmithKline Best Practices Document for the Development of the Local ICF |
| Type of section <br> changes |


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| :--- |
| GlaxoSmithKline Best Practices Document for the Development of the Local ICF |
| ICF section Type of <br> changes <br> Check if the QA (Quality <br> Assurance) on tests related to <br> the study vaccine/ disease <br> (type 2 testing) is reported in <br> the Local ICF. Not permitted |
| QA testing will be done at all times, <br> assuming it is allowed as per <br> individual subject's/patient's <br> consent. If QA testing is not <br> mentioned in the ICF, there is a risk <br> that GSK will be unable to perform <br> the protocol tests and therefore this <br> type of testing cannot be omitted. |
| Check local regulations <br> regarding tests related to the <br> product/disease under study <br> (type 3a and 3b testing). <br> [If there are concerns <br> regarding this text then this <br> should be discussed with the <br> central team and GSK <br> Biologicals' central ICF <br> taskforce for alignment prior to <br> the finalization of the local <br> ICF] |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| Check Local regulations regarding storage duration. Check if the wording "for a maximum of 20 years" is not changed into "for 20 years". [If there are concerns regarding this text then this should be discussed with the central project team and GSK Biologicals' central ICF taskforce for alignment prior to the finalization of the local ICF] | Justified | It is necessary to put a defined storage period in the ICF. As a standard, GSK proposes to store samples for "for a maximum of" 20 years. Attention should be paid to the used wording "for a maximum of" 20 years. This wording allows GSK to cover different situations (e.g. to keep samples for maximum 20 years, to destroy samples when GSK no longer wants to store them or no longer is interested in testing, when physical integrity of some type of samples does not permit such long storage, etc). <br> Any changes to this section should be captured in the UHSF. This will allow the laboratory to take the appropriate measures for sample storage, "for a maximum of 20 " years or as defined in the ICF and documented in the UHSF section called "other". |
| Check local regulations regarding future research. [If there are concerns regarding this text then this should be discussed with the central project team and GSK Biologicals' central ICF taskforce for alignment prior to the finalization of the local ICF] | Justified | A change to this section is justified, since depending on local regulations, this type of testing is allowed or not. However, the wording of the text itself, should not be changed and nothing should be added! We capture this info in the CRF/eCRF by the mean of the UHSF, which contains standard wording so if the wording in the ICF is changed, this will not be matching with the UHSF. This form allows the central project team to track the actual testing at GSK (or laboratories used for GSKsponsored studies) with the individual subject's/patient's consent and local regulations. If this text is changed, there is a risk to use human samples outside the |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
|  |  | subject‘s consent. <br> This has major ethical and legal implications and can lead to a loss of company reputation, lack of confidence, invalid study data, etc.... |
| What side effects or risks can you expect in the study? |  |  |
| Check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | The content of this section is required by ICH-GCP. The reasonably foreseeable risks or inconveniences to the subject should be mentioned in the ICF. If any of this information is omitted in the local ICF, the subject may not receive the complete information required to make an informed consent. Text can be simplified if necessary. <br> Refer to the GSK Position Paper on 'Communication of Individual Immunological Assay Results to Study Sites' for additional information. |
| Check if the text on autoimmune diseases (applicable if product/vaccine contains an adjuvant) is identical to the Model ICF. | Not permitted | The text on autoimmune diseases has been approved by GSK upper management following feedback from Authorities. The AID wording should remain consistent in all projects and countries. There is a reputational risk associated to the fact that GSK might seem to be sharing different information with Subjects/Patients/Externally on AID. |
| Check if the text on Rotarix, if applicable, is identical to the Model ICF. | Not permitted | This text has been approved by GSK upper management following feedback from Authorities. |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| What benefits can you expect in the study? |  |  |
| Check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | The content of this section is required by ICH-GCP. The reasonably expected benefits or indirect benefits or if there is no direct clinical benefit for the subjects/patients must be included in the local ICF. Text can be simplified if necessary |
| Are there other products or treatment? |  |  |
| Check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | It is an ICH-GCP requirement to provide to the subject information on alternative procedures or treatment that may be available and their important potential benefits and risks. <br> Omitting any of this information would be violating the rights of the subject/patient to freely participate to the study and would be putting the company reputation at risk. Text can be simplified if necessary. |
| Add currently available local alternatives, if applicable. | Required | This information must be added locally to the ICF using the most current information regarding the treatments that are available in the country. |
| Do you have to stay in the study? |  |  |
| Explain voluntary participation and check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | The content of this section is required by ICH-GCP. <br> Omitting any of this information would be violating the rights of the subject/patient to freely participate to the study and would be putting the company reputation at risk. Text can be simplified if necessary. |
| What happens if you leave the study? |  |  |
| Check if the text on the use of data after subject/patient withdrawal is identical to the | Justified | The bold text in this section has been approved by Medical Governance. Changes to this |


| gSK |
| :--- |
| GSlaxoSmithKline |
| Best Practices Document for the Development of the Local ICF |
| Type of <br> changes |
| Model ICF. <br> [Check local regulations and <br> seek local legal advice] <br> [If the text needs to be changed <br> it should be discussed with the <br> central projet team and GSK <br> Biologicals' central ICF <br> taskforce for alignment prior to <br> the finalization of the local |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| Will you be paid for being in the study? |  |  |
| Information related to this section is added at a regional or country level. | Required | The content of this section is required by ICH-GCP and must be included in the ICF so that the subject/patient is well informed before consenting to participation. The anticipated prorated payment or other financial benefit, if any, to the subject for participating in the study should be mentioned in the ICF. <br> Explain if expenses incurred by subjects for clinical visits made because of their participation in the study will be reimbursed or not. |
| Do you have to pay anything to be in the study? |  |  |
| This section is optional. Information related to this section is added at a regional or country level when it is appropriate for a study and/or is required by local practice. | Justified | If appropriate for a study, include here information on cost/expenses that subject/patient will have to bear for taking part in the study i.e., whether the subject/patient or the subject's/patient's insurance will be charged for any study item or procedure. According to ICH-GCP, the anticipated expenses, if any, to the subject/patient for participating in the study should be mentioned. |
| Who should you contact if you have questions? |  |  |
| Add local contact details. | Required | The content of this section is required by ICH-GCP. The subject/patient must have a contact person for further information regarding the study, his rights and who to contact in the event of trialrelated injury. |
| Consent statement |  |  |
| Check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | The consent statement should be aligned with ICH-GCP requirements. Omitting any of the information can have legal |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
|  |  | implications |
| Check local regulations regarding future research (type 4 testing). <br> Check if the wording is identical to the wording in the body of the ICF. <br> [If there are concerns regarding this text then this should be discussed with the central project team and GSK Biologicals' central ICF taskforce for alignment prior to the finalization of the local ICF] | Justified | A change to this section is justified, since depending on local regulations, this type of testing is allowed or not. This type of testing is optional for the subject/patient, meaning that if this testing is mentioned in the body of the ICF, a tick box should be available in the consent statement. The wording of the text itself, should not be changed and nothing should be added! We capture this info in the CRF/eCRF by using the UHSF, which contains standard wording so if the wording in the ICF is changed, this will not be matching with the UHSF. |

## References

SOP_54823, Development and implementation of Informed Consent for clinical studies.
GUI_51905, Guidance for Informed Consent documents.
GUI-BIO-CLIN-0014, Guidance for the development of Informed Consent-related documents.

GSK's Position Paper on Communication of Individual Immunological Assay Results To Study Sites.

GSK's Clarification Paper on Handling Data after Subject withdrawal.
GSK's Clarification Paper on Future Use of Biospecimens

## CONFIDENTIAL

## Instructions for Local ICF development

The LOC should ensure that all local legal regulatory requirements are satisfied before finalizing the Local ICF. It is strongly recommended to align the content of the Local ICF with the content of the Model ICF and this template.

When developing a Local ICF, all changes to the content that affect the meaning of the Model ICF should be justified and documented locally. Any black bold text in the final Model ICF is GSK Biologicals' mandatory wording and should be retained, any alterations or additions to this text must be communicated to the central team prior to the finalization of the local ICF.

Refer to Appendix B Best Practices document for the development of the Local ICF.
Note: In the final Local ICF all text should be in the same format i.e. any bold text must be in normal font and red hidden text must not be retained.

Refer to INS_51928, SOP_54823, GUI_51905 and GUI-BIO-CLIN-0014 for more information.
(Delete the instructions above from the Final Local ICF).

## INFORMED CONSENT FORM

Study Identification: ZOSTER-028 (116427)

## Study Title: An observer-bind study to evaluate immunogenicity and safety of GSK Biologicals' Herpes Zoster vaccine GSK1437173A in adults $\geq 18$ years of age with solid tumours receiving chemotherapy

Model ICF Version Number: 03 (replace with Version of Local ICF)
Date: 14/NOV/2012 (replace with Date of Local ICF)
Company Name: GlaxoSmithKline (GSK) Biologicals S.A.
Subject/Patient Identification: Insert subject/patient ID here What is consent?

Consent means agreeing to take part in this research study. You can decide if you want to take part in this study or not. Please take time to read the following information and ask the study doctor or study staff if you have any questions. They will explain the study fully to you. You can talk in confidence with family, friends and your doctor to help you make a decision. You must sign the Consent pages at the end of this form if you decide to join this study. You will receive a copy of this form.

## Why is this study being done?

This study is to test how well a new vaccine works to protect against shingles. The vaccine will be tested in people who received chemotherapy for solid tumours. You will soon get such a treatment or have just gotten the first cycle of chemotherapy. Therefore, we invite you to join this research study.

Shingles is a disease caused by a virus. The same virus causes chickenpox. You can get chickenpox when you are a child. After that, the virus stays in the body but is asleep. You can get shingles when the virus wakes up.

If your immunity (resistance to disease) decreases, the risk of getting shingles increases. This can happen from a disease or some treatments (such as chemotherapy). A decreased immunity could also impact the way you are responding to a vaccine.

Shingles most often occurs on the chest or back. But it can occur anywhere on the body such as the face or on an arm or leg. The first sign of shingles is often pain, tingling, itching or burning. The first sign is mostly on only one side of your body. This pain can even be caused by air blowing on the skin. Clothes rubbing against the skin or hot or cold temperatures can also cause pain. Within a few days, a rash appears in the same place. The rash may begin as red spots, but blisters soon form. This typical rash is mostly painful and may be itchy. Some people with shingles also have fever, muscle aches and headaches. After the rash has healed, sometimes people can still feel pain in the same place. This is called post-herpetic neuralgia, or PHN and can last for months or even years.

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Study Identification ZOSTER-028 (116427)
The new vaccine against shingles that GlaxoSmithKline (GSK) Biologicals is testing in people is not yet approved. The doctors cannot yet prescribe it to the public. It is being studied first. That is why we call it a study vaccine. One part of the study vaccine is recognised by the part of the body that makes defense responses. The study vaccine is made from only a part of the shingles virus. So there is no risk that the study vaccine itself will cause shingles or chicken pox. It is thought that the body's defense response to the study vaccine will protect you from getting shingles. A substance known as adjuvant is part of the study vaccine to help make a better response. This study will look at your body's defense responses during your course of chemotherapy. For this, we will need to collect blood samples before and after vaccination.

If you decide to take part in this study, you will be enrolled into 1 of 2 treatment groups. Both groups will get 2 shots ( 1 to 2 months apart). Both shots will either be the active study vaccine or a solution without active ingredients called placebo.

In both groups you can receive the first vaccination either at least 10 days before chemotherapy or on the first day of the first (or second) chemotherapy cycle.

## How is GSK involved?

GSK is a company that studies and makes vaccines, medicines and other health products. GSK planned and organized this study. GSK pays the study doctor and the institution to run this study.

GSK will be the owner of the study results. GSK plans to use these to get patents, sell the vaccine in the future or make profits in other ways. You will not be paid for any part of this.

The information and materials we give you about this study are confidential and belong to GSK. We ask that you keep it private. You can share this information with your doctor, family or friends when discussing about your participation in this study and your healthcare.

## Who can join this study?

You can only be in this study if:
a. You are aged 18 years or older [Please update in accordance with the age of legal consent in your country] when you join the study. You can follow the study procedures;
b. You will be receiving chemotherapy for solid tumours and have not had more than two cycles of chemotherapy;
c. You have not had chickenpox or shingles in the year before you get the first shot of the study vaccine or placebo;
d. You did not get a vaccine against chickenpox or shingles in the year before;
e. You did not get in the past and are not planning to get certain medication, vaccines or therapy. Your study doctor will explain this;

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Study Identification ZOSTER-028 (116427)
f. If you are a woman, you must not be pregnant or nursing a baby;
g. If you are a woman and can get pregnant, for a certain time you must agree to use contraception. This time is from 30 days before your first injection. It lasts until 2 months after your second injection.

The study doctor will also check some other aspects before you can join this study.
You can ask your study doctor for more details.

## What does this study involve?

About 200 people will take part in this study. When we have enough people taking part in this study, we will not include or invite any more. It is possible that you will be screened, but not vaccinated, even if you meet all criteria.

The study will be done in different countries worldwide.
If you agree to take part then you will receive either the study vaccine or the placebo. A computer will be used to put you into one of these 2 treatment groups (study vaccine or placebo). You have an equal chance of being in either of these two groups. Neither you nor the study doctor, or other study staff, will know which treatment group you are in. You will find out what group you are in after the whole study is finished. The study doctor can also tell you in case of a medical emergency.

A computer will also decide if you should start your vaccination (study vaccine or placebo) at least 10 days before the start of chemotherapy (PreChemo) or on the first day of the first (or second) chemotherapy cycle (OnChemo). Since the study has 4 times more subjects in the PreChemo group than in the OnChemo group, you will be four times more likely of being in the PreChemo group. Neither you nor the study doctor can choose either a treatment group or one of these scheduling groups.

A total of 6 office visits planned for the study. There is a visit some time before the day of the first vaccination (called the Pre-vaccination visit). This visit is followed by 5 study visits (Visits 1 to 5 ) and 2 phone contacts (Month 5 and Month 9).

The procedures during the study visits are listed below. They are also summarized in Appendix A.

If you agree to take part in this study, it is important that you follow all the study procedures explained below.

- The Pre-vaccination visit will occur up to about 30 days before Visit 1 and can occur on the same day as Visit 1 .
- The study staff will explain the study to you. They will ask you questions about your health and medications that you are taking. This is needed to see if you can take part in this study.
- You will be asked to read and sign this Informed Consent Form (ICF).


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- If you are a woman, you will have a urine pregnancy test at the Pre-vaccination visit.
- Visit 1 will be scheduled in relation to your first chemotherapy cycle.
- Visit 1 will occur at most 1 month before, to as few as, 10 days before the start of your first chemotherapy cycle; or at the first day of your first or second chemotherapy cycle (allowing a 1 day window before or after).
- You will reconfirm if you agree to join [If required by local regulations].
- The study staff will ask you if any changes occurred with respect to your health since the Pre-vaccination visit to confirm that you can take part in the study.
- If needed, the study doctor will check you (called a physical exam) to make sure you are healthy enough to be in the study.
- If you are a woman, we will collect a urine sample for a pregnancy test before vaccination. [Local, if applicable: If a serum pregnancy test is required at your site (e.g., due to requirement of EC/IRB) prior to vaccination at Visits 1 and 2, insert "blood" instead of "urine", and add the appropriate blood sample volume].
- At Visit 1 and all the following visits you will have a blood sampling (*see below) to test your response to the study vaccine.
- At Visit 1 you will get the first injection of either the study vaccine or placebo in the arm. You will have to wait at the study office for at least 30 minutes. This is so the study staff can make sure you are well enough to leave.
- You will receive a safety diary card on the day of each vaccination, for you to fill out at home, and return at your next visit (**see below).
- You should contact the study doctor or the study staff immediately if you get any symptoms that you feel may be serious at any time during the study.
- Visit 2 will occur 1 to 2 months after Visit 1.
- The study staff will ask you if any changes occurred with respect to your health since Visit 1.
- You will return the safety diary card you received at Visit 1 and you will receive a second diary card to write down safety information and information regarding any medication/vaccination taken for the next 30 days ( $* *$ see below).
- If you are a woman, we will collect a urine sample for a pregnancy test before vaccination. [Local, if applicable: If a serum pregnancy test is required at your site (e.g., due to requirement of EC/IRB) prior to vaccination at Visits 1 and 2, insert "blood" instead of "urine", and add the appropriate blood sample volume].
- You will have a blood sampling (*see below) to test your response to the study vaccine.
- At Visit 2 you will receive the second injection of either the study vaccine or placebo in the arm. You will have to wait at the study office for at least 30 minutes. This is so the study staff can make sure you are well enough to leave.

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- Visit 3 will occur 1 month after Visit 2.
- The study staff will ask you if any changes occurred with respect to your health since Visit 2.
- You will return the safety diary card you filled out since the last vaccination (**see below).
- You will have a blood sampling (*see below) to test your response to the study vaccine.
- A Month 5 Phone Contact will happen about 2 months after Visit 3 ( ${ }^{* * *}$ see below), and the study office will contact you by a phone call.
- You will be asked about certain changes in your medical condition and medications.
- Visit 4, is a conditional visit and may occur within Months 4 to 13 ( $*^{* *}$ see below) at the start of your last cycle of chemotherapy (if at least two months after the previous Visit 3).
- Thus, the timing of this particular visit will be variable depending on your chemotherapy schedule and on when you started vaccination in relation to your chemotherapy.
- You will have a blood sampling (*see below) to test your response to the study vaccine.
- A Month 9 Phone Contact will happen about 4 months after the Month 5 Phone Contact $\left({ }^{* * *}\right.$ see below), and the study office will contact you by a phone call.
- You will be asked about certain changes in your medical condition and medications.
- Should Visit 4 occur around Month 9, it will replace the Month 9 Phone Contact.
- Visit 5 will be about 12 months after the second vaccination.
- You will have a blood sampling (*see below) to test your response to the study vaccine.
- You will be in the study for at least 14 months and will be told at that time your participation in the study has ended.

At each Visit and during the Phone Contacts, the study staff will ask about your health, any medicines you took since your previous visit and for how long you took them, as well as if you have received any other vaccination.

At any time during the study, you should contact the study doctor or the study staff immediately should you get any symptoms that you feel may be serious.
*Before the first and second injections at Visit 1 and Visit 2, and at all subsequent visits, about one and a half teaspoonfuls ( $\sim 8 \mathrm{~mL}$ ) of blood will be taken from you. This will be used to test your body's immune response. For some subjects only in the PreChemo groups, about one ounce ( $\sim 30 \mathrm{~mL}$ ) of blood will also be taken (at Visits 1, 2, 3 and 5).

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This is for a different kind of immune test. The study staff will inform you if you are part of this sub-group.
**You will receive a safety diary card on the day of each vaccination. The study staff will explain to you how to complete the safety diary card. The card must be returned to the study office at your next visit. Completion of the safety diary card involves writing:

- On the day of each vaccination and the following 6 days: write down your temperature, any pain, redness or swelling at the injection site and any medical consultation you had.
- On the day of each vaccination and the following 29 days: write down any other unusual things you experience, any medical consultation you had (outside the regular chemotherapy cycles), and any medication or vaccination you may have taken (outside the regular chemotherapy cycles).
***Should Visit 4 coincide with Month 5 or Month 9, it will replace the Month 5 or the Month 9 Phone Contact, respectively. The study staff will inform you accordingly.
[Include the following statement if material about shingles is provided.] The study doctor will give you material with pictures and information on the signs and symptoms of shingles.

You will receive a card with study contact information. Keep this card with you at all times during the study. Show this card to the medical staff if you need emergency care during the study. The medical staff can then contact your study doctor if needed to ask about the vaccine or product you received.

You will be asked at the end of the study if we can contact you for future related studies. If you agree to be contacted, it does not mean that you have to take part in future related studies. If you do not want to be contacted, we would like to know why. We will record your answer.

## What about pregnancy and breastfeeding?

It is not known if the vaccine used in this study may have an effect on the unborn baby. You will not be able to join this study if you are pregnant or nursing a baby.

If you are a woman who can get pregnant, you will need to use birth control. This will be from 30 days before the first shot, until 2 months after the second shot. The study doctor will tell you about birth control methods that can be used during this study.

You will have a urine pregnancy test at the Pre-vaccination visit and before each vaccination at Visits 1 and 2. [Local, if applicable: If a serum pregnancy test is required at your site (e.g., due to requirement of $E C / I R B$ ) prior to vaccination at Visits 1 and 2; insert: "blood" instead of "urine"; and delete: "at the Prevaccination visit and"] The pregnancy test must be negative in order for you to receive the study vaccine.

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Tell the study doctor if you are pregnant. If you get pregnant during the study, you may not receive any more vaccine but may remain in the study for follow-up.

## What will happen to samples taken in this study?

As part of the study, you will be asked to give samples of your blood. Your blood samples may be sent to GSK or other laboratories working with GSK including those outside [insert name of country] to:

- measure how your body reacts to the study vaccine.
- ensure the quality of the tests we use for the study vaccine and/or disease(s)
- improve tests and develop new tests linked to the study vaccine and/or disease(s). These tests will never include testing related to your genes' hereditary characteristics.
- Urine samples will be collected from women for pregnancy testing at the Prevaccination Visit and before each vaccination at Visits 1 and 2. [Local, if applicable: If a serum pregnancy test is required at your site (e.g., due to requirement of $E C / I R B$ ) prior to vaccination at Visits 1 and 2, insert "Blood" instead of "Urine", and delete "at the Pre-vaccination Visit and"].

Your samples will be given a code so that it does not directly identify you.
Your samples will be kept for a maximum of 20 years from the end of the study. Any sample remaining at that time will be destroyed.

## Optional tests on your samples:

If you agree, your sample(s) may also be used for future research. GSK will always ask approval for this research to an independent ethics committee or independent review board.

You can choose not to allow these optional tests and still be in the study.

## What side effects or risks can you expect in this study?

The shingles vaccine used in this study has been tested previously in clinical research studies.

We have results from about a thousand people. They all received the active study vaccine. Most of these people ( $95 \%$ ) were 50 years or older. The vaccine has mostly been well tolerated. The most common side effects were at the site of injection. Side effects at the site of the injection included pain, redness, and swelling. They occurred in more than 1 in 10 people (more than $10 \%$ ) who got the vaccine. In fact, more than $50 \%$ of people who got the study vaccine had pain at the injection site. These symptoms were usually mild and resolved within a few days. Other side effects seen in more than $10 \%$ of people who got the vaccine included tiredness, muscle pain, headache, fever and symptoms such as nausea, vomiting, diarrhea and/or abdominal pain. The side effect of shivering was less

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likely. It occurred in about 1 to $10 \%$ of people who got the vaccine. These symptoms were also usually mild and resolved within a few days.

The shingles vaccine may cause some side effects that are not known at the present time. However, should any new findings (including findings from other studies or in animals) regarding any risks involved with the study vaccine be discovered during the course of the research, you will be notified immediately.

Unexpected side-effects, like serious allergic reactions, to the vaccine may occur. All the medical equipment to help you in such a case will be available.

When you give blood you may feel faint, or have mild pain, bruising, irritation or redness where the blood is taken. These reactions usually last only a short time.

There may be possible risks to a pregnant woman, embryo, foetus or nursing infant. Such risks are not known at this time. Therefore, you will not be allowed to enter this study if you are pregnant or breastfeeding. You should also not plan a pregnancy or breastfeed before 2 months after you have received the second vaccine dose.

The side effects that you may report in this study will be shared with experts on shingles. The experts will make any recommendations to ensure the safety of the people participating to the study.

Many adults and children have received vaccines that contain a substance known as an "adjuvant". These adjuvants are similar to what is in the vaccine that you may get in this study. Rarely, some of these people have developed illnesses, sometimes serious, called autoimmune diseases, where their immune system harms their own body. These illnesses have also developed in people who have not received these vaccines. We do not know if the study vaccine(s) can actually cause autoimmune diseases. GSK therefore follows this question closely.

## What benefits can you expect in this study?

Taking part in this study may not have a direct benefit for you.
If you get the placebo, there is no expected benefit.
If you get the study vaccine, we do not know yet if it will protect you against shingles.
The study vaccine, study tests, and follow-up by the study doctor will be free of charge. You do not need to pay for these.

Information from this study will help us learn more about shingles vaccines.

## Are there other products or treatment?

Shingles can be treated with:

- Antiviral medication;

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- Medication to treat the pain when you have shingles.

There is no approved vaccine available to prevent shingles in people who have received chemotherapy to treat solid tumours.

This section should be completed locally using the most current information regarding the treatments/ vaccines/ products that are available in the country and their important potential benefits and risks. State if there are no alternate treatments.

## Do you have to stay in the study?

You may choose to leave the study at any time, without giving a reason. If you do give a reason, then it may be recorded. Your choice will not change the medical care you receive outside of this study.

We will share with you any new information that may change your choice to stay in the study. We will share this information with you as soon as possible.

Tell the study doctor if you no longer want to take part.
GSK may choose to stop the study or the study doctor may choose to stop your participation in the study at any time. We will then tell you why.

We may ask you to leave the study if:

- Test results show that this study is not right for you;
- You do not follow instructions for treatment or follow-up visits;
- You decide that you want to become pregnant or plan to discontinue contraceptive precautions before 2 months after you received the second vaccination;
- The study doctor thinks it is in your best interest to stop, e.g., if you have specific health problems.


## What happens if you leave the study?

Check local regulations and seek local legal advice for the use of data after subject withdrawal. If any changes are made to this section in the Local ICF compared to the Model ICF, in response to a request from any source, these should be discussed with the central study team and GSK Biologicals ICF taskforce for alignment prior to the finalization of the local ICF, so that the impact for database collection can be taken into account.

No more information about you will be collected after you leave the study. All the information and samples collected before you left the study will still be used.

If the doctor becomes aware of any relevant safety information about you after you left the study, this will be collected.

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We may also contact you later for information. This is to help us better understand the safety profile of the vaccine.

## What about your personal and medical information?

If changes are made to this text it needs to be checked with the local Legal team that this is aligned with local rules and regulations.

It is very important that your personal and medical information stay confidential and secure. Your personal and medical information will be protected in accordance with current law.

When you sign this consent form you agree that your personal and medical information can be used as described here.

- Your personal and medical information may be checked by GSK and others (like agencies that approve and monitor studies). This is to make sure that the study is being run properly.
- Besides that, only the researchers at this study site can use information that identifies you (such as name and address) and only for the purpose of the study.
- Your information collected during the study will be labeled with a code number (for example, PPD It will not include your name or address. The study doctor will have the link between your name and the code number.
- The link between your name and the code number will not be shared. Only the code number and coded information will be sent to GSK.
- GSK will use your coded information for research only, including research looking at improving the quality and efficiency in conducting clinical research trials in general.
- GSK may:
- keep it electronically, and analyse it by computer to find out what the study is telling us. This may be done by GSK or a third party, in which case GSK will ensure that the third party is required to keep your data secure.
- share it with regulatory agencies that approve new vaccines and medicines,
- share it with people who check that the study is done properly (like the independent ethics committee or review boards),
- combine it with results from other studies to learn more about the vaccine and this disease and related conditions. This may help us to assess the risks and benefits of GSK (or other) vaccines or medicines, or to improve disease understanding,
- publish study results in medical journals, for meetings and on the internet for other researchers to use. Your name will not appear in any publication.
- share coded information with other companies, organisations or universities to carry out research, including research looking at improving the quality and efficiency in conducting clinical research trials in general.

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Personal and medical data collected during the trial may be moved to, stored and used in the country where you live or another country where GSK or those working with GSK work.

Use of this information may take place in countries with lower data protection rules than the country where you live. GSK will make sure that if your data are moved to another country, it will still be treated as stated in this Informed Consent Form.

A description of this clinical trial will be available on the GSK Clinical Study Register http://www.gsk-clinicalstudyregister.com/ and may also appear in clinical trial registries in countries in which the clinical study is conducted.

If you withdraw your consent for us to use your personal information you will no longer be able to continue in the study.

At any time, you may ask to see your personal information and correct it if necessary.
In some circumstances you may not be able to access your study information while the study is ongoing. However the study doctor will share any important medical information if it is relevant to your health during the course of the study.

## What happens if you get hurt while taking part in this study?

[Please add appropriate local compensation for injury terms.]
Compensation for injury language to be used for GSK sponsored studies in the UK (and in countries which have no special local requirements)

If you are hurt by a vaccine / product or a clinical procedure that you would not have been given outside this study, you will be compensated. Your study doctor can give you information about the compensation guidelines for this kind of hurt.

## GSK sponsored studies in Other Regions

[The participating countries should complete if there are local compensation for injury requirements.]

## Will you be paid for being in the study?

[This section should be completed locally.]
You will not be paid for taking part in this study. OR
We will reimburse you for the cost of travelling to your study visits. You may receive up to [amount] for travel / per visit.

## Do you have to pay anything to be in the study?

[Information related to this section is added at a regional or country level when it is appropriate for a study and/or is required by local practice)]

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## CONFIDENTIAL

Study Identification ZOSTER-028 (116427)
Who should you contact if you have questions?
Person to contact for any questions: name, address, telephone number.

Person to contact about your rights: name, address, telephone number.
Person to contact in case of injury: name, address, telephone number.
$\qquad$
CONFIDENTIAL
Study Identification ZOSTER-028 (116427)

## Consent statement

I,
(Printed name of Subject)

- confirm that I have read the written information (or have had the information read to me) for study 116427 (ZOSTER-028) ICF Version 03, 14 NOV 2012 (16 pages) (to be updated locally), and the study procedures have been explained to me by study staff during the consent process for this study.
- confirm that I have had the chance to ask questions about this study and I am satisfied with the answers and explanations that have been given.
- understand that I give access to data about me to authorised persons described in this information sheet.
- I know what will happen to my blood/tissue samples.
- have been given time and opportunity to consider taking part in this study.

Tick as appropriate (this decision will not affect your ability to enter the study):
I agree that my family doctor will be told that I am taking part in the study.
[Note: Not applicable if investigator is family doctor or if there is no family doctor.]
$\square$
Yes $\square$
No

## Tick as appropriate:

I agree that my biological samples may be used for future research. GSK will always ask approval for this research to an independent ethics committee or independent review board. I understand that if I select "No", I can still take part in the study.


Subject ID $\qquad$
CONFIDENTIAL
Study Identification ZOSTER-028 (116427)
[Note: If more than one page, the subsequent page must contain the subject's name.]
*Printed name of subject

I agree to take part in this study.
Signature of subject
Date day/month/ year
Thumbprint of subject*
Date: day/month/year

* In case the subject is unable to write.

Printed name of person conducting consent

Signature of person conducting consent
$\qquad$
Date: day/month/ year

I confirm that I am independent of the study, that I attended the informed consent process and that I have read the written information for the study.
**Printed name of Witness

Signature of Witness
Date: day/month/ year
** Witness is only required if the subject is unable to read.

## YOU MAY HAVE HAD A PRE-VACCINATION VISIT AND YOU MAY HAVE SIGNED THE ICF MORE THAN 30 DAYS AGO. IN THIS CASE, YOU NEED TO CONFIRM CONSENT BEFORE VISIT 1.

Signature of subject
Date: day/month/ year
Thumbprint of subject*
Date: day/month/ year

* In case the subject is unable to write.

Informed Consent Form

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Study Identification ZOSTER-028 (116427)

## Appendix A Summary of activities during the study

The table shows what will happen at each study visit for all participants in the study.

| Visit number and time point | What will happen at this visit |
| :---: | :---: |
| Pre-vaccination visit (up to 30 days before Visit 1 and can be on the same day as Visit 1) | 1. The study doctor or staff will explain the study. <br> 2. If you agree to join, you will sign the consent form. <br> 3. You will answer medical questions to see if you can join the study. <br> 4. Women who may get pregnant will have a urinary pregnancy test. |
| Visit 1 at Day 0/Month 0 (visit of your first vaccination) | 1. You will reconfirm if you agree to join [If required by local regulations]. <br> 2. The study staff will ask you if any changes occurred with respect to your health. since the Pre-vaccination visit to confirm that you can take part in the study <br> 3. You will answer questions about your Health in the past. <br> 4. If needed, the study doctor will check you (called a physical exam) to make sure you are healthy enough to be in the study. <br> 5. You will get a urine test for pregnancy (only if you are a woman who can get pregnant) ['serum test', in case a serum pregnancy test is required in your site (e.g., due to requirement of EC/IRB)]. <br> 6. The study doctor or staff will take your temperature. <br> 7. The study staff will take a blood sample* for baseline that can be used to compare with immune responses after you receive the study vaccine or placebo. <br> 8. You will receive the first injection of the study vaccine or placebo. <br> 9. You must wait for 30 minutes in the study office to make sure there are no serious reactions before you leave the study office. <br> 10. You will receive a safety diary card to write down: <br> - Your temperature, any pain, redness or swelling at the injection site and any medical consultation you had from the day of vaccination and the next 6 days, <br> - If you were not scheduled to have the vaccination during your chemotherapy cycle, you will write down if you experience tiredness, headache, muscle ache or gastrointestinal symptoms (nausea, vomiting, diarrhea or stomach ache) or shivering from the day of vaccination and the next 6 days, <br> - Any other unusual things you experience, any medical consultation you had, and any medication or vaccination you may have taken from the day of vaccination and the next 29 days. |
| Visit 2 at Month 1 (1 to 2 months after Visit 1) | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. <br> 4. You will get a urine test for pregnancy (only if you are a woman who can get pregnant) [Local: If a serum pregnancy test is required at your site (e.g., due to requirement of EC/IRB) prior to vaccination at Visits 1 and 2, insert "blood" instead of "urine"]. <br> 5. The study doctor or staff will take your temperature. <br> 6. The study staff will take a blood sample* for measurement of immune responses. <br> 7. You will receive the second injection. <br> 8. You must wait for 30 minutes in the study office to make sure there are no serious reactions before you leave the study office. <br> 9. You will return the safety diary card you received at Visit 1 and you will receive a second diary card to write down safety information and information regarding any medication/vaccination taken for 30 days. |

Indicate version: i.e. Local (specify country and subset if applicable) ICF Version Number NN, Dated: DD/MMM/YYYY, based on Model ICF Version Number 03, Dated: 14/NOV/2012 (Page 15 of 16)
[Template Edition 6.1]

Informed Consent Form

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Study Identification ZOSTER-028 (116427)

| Visit number and time point | What will happen at this visit |
| :---: | :---: |
| Visit 3 at Month 2 (1 month after Visit 2) | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. <br> 4. The study staff will take a blood sample ${ }^{\star}$ for measurement of immune responses. <br> 5. You will return the safety diary card you received at Visit 2. |
| Phone Contact at Month 5** | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. |
| Visit 4 between Month 4 and Month $13^{* *}$ | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. <br> 4. The study staff will take a blood sample* for measurement of immune responses. |
| Phone Contact at Month ${ }^{* *}$ | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. |
| Visit 5 <br> (12 months after Visit 2) | 1. You will answer questions about your health. <br> 2. The study staff will ask you if you had symptoms of shingles or serious symptoms. You also need to talk about any medicines or vaccinations you have taken. <br> 3. The study staff will ask if you have become pregnant if you are a woman who can get pregnant. <br> 4. The study staff will take a blood sample* for measurement of immune responses. <br> 5. You will be informed that your participation in the study has ended. <br> 6. The study staff will ask you if you would be willing to participate to a follow-up study. |

* Before the first and second injections at Visit 1 and Visit 2, and at all subsequent visits, about one and a half teaspoonfuls ( $\sim 8 \mathrm{~mL}$ ) of blood will be taken. For a sub-group of only the PreChemo_subjects, about an ounce ( $\sim 30 \mathrm{~mL}$ ) of blood will also be taken (at Visits 1, 2, 3 and 5).
** Should Visit 4 coincide with Month 5 or Month 9 , it will replace the Month 5 or the Month 9 Phone Contact, respectively. The study staff will inform you accordingly.

Best Practices Document for the Development of the Local ICF Delete the following Appendix in the Final local ICF.

## Appendix B GlaxoSmithKline Biologicals Best Practices Document for the Development of the Local ICF

## Introduction

The local informed consent form (ICF) is created based on the GSK Biologicals internally approved model ICF and is adapted according to country or local requirements.

The model ICF is the recommended content and structure which contains all ICH and GSK required elements and is aligned with the study protocol.

The content of the local ICF should be aligned with the Model ICF and any local specifications and regulations included.

The local GSK approved version should be submitted for ethical/regulatory approval and should be presented to the subject/patient and/or their legally acceptable representative.

It is essential that the version of the local ICF is accurately tracked, with a unique version number, date and reference to the model ICF on which it is based, to ensure that the correct version of the ICF is used and can be identified if needed.

It is strongly recommended to have a final local ICF, back-translated in English, available in the Investigator's study file to ensure site readiness in case of audits and/or inspections.

## Objective

These best practices are intended to give adequate support and to ensure consistency while developing the local ICF from the model ICF.

It is a tool to know what changes are not permitted and what changes can be justified and/or are required per local regulations and site specific information.

The development of the accurate and complete local ICF is a local responsibility and alignment with the model ICF is essential to study conduct.

Any changes made to the local ICF from the model ICF must be documented at local level.

## Human Sample Management

The collection of human tissue samples, the intended use, and secondary use, if retained, and how the subject's confidentiality would be maintained for the retained samples, must be reported in the ICF.

The content of this section must be fully aligned with the Use of Human Samples form. This form allows the central project team to track the actual testing at GSK (or laboratories used for GSK-sponsored studies) with the individual subject's consent and

Best Practices Document for the Development of the Local ICF local regulations. To avoid ethical and legal implications and invalidating the study data, any changes made to this section must be discussed with the central project team and GSK Biologicals' central ICF taskforce for alignment prior to the finalization of the local ICF.

## Subject/patient data after withdrawal

The retention of samples collected and data recorded before withdrawal and the continued collection of safety information after withdrawal must be reported in the ICF. Check local regulations and seek local legal advice for the use of data after subject/patient withdrawal. If any changes are made to this section in response to a request from any source, these changes must be discussed with the central project team and GSK Biologicals' central ICF taskforce for alignment prior to the finalization of the local ICF, so that the impact for database collection and sample destruction can be taken into account

## Type of changes

Changes to the local ICF can be classified into 3 categories:

## 'Not permitted' changes

BOLD BLACK mandatory text in the model ICF should not be changed.

## 'Required' changes

Required changes must be made in the local ICF to add country-specific or centerspecific information. (Indicated as BOLD RED text in the model ICF e.g. investigator details).

## ‘Justified’ changes

Justified changes may be necessary in some countries to comply with local requirements / regulations or to comply with a specific template e.g. country specific compensation guidance text.

In addition, some text can be clarified / simplified, provided the meaning remains the same as in the model ICF and does not contradict or change the intended meaning of the model ICF.

Changes that require a specific rationale or justification, that may be necessary in specific situations e.g. storage duration of samples, or changes required by the relevant Ethics Committees, can also be justified.

## Best Practices per ICF Section

This table describes the type of changes (not permitted, required or justified) for each ICF section of the local ICF compared to the model ICF.

| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| Study Identification |  |  |
| Check if study identification is identical to Model ICF. | Not permitted | The study identification and study number allows us to link the document to the study protocol, the corresponding IRB/IEC approvals, all relevant study documentation and ensures that the subject/patient is linked to the correct study. |
| Study Title |  |  |
| Check if study title is identical to Model ICF. | Not permitted | The study title allows us to link the document to the study protocol, the corresponding IRB/IEC approvals, all relevant study documentation and ensures that the subject/patient is linked to the correct study. |
| ICF Version Number and Date |  |  |
| Update with version and date of Local ICF and check if reference to the Model ICF version and date is included. Specify country and subset if applicable. | Required | It is mandatory to include an ICF version number, the date of the final version, the page number and the total number of pages (for the Local and Model ICF). <br> Each ICF type has to be uniquely identified and must include a reference to the source. The version of the local ICF allows us to link the ICF to the corresponding approval documents. If the version is omitted in the local ICF, the subject may not receive the most up to date ICF and thus may not receive the complete information required to make an informed consent. |
| Company Name |  |  |
| Check if company name is GlaxoSmithKline (GSK) Biologicals S.A. or the local GSK affiliate if this is required by local regulations. | Justified | A change to this section is permitted if it is justified by local regulations. <br> For some countries, the local GSK affiliate should be indicated as Company Name. |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| Subject/Patient Identification |  |  |
| Check whether there is space foreseen to insert the subject ID. | Required | The subject/patient ID should be mentioned on the ICF to be able to link the subject/patient ID with the corresponding source documents and RDE entries. |
| Header |  |  |
| Check if study identification in header is identical to Model ICF. | Not permitted | The study identification and study number allows us to link the document to the study protocol, the corresponding IRB/IEC approvals, all relevant study documentation and ensures that the subject/patient is linked to the correct study. |
| Footer |  |  |
| Indicate version of Local ICF and check if reference to the Model ICF version is included. Specify country and subset if applicable. | Required | It is mandatory to include an ICF version number, the date of the final version, the page number and the total number of pages (for the Local and Model ICF). <br> Each ICF type has to be uniquely identified and must include a reference to the source. The version of the local ICF allows us to link the ICF to the corresponding approval documents. <br> If the version is omitted in the local ICF, the subject/patient may not receive the most up to date ICF and thus may not receive the complete information required to make an informed consent. |
| What is consent? |  |  |
| Explain the consent process and check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | Freely given and written informed consent must be obtained from each subject/patient/LAR prior to study participation. Informed consent involves an education and information exchange that takes place between the researcher and the potential subject/patient. How the process of consenting looks like, needs to be explained in the |

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\hline \multicolumn{1}{|c|}{ ICF section } \& \multicolumn{1}{|c|}{| Type of |
| :--- |
| changes |} \& \multicolumn{1}{c|}{ Rationale/Impact }

\end{tabular}

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| Type of section <br> changes |


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| GlaxoSmithKline Best Practices Document for the Development of the Local ICF |
| ICF section Type of <br> changes <br> Check if the QA (Quality <br> Assurance) on tests related to <br> the study vaccine/ disease <br> (type 2 testing) is reported in <br> the Local ICF. Not permitted |
| QA testing will be done at all times, <br> assuming it is allowed as per <br> individual subject's/patient's <br> consent. If QA testing is not <br> mentioned in the ICF, there is a risk <br> that GSK will be unable to perform <br> the protocol tests and therefore this <br> type of testing cannot be omitted. |
| Check local regulations <br> regarding tests related to the <br> product/disease under study <br> (type 3a and 3b testing). <br> [If there are concerns <br> regarding this text then this <br> should be discussed with the <br> central team and GSK <br> Biologicals' central ICF <br> taskforce for alignment prior to <br> the finalization of the local <br> ICF] |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| Check Local regulations regarding storage duration. Check if the wording "for a maximum of 20 years" is not changed into "for 20 years". [If there are concerns regarding this text then this should be discussed with the central project team and GSK Biologicals' central ICF taskforce for alignment prior to the finalization of the local ICF] | Justified | It is necessary to put a defined storage period in the ICF. As a standard, GSK proposes to store samples for "for a maximum of" 20 years. Attention should be paid to the used wording "for a maximum of" 20 years. This wording allows GSK to cover different situations (e.g. to keep samples for maximum 20 years, to destroy samples when GSK no longer wants to store them or no longer is interested in testing, when physical integrity of some type of samples does not permit such long storage, etc). <br> Any changes to this section should be captured in the UHSF. This will allow the laboratory to take the appropriate measures for sample storage, "for a maximum of 20 " years or as defined in the ICF and documented in the UHSF section called "other". |
| Check local regulations regarding future research. [If there are concerns regarding this text then this should be discussed with the central project team and GSK Biologicals' central ICF taskforce for alignment prior to the finalization of the local ICF] | Justified | A change to this section is justified, since depending on local regulations, this type of testing is allowed or not. However, the wording of the text itself, should not be changed and nothing should be added! We capture this info in the CRF/eCRF by the mean of the UHSF, which contains standard wording so if the wording in the ICF is changed, this will not be matching with the UHSF. This form allows the central project team to track the actual testing at GSK (or laboratories used for GSKsponsored studies) with the individual subject's/patient's consent and local regulations. If this text is changed, there is a risk to use human samples outside the |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
|  |  | subject‘s consent. <br> This has major ethical and legal implications and can lead to a loss of company reputation, lack of confidence, invalid study data, etc.... |
| What side effects or risks can you expect in the study? |  |  |
| Check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | The content of this section is required by ICH-GCP. The reasonably foreseeable risks or inconveniences to the subject should be mentioned in the ICF. If any of this information is omitted in the local ICF, the subject may not receive the complete information required to make an informed consent. Text can be simplified if necessary. <br> Refer to the GSK Position Paper on 'Communication of Individual Immunological Assay Results to Study Sites' for additional information. |
| Check if the text on autoimmune diseases (applicable if product/vaccine contains an adjuvant) is identical to the Model ICF. | Not permitted | The text on autoimmune diseases has been approved by GSK upper management following feedback from Authorities. The AID wording should remain consistent in all projects and countries. There is a reputational risk associated to the fact that GSK might seem to be sharing different information with Subjects/Patients/Externally on AID. |
| Check if the text on Rotarix, if applicable, is identical to the Model ICF. | Not permitted | This text has been approved by GSK upper management following feedback from Authorities. |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| What benefits can you expect in the study? |  |  |
| Check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | The content of this section is required by ICH-GCP. The reasonably expected benefits or indirect benefits or if there is no direct clinical benefit for the subjects/patients must be included in the local ICF. Text can be simplified if necessary |
| Are there other products or treatment? |  |  |
| Check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | It is an ICH-GCP requirement to provide to the subject information on alternative procedures or treatment that may be available and their important potential benefits and risks. <br> Omitting any of this information would be violating the rights of the subject/patient to freely participate to the study and would be putting the company reputation at risk. Text can be simplified if necessary. |
| Add currently available local alternatives, if applicable. | Required | This information must be added locally to the ICF using the most current information regarding the treatments that are available in the country. |
| Do you have to stay in the study? |  |  |
| Explain voluntary participation and check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | The content of this section is required by ICH-GCP. <br> Omitting any of this information would be violating the rights of the subject/patient to freely participate to the study and would be putting the company reputation at risk. Text can be simplified if necessary. |
| What happens if you leave the study? |  |  |
| Check if the text on the use of data after subject/patient withdrawal is identical to the | Justified | The bold text in this section has been approved by Medical Governance. Changes to this |


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| Type of <br> changes |
| Model ICF. <br> [Check local regulations and <br> seek local legal advice] <br> [If the text needs to be changed <br> it should be discussed with the <br> central projet team and GSK <br> Biologicals' central ICF <br> taskforce for alignment prior to <br> the finalization of the local |


| ICF section | Type of changes | Rationale/Impact |
| :---: | :---: | :---: |
| Will you be paid for being in the study? |  |  |
| Information related to this section is added at a regional or country level. | Required | The content of this section is required by ICH-GCP and must be included in the ICF so that the subject/patient is well informed before consenting to participation. The anticipated prorated payment or other financial benefit, if any, to the subject for participating in the study should be mentioned in the ICF. <br> Explain if expenses incurred by subjects for clinical visits made because of their participation in the study will be reimbursed or not. |
| Do you have to pay anything to be in the study? |  |  |
| This section is optional. Information related to this section is added at a regional or country level when it is appropriate for a study and/or is required by local practice. | Justified | If appropriate for a study, include here information on cost/expenses that subject/patient will have to bear for taking part in the study i.e., whether the subject/patient or the subject's/patient's insurance will be charged for any study item or procedure. According to ICH-GCP, the anticipated expenses, if any, to the subject/patient for participating in the study should be mentioned. |
| Who should you contact if you have questions? |  |  |
| Add local contact details. | Required | The content of this section is required by ICH-GCP. The subject/patient must have a contact person for further information regarding the study, his rights and who to contact in the event of trialrelated injury. |
| Consent statement |  |  |
| Check if the meaning of the text is not changed compared to the Model ICF (Text can be simplified if necessary). | Justified | The consent statement should be aligned with ICH-GCP requirements. Omitting any of the information can have legal |


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| :--- |
| Best Practices Document for the Development of the Local ICF |
| Type of <br> changes |

## References

SOP_54823, Development and implementation of Informed Consent for clinical studies.
GUI_51905, Guidance for Informed Consent documents.
GUI-BIO-CLIN-0014, Guidance for the development of Informed Consent-related documents.

GSK's Position Paper on Communication of Individual Immunological Assay Results To Study Sites.

GSK's Clarification Paper on Handling Data after Subject withdrawal.
GSK's Clarification Paper on Future Use of Biospecimens

## Investigator CVs or equivalent summaries of training and experience relevant to the performance of the clinical study

Page(s) removed - Out of Scope of phase 1 of Policy 0070 - Investigator CVs

## Signature of principal or coordinating investigator

## GlaxoSmithKline Biologicals <br> Vaccines R\&D <br> Investigator Approval Page

STUDY TITLE: A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster $\mathrm{HZ} /$ su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy.

Study: 116427 (ZOSTER-028) Development Phase: II/III
I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

Name of Investigator: Ignacio Delgado Mingorance
Affiliation/investigational
Hospital Infanta Cristina,
Unidad De Cuidados Intensivos, Avenida de Elvas S/N, Badajoz, Spain, 6080

Signature of Investigator:
Date:

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[^19]
## GlaxoSmithKline Biologicals <br> Vaccines R\&D <br> Sponsor Signatory Approval Page

Please note that by signing this page, you take responsibility for the content of the Study Report including appendices

STUDY TITLE: A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster $\mathrm{HZ} /$ su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy

Study: 116427 (ZOSTER-028) Development Phase: II/III
I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

Name of Sponsor Signatory: Lidia Oostvogels

Title of Sponsor Signatory:
Director, Clinical and Epidemiology Project Leader Zoster Program
Belgian Research and Development Care
GlaxoSmithKline Vaccines

Signature:
Date:

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[^20]
## Listings of patients receiving test drug(s) /investigational product(s) from specific batches, where more than one batch was used

Not applicable.

## Randomisation list

## Randomisation list

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ZOSTER-028 (A.10FEB2017)

Randomisation list

Treatment number associated to material : Hz/su-PreChemo

| PPD | 1 | PPD | 11 | PPD | 21 | PPD | 31 | PPD | 42 | PPD | 52 | PPD | 62 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | 1 |  | 11 |  | 21 |  | 32 |  | 42 |  | 52 |  | 62 |
|  | 1 |  | 11 |  | 22 |  | 32 |  | 42 |  | 52 |  | 63 |
|  | 1 |  | 12 |  | 22 |  | 32 |  | 42 |  | 53 |  | 63 |
|  | 2 |  | 12 |  | 22 |  | 32 |  | 43 |  | 53 |  | 63 |
|  | 2 |  | 12 |  | 22 |  | 33 |  | 43 |  | 53 |  | 63 |
|  | 2 |  | 12 |  | 23 |  | 33 |  | 43 |  | 53 |  | 64 |
|  | 2 |  | 13 |  | 23 |  | 33 |  | 43 |  | 54 |  | 64 |
|  | 3 |  | 13 |  | 23 |  | 33 |  | 44 |  | 54 |  | 64 |
|  | 3 |  | 13 |  | 23 |  | 34 |  | 44 |  | 54 |  | 64 |
|  | 3 |  | 13 |  | 24 |  | 34 |  | 44 |  | 54 |  | 65 |
|  | 3 |  | 14 |  | 24 |  | 34 |  | 44 |  | 55 |  | 65 |
|  | 4 |  | 14 |  | 24 |  | 34 |  | 45 |  | 55 |  | 65 |
|  | 4 |  | 14 |  | 24 |  | 35 |  | 45 |  | 55 |  | 65 |
|  | 4 |  | 14 |  | 25 |  | 35 |  | 45 |  | 55 |  | 66 |
|  | 4 |  | 15 |  | 25 |  | 35 |  | 45 |  | 56 |  | 66 |
|  | 5 |  | 15 |  | 25 |  | 35 |  | 46 |  | 56 |  | 66 |
|  | 5 |  | 15 |  | 25 |  | 36 |  | 46 |  | 56 |  | 66 |
|  | 5 |  | 15 |  | 26 |  | 36 |  | 46 |  | 56 |  | 67 |
|  | 5 |  | 16 |  | 26 |  | 36 |  | 46 |  | 57 |  | 67 |
|  | 6 |  | 16 |  | 26 |  | 36 |  | 47 |  | 57 |  | 67 |
|  | 6 |  | 16 |  | 26 |  | 37 |  | 47 |  | 57 |  | 67 |
|  | 6 |  | 16 |  | 27 |  | 37 |  | 47 |  | 57 |  | 68 |
|  | 6 |  | 17 |  | 27 |  | 37 |  | 47 |  | 58 |  | 68 |
|  | 7 |  | 17 |  | 27 |  | 37 |  | 48 |  | 58 |  | 68 |
|  | 7 |  | 17 |  | 27 |  | 38 |  | 48 |  | 58 |  | 68 |
|  | 7 |  | 17 |  | 28 |  | 38 |  | 48 |  | 58 |  | 69 |
|  | 7 |  | 18 |  | 28 |  | 38 |  | 48 |  | 59 |  | 69 |
|  | 8 |  | 18 |  | 28 |  | 38 |  | 49 |  | 59 |  | 69 |
|  | 8 |  | 18 |  | 28 |  | 39 |  | 49 |  | 59 |  | 69 |
|  | 8 |  | 18 |  | 29 |  | 39 |  | 49 |  | 59 |  | 70 |
|  | 8 |  | 19 |  | 29 |  | 39 |  | 49 |  | 60 |  | 70 |
|  | 9 |  | 19 |  | 29 |  | 39 |  | 50 |  | 60 |  | 70 |
|  | 9 |  | 19 |  | 29 |  | 40 |  | 50 |  | 60 |  | 70 |
|  | 9 |  | 19 |  | 30 |  | 40 |  | 50 |  | 60 |  | 71 |
|  | 9 |  | 20 |  | 30 |  | 40 |  | 50 |  | 61 |  | 71 |
|  | 10 |  | 20 |  | 30 |  | 40 |  | 51 |  | 61 |  | 71 |
|  | 10 |  | 20 |  | 30 |  | 41 |  | 51 |  | 61 |  | 71 |
|  | 10 |  | 20 |  | 31 |  | 41 |  | 51 |  | 61 |  | 72 |
|  | 10 |  | 21 |  | 31 |  | 41 |  | 51 |  | 62 |  | 72 |
|  | 11 |  | 21 |  | 31 |  | 41 |  | 52 |  | 62 |  | 72 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo


SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo


SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

|  | Bl. |  |  |  | Bl. |  |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 308 | PPD | 318 | PPD | 329 | PPD | 339 | PPD | 349 |
|  | 308 |  | 319 |  | 329 |  | 339 |  | 349 |
|  | 309 |  | 319 |  | 329 |  | 339 |  | 350 |
|  | 309 |  | 319 |  | 329 |  | 340 |  | 350 |
|  | 309 |  | 319 |  | 330 |  | 340 |  | 350 |
|  | 309 |  | 320 |  | 330 |  | 340 |  | 350 |
|  | 310 |  | 320 |  | 330 |  | 340 |  | 351 |
|  | 310 |  | 320 |  | 330 |  | 341 |  | 351 |
|  | 310 |  | 320 |  | 331 |  | 341 |  | 351 |
|  | 310 |  | 321 |  | 331 |  | 341 |  | 351 |
|  | 311 |  | 321 |  | 331 |  | 341 |  | 352 |
|  | 311 |  | 321 |  | 331 |  | 342 |  | 352 |
|  | 311 |  | 321 |  | 332 |  | 342 |  | 352 |
|  | 311 |  | 322 |  | 332 |  | 342 |  | 352 |
|  | 312 |  | 322 |  | 332 |  | 342 |  | 353 |
|  | 312 |  | 322 |  | 332 |  | 343 |  | 353 |
|  | 312 |  | 322 |  | 333 |  | 343 |  | 353 |
|  | 312 |  | 323 |  | 333 |  | 343 |  | 353 |
|  | 313 |  | 323 |  | 333 |  | 343 |  | 354 |
|  | 313 |  | 323 |  | 333 |  | 344 |  | 354 |
|  | 313 |  | 323 |  | 334 |  | 344 |  | 354 |
|  | 313 |  | 324 |  | 334 |  | 344 |  | 354 |
|  | 314 |  | 324 |  | 334 |  | 344 |  | 355 |
|  | 314 |  | 324 |  | 334 |  | 345 |  | 355 |
|  | 314 |  | 324 |  | 335 |  | 345 |  | 355 |
|  | 314 |  | 325 |  | 335 |  | 345 |  | 355 |
|  | 315 |  | 325 |  | 335 |  | 345 |  | 356 |
|  | 315 |  | 325 |  | 335 |  | 346 |  | 356 |
|  | 315 |  | 325 |  | 336 |  | 346 |  | 356 |
|  | 315 |  | 326 |  | 336 |  | 346 |  | 356 |
|  | 316 |  | 326 |  | 336 |  | 346 |  | 357 |
|  | 316 |  | 326 |  | 336 |  | 347 |  | 357 |
|  | 316 |  | 326 |  | 337 |  | 347 |  | 357 |
|  | 316 |  | 327 |  | 337 |  | 347 |  | 357 |
|  | 317 |  | 327 |  | 337 |  | 347 |  | 358 |
|  | 317 |  | 327 |  | 337 |  | 348 |  | 358 |
|  | 317 |  | 327 |  | 338 |  | 348 |  | 358 |
|  | 317 |  | 328 |  | 338 |  | 348 |  | 358 |
|  | 318 |  | 328 |  | 338 |  | 348 |  | 359 |
|  | 318 |  | 328 |  | 338 |  | 349 |  | 359 |
|  | 318 |  | 328 |  | 339 |  | 349 |  | 359 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

|  |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 380 | PPD | 390 | PPD | 400 | PPD | 411 | PPD | 421 |
|  | 380 |  | 390 |  | 401 |  | 411 |  | 421 |
|  | 380 |  | 391 |  | 401 |  | 411 |  | 421 |
|  | 381 |  | 391 |  | 401 |  | 411 |  | 422 |
|  | 381 |  | 391 |  | 401 |  | 412 |  | 422 |
|  | 381 |  | 391 |  | 402 |  | 412 |  | 422 |
|  | 381 |  | 392 |  | 402 |  | 412 |  | 422 |
|  | 382 |  | 392 |  | 402 |  | 412 |  | 423 |
|  | 382 |  | 392 |  | 402 |  | 413 |  | 423 |
|  | 382 |  | 392 |  | 403 |  | 413 |  | 423 |
|  | 382 |  | 393 |  | 403 |  | 413 |  | 423 |
|  | 383 |  | 393 |  | 403 |  | 413 |  | 424 |
|  | 383 |  | 393 |  | 403 |  | 414 |  | 424 |
|  | 383 |  | 393 |  | 404 |  | 414 |  | 424 |
|  | 383 |  | 394 |  | 404 |  | 414 |  | 424 |
|  | 384 |  | 394 |  | 404 |  | 414 |  | 425 |
|  | 384 |  | 394 |  | 404 |  | 415 |  | 425 |
|  | 384 |  | 394 |  | 405 |  | 415 |  | 425 |
|  | 384 |  | 395 |  | 405 |  | 415 |  | 425 |
|  | 385 |  | 395 |  | 405 |  | 415 |  | 426 |
|  | 385 |  | 395 |  | 405 |  | 416 |  | 426 |
|  | 385 |  | 395 |  | 406 |  | 416 |  | 426 |
|  | 385 |  | 396 |  | 406 |  | 416 |  | 426 |
|  | 386 |  | 396 |  | 406 |  | 416 |  | 427 |
|  | 386 |  | 396 |  | 406 |  | 417 |  | 427 |
|  | 386 |  | 396 |  | 407 |  | 417 |  | 427 |
|  | 386 |  | 397 |  | 407 |  | 417 |  | 427 |
|  | 387 |  | 397 |  | 407 |  | 417 |  | 428 |
|  | 387 |  | 397 |  | 407 |  | 418 |  | 428 |
|  | 387 |  | 397 |  | 408 |  | 418 |  | 428 |
|  | 387 |  | 398 |  | 408 |  | 418 |  | 428 |
|  | 388 |  | 398 |  | 408 |  | 418 |  | 429 |
|  | 388 |  | 398 |  | 408 |  | 419 |  | 429 |
|  | 388 |  | 398 |  | 409 |  | 419 |  | 429 |
|  | 388 |  | 399 |  | 409 |  | 419 |  | 429 |
|  | 389 |  | 399 |  | 409 |  | 419 |  | 430 |
|  | 389 |  | 399 |  | 409 |  | 420 |  | 430 |
|  | 389 |  | 399 |  | 410 |  | 420 |  | 430 |
|  | 389 |  | 400 |  | 410 |  | 420 |  | 430 |
|  | 390 |  | 400 |  | 410 |  | 420 |  | 431 |
|  | 390 |  | 400 |  | 410 |  | 421 |  | 431 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)


SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

| Trt. No |  |  |  |  |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 503 | PPD | 513 | PPD | 523 | PPD | 534 | PPD | 544 | PPD | 554 | PPD | 564 |
|  | 503 |  | 513 |  | 524 |  | 534 |  | 544 |  | 554 |  | 565 |
|  | 503 |  | 514 |  | 524 |  | 534 |  | 544 |  | 555 |  | 565 |
|  | 504 |  | 514 |  | 524 |  | 534 |  | 545 |  | 555 |  | 565 |
|  | 504 |  | 514 |  | 524 |  | 535 |  | 545 |  | 555 |  | 565 |
|  | 504 |  | 514 |  | 525 |  | 535 |  | 545 |  | 555 |  | 566 |
|  | 504 |  | 515 |  | 525 |  | 535 |  | 545 |  | 556 |  | 566 |
|  | 505 |  | 515 |  | 525 |  | 535 |  | 546 |  | 556 |  | 566 |
|  | 505 |  | 515 |  | 525 |  | 536 |  | 546 |  | 556 |  | 566 |
|  | 505 |  | 515 |  | 526 |  | 536 |  | 546 |  | 556 |  | 567 |
|  | 505 |  | 516 |  | 526 |  | 536 |  | 546 |  | 557 |  | 567 |
|  | 506 |  | 516 |  | 526 |  | 536 |  | 547 |  | 557 |  | 567 |
|  | 506 |  | 516 |  | 526 |  | 537 |  | 547 |  | 557 |  | 567 |
|  | 506 |  | 516 |  | 527 |  | 537 |  | 547 |  | 557 |  | 568 |
|  | 506 |  | 517 |  | 527 |  | 537 |  | 547 |  | 558 |  | 568 |
|  | 507 |  | 517 |  | 527 |  | 537 |  | 548 |  | 558 |  | 568 |
|  | 507 |  | 517 |  | 527 |  | 538 |  | 548 |  | 558 |  | 568 |
|  | 507 |  | 517 |  | 528 |  | 538 |  | 548 |  | 558 |  | 569 |
|  | 507 |  | 518 |  | 528 |  | 538 |  | 548 |  | 559 |  | 569 |
|  | 508 |  | 518 |  | 528 |  | 538 |  | 549 |  | 559 |  | 569 |
|  | 508 |  | 518 |  | 528 |  | 539 |  | 549 |  | 559 |  | 569 |
|  | 508 |  | 518 |  | 529 |  | 539 |  | 549 |  | 559 |  | 570 |
|  | 508 |  | 519 |  | 529 |  | 539 |  | 549 |  | 560 |  | 570 |
|  | 509 |  | 519 |  | 529 |  | 539 |  | 550 |  | 560 |  | 570 |
|  | 509 |  | 519 |  | 529 |  | 540 |  | 550 |  | 560 |  | 570 |
|  | 509 |  | 519 |  | 530 |  | 540 |  | 550 |  | 560 |  | 571 |
|  | 509 |  | 520 |  | 530 |  | 540 |  | 550 |  | 561 |  | 571 |
|  | 510 |  | 520 |  | 530 |  | 540 |  | 551 |  | 561 |  | 571 |
|  | 510 |  | 520 |  | 530 |  | 541 |  | 551 |  | 561 |  | 571 |
|  | 510 |  | 520 |  | 531 |  | 541 |  | 551 |  | 561 |  | 572 |
|  | 510 |  | 521 |  | 531 |  | 541 |  | 551 |  | 562 |  | 572 |
|  | 511 |  | 521 |  | 531 |  | 541 |  | 552 |  | 562 |  | 572 |
|  | 511 |  | 521 |  | 531 |  | 542 |  | 552 |  | 562 |  | 572 |
|  | 511 |  | 521 |  | 532 |  | 542 |  | 552 |  | 562 |  | 573 |
|  | 511 |  | 522 |  | 532 |  | 542 |  | 552 |  | 563 |  | 573 |
|  | 512 |  | 522 |  | 532 |  | 542 |  | 553 |  | 563 |  | 573 |
|  | 512 |  | 522 |  | 532 |  | 543 |  | 553 |  | 563 |  | 573 |
|  | 512 |  | 522 |  | 533 |  | 543 |  | 553 |  | 563 |  | 574 |
|  | 512 |  | 523 |  | 533 |  | 543 |  | 553 |  | 564 |  | 574 |
|  | 513 |  | 523 |  | 533 |  | 543 |  | 554 |  | 564 |  | 574 |
|  | 513 |  | 523 |  | 533 |  | 544 |  | 554 |  | 564 |  | 574 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)


Randomisation list

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo


SD4 $\backslash$ RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 718 | PPD | 728 | PPD | 739 | PPD | 749 | PPD | 759 | PPD | 769 | PPD | 780 |
|  | 718 |  | 729 |  | 739 |  | 749 |  | 759 |  | 770 |  | 780 |
|  | 719 |  | 729 |  | 739 |  | 749 |  | 760 |  | 770 |  | 780 |
|  | 719 |  | 729 |  | 739 |  | 750 |  | 760 |  | 770 |  | 780 |
|  | 719 |  | 729 |  | 740 |  | 750 |  | 760 |  | 770 |  | 781 |
|  | 719 |  | 730 |  | 740 |  | 750 |  | 760 |  | 771 |  | 781 |
|  | 720 |  | 730 |  | 740 |  | 750 |  | 761 |  | 771 |  | 781 |
|  | 720 |  | 730 |  | 740 |  | 751 |  | 761 |  | 771 |  | 781 |
|  | 720 |  | 730 |  | 741 |  | 751 |  | 761 |  | 771 |  | 782 |
|  | 720 |  | 731 |  | 741 |  | 751 |  | 761 |  | 772 |  | 782 |
|  | 721 |  | 731 |  | 741 |  | 751 |  | 762 |  | 772 |  | 782 |
|  | 721 |  | 731 |  | 741 |  | 752 |  | 762 |  | 772 |  | 782 |
|  | 721 |  | 731 |  | 742 |  | 752 |  | 762 |  | 772 |  | 783 |
|  | 721 |  | 732 |  | 742 |  | 752 |  | 762 |  | 773 |  | 783 |
|  | 722 |  | 732 |  | 742 |  | 752 |  | 763 |  | 773 |  | 783 |
|  | 722 |  | 732 |  | 742 |  | 753 |  | 763 |  | 773 |  | 783 |
|  | 722 |  | 732 |  | 743 |  | 753 |  | 763 |  | 773 |  | 784 |
|  | 722 |  | 733 |  | 743 |  | 753 |  | 763 |  | 774 |  | 784 |
|  | 723 |  | 733 |  | 743 |  | 753 |  | 764 |  | 774 |  | 784 |
|  | 723 |  | 733 |  | 743 |  | 754 |  | 764 |  | 774 |  | 784 |
|  | 723 |  | 733 |  | 744 |  | 754 |  | 764 |  | 774 |  | 785 |
|  | 723 |  | 734 |  | 744 |  | 754 |  | 764 |  | 775 |  | 785 |
|  | 724 |  | 734 |  | 744 |  | 754 |  | 765 |  | 775 |  | 785 |
|  | 724 |  | 734 |  | 744 |  | 755 |  | 765 |  | 775 |  | 785 |
|  | 724 |  | 734 |  | 745 |  | 755 |  | 765 |  | 775 |  | 786 |
|  | 724 |  | 735 |  | 745 |  | 755 |  | 765 |  | 776 |  | 786 |
|  | 725 |  | 735 |  | 745 |  | 755 |  | 766 |  | 776 |  | 786 |
|  | 725 |  | 735 |  | 745 |  | 756 |  | 766 |  | 776 |  | 786 |
|  | 725 |  | 735 |  | 746 |  | 756 |  | 766 |  | 776 |  | 787 |
|  | 725 |  | 736 |  | 746 |  | 756 |  | 766 |  | 777 |  | 787 |
|  | 726 |  | 736 |  | 746 |  | 756 |  | 767 |  | 777 |  | 787 |
|  | 726 |  | 736 |  | 746 |  | 757 |  | 767 |  | 777 |  | 787 |
|  | 726 |  | 736 |  | 747 |  | 757 |  | 767 |  | 777 |  | 788 |
|  | 726 |  | 737 |  | 747 |  | 757 |  | 767 |  | 778 |  | 788 |
|  | 727 |  | 737 |  | 747 |  | 757 |  | 768 |  | 778 |  | 788 |
|  | 727 |  | 737 |  | 747 |  | 758 |  | 768 |  | 778 |  | 788 |
|  | 727 |  | 737 |  | 748 |  | 758 |  | 768 |  | 778 |  | 789 |
|  | 727 |  | 738 |  | 748 |  | 758 |  | 768 |  | 779 |  | 789 |
|  | 728 |  | 738 |  | 748 |  | 758 |  | 769 |  | 779 |  | 789 |
|  | 728 |  | 738 |  | 748 |  | 759 |  | 769 |  | 779 |  | 789 |
|  | 728 |  | 738 |  | 749 |  | 759 |  | 769 |  | 779 |  | 790 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| Tret. | Bl. | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 790 | PPD | 800 | PPD | 810 | PPD | 821 | PPD | 831 | PPD | 841 | PPD | 851 |
|  | 790 |  | 800 |  | 811 |  | 821 |  | 831 |  | 841 |  | 852 |
|  | 790 |  | 801 |  | 811 |  | 821 |  | 831 |  | 842 |  | 852 |
|  | 791 |  | 801 |  | 811 |  | 821 |  | 832 |  | 842 |  | 852 |
|  | 791 |  | 801 |  | 811 |  | 822 |  | 832 |  | 842 |  | 852 |
|  | 791 |  | 801 |  | 812 |  | 822 |  | 832 |  | 842 |  | 853 |
|  | 791 |  | 802 |  | 812 |  | 822 |  | 832 |  | 843 |  | 853 |
|  | 792 |  | 802 |  | 812 |  | 822 |  | 833 |  | 843 |  | 853 |
|  | 792 |  | 802 |  | 812 |  | 823 |  | 833 |  | 843 |  | 853 |
|  | 792 |  | 802 |  | 813 |  | 823 |  | 833 |  | 843 |  | 854 |
|  | 792 |  | 803 |  | 813 |  | 823 |  | 833 |  | 844 |  | 854 |
|  | 793 |  | 803 |  | 813 |  | 823 |  | 834 |  | 844 |  | 854 |
|  | 793 |  | 803 |  | 813 |  | 824 |  | 834 |  | 844 |  | 854 |
|  | 793 |  | 803 |  | 814 |  | 824 |  | 834 |  | 844 |  | 855 |
|  | 793 |  | 804 |  | 814 |  | 824 |  | 834 |  | 845 |  | 855 |
|  | 794 |  | 804 |  | 814 |  | 824 |  | 835 |  | 845 |  | 855 |
|  | 794 |  | 804 |  | 814 |  | 825 |  | 835 |  | 845 |  | 855 |
|  | 794 |  | 804 |  | 815 |  | 825 |  | 835 |  | 845 |  | 856 |
|  | 794 |  | 805 |  | 815 |  | 825 |  | 835 |  | 846 |  | 856 |
|  | 795 |  | 805 |  | 815 |  | 825 |  | 836 |  | 846 |  | 856 |
|  | 795 |  | 805 |  | 815 |  | 826 |  | 836 |  | 846 |  | 856 |
|  | 795 |  | 805 |  | 816 |  | 826 |  | 836 |  | 846 |  | 857 |
|  | 795 |  | 806 |  | 816 |  | 826 |  | 836 |  | 847 |  | 857 |
|  | 796 |  | 806 |  | 816 |  | 826 |  | 837 |  | 847 |  | 857 |
|  | 796 |  | 806 |  | 816 |  | 827 |  | 837 |  | 847 |  | 857 |
|  | 796 |  | 806 |  | 817 |  | 827 |  | 837 |  | 847 |  | 858 |
|  | 796 |  | 807 |  | 817 |  | 827 |  | 837 |  | 848 |  | 858 |
|  | 797 |  | 807 |  | 817 |  | 827 |  | 838 |  | 848 |  | 858 |
|  | 797 |  | 807 |  | 817 |  | 828 |  | 838 |  | 848 |  | 858 |
|  | 797 |  | 807 |  | 818 |  | 828 |  | 838 |  | 848 |  | 859 |
|  | 797 |  | 808 |  | 818 |  | 828 |  | 838 |  | 849 |  | 859 |
|  | 798 |  | 808 |  | 818 |  | 828 |  | 839 |  | 849 |  | 859 |
|  | 798 |  | 808 |  | 818 |  | 829 |  | 839 |  | 849 |  | 859 |
|  | 798 |  | 808 |  | 819 |  | 829 |  | 839 |  | 849 |  | 860 |
|  | 798 |  | 809 |  | 819 |  | 829 |  | 839 |  | 850 |  | 860 |
|  | 799 |  | 809 |  | 819 |  | 829 |  | 840 |  | 850 |  | 860 |
|  | 799 |  | 809 |  | 819 |  | 830 |  | 840 |  | 850 |  | 860 |
|  | 799 |  | 809 |  | 820 |  | 830 |  | 840 |  | 850 |  | 861 |
|  | 799 |  | 810 |  | 820 |  | 830 |  | 840 |  | 851 |  | 861 |
|  | 800 |  | 810 |  | 820 |  | 830 |  | 841 |  | 851 |  | 861 |
|  | 800 |  | 810 |  | 820 |  | 831 |  | 841 |  | 851 |  | 861 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{gathered} \text { Trt. } \\ \text { No } \end{gathered}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | Trt. Bl. |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 862 | PPD | 872 | PPD | 882 | PPD | 892 | PPD | 903 | PPD | 913 | PPD | 923 |
|  | 862 |  | 872 |  | 882 |  | 893 |  | 903 |  | 913 |  | 923 |
|  | 862 |  | 872 |  | 883 |  | 893 |  | 903 |  | 913 |  | 924 |
|  | 862 |  | 873 |  | 883 |  | 893 |  | 903 |  | 914 |  | 924 |
|  | 863 |  | 873 |  | 883 |  | 893 |  | 904 |  | 914 |  | 924 |
|  | 863 |  | 873 |  | 883 |  | 894 |  | 904 |  | 914 |  | 924 |
|  | 863 |  | 873 |  | 884 |  | 894 |  | 904 |  | 914 |  | 925 |
|  | 863 |  | 874 |  | 884 |  | 894 |  | 904 |  | 915 |  | 925 |
|  | 864 |  | 874 |  | 884 |  | 894 |  | 905 |  | 915 |  | 925 |
|  | 864 |  | 874 |  | 884 |  | 895 |  | 905 |  | 915 |  | 925 |
|  | 864 |  | 874 |  | 885 |  | 895 |  | 905 |  | 915 |  | 926 |
|  | 864 |  | 875 |  | 885 |  | 895 |  | 905 |  | 916 |  | 926 |
|  | 865 |  | 875 |  | 885 |  | 895 |  | 906 |  | 916 |  | 926 |
|  | 865 |  | 875 |  | 885 |  | 896 |  | 906 |  | 916 |  | 926 |
|  | 865 |  | 875 |  | 886 |  | 896 |  | 906 |  | 916 |  | 927 |
|  | 865 |  | 876 |  | 886 |  | 896 |  | 906 |  | 917 |  | 927 |
|  | 866 |  | 876 |  | 886 |  | 896 |  | 907 |  | 917 |  | 927 |
|  | 866 |  | 876 |  | 886 |  | 897 |  | 907 |  | 917 |  | 927 |
|  | 866 |  | 876 |  | 887 |  | 897 |  | 907 |  | 917 |  | 928 |
|  | 866 |  | 877 |  | 887 |  | 897 |  | 907 |  | 918 |  | 928 |
|  | 867 |  | 877 |  | 887 |  | 897 |  | 908 |  | 918 |  | 928 |
|  | 867 |  | 877 |  | 887 |  | 898 |  | 908 |  | 918 |  | 928 |
|  | 867 |  | 877 |  | 888 |  | 898 |  | 908 |  | 918 |  | 929 |
|  | 867 |  | 878 |  | 888 |  | 898 |  | 908 |  | 919 |  | 929 |
|  | 868 |  | 878 |  | 888 |  | 898 |  | 909 |  | 919 |  | 929 |
|  | 868 |  | 878 |  | 888 |  | 899 |  | 909 |  | 919 |  | 929 |
|  | 868 |  | 878 |  | 889 |  | 899 |  | 909 |  | 919 |  | 930 |
|  | 868 |  | 879 |  | 889 |  | 899 |  | 909 |  | 920 |  | 930 |
|  | 869 |  | 879 |  | 889 |  | 899 |  | 910 |  | 920 |  | 930 |
|  | 869 |  | 879 |  | 889 |  | 900 |  | 910 |  | 920 |  | 930 |
|  | 869 |  | 879 |  | 890 |  | 900 |  | 910 |  | 920 |  | 931 |
|  | 869 |  | 880 |  | 890 |  | 900 |  | 910 |  | 921 |  | 931 |
|  | 870 |  | 880 |  | 890 |  | 900 |  | 911 |  | 921 |  | 931 |
|  | 870 |  | 880 |  | 890 |  | 901 |  | 911 |  | 921 |  | 931 |
|  | 870 |  | 880 |  | 891 |  | 901 |  | 911 |  | 921 |  | 932 |
|  | 870 |  | 881 |  | 891 |  | 901 |  | 911 |  | 922 |  | 932 |
|  | 871 |  | 881 |  | 891 |  | 901 |  | 912 |  | 922 |  | 932 |
|  | 871 |  | 881 |  | 891 |  | 902 |  | 912 |  | 922 |  | 932 |
|  | 871 |  | 881 |  | 892 |  | 902 |  | 912 |  | 922 |  | 933 |
|  | 871 |  | 882 |  | 892 |  | 902 |  | 912 |  | 923 |  | 933 |
|  | 872 |  | 882 |  | 892 |  | 902 |  | 913 |  | 923 |  | 933 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{gathered} \text { Trt. } \\ \text { No } \end{gathered}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | Trt. Bl. |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. } \mathrm{Bl} . \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 933 | PPD | 944 | PPD | 954 | PPD | 964 | PPD | 974 | PPD | 985 | PPD | 995 |
|  | 934 |  | 944 |  | 954 |  | 964 |  | 975 |  | 985 |  | 995 |
|  | 934 |  | 944 |  | 954 |  | 965 |  | 975 |  | 985 |  | 995 |
|  | 934 |  | 944 |  | 955 |  | 965 |  | 975 |  | 985 |  | 996 |
|  | 934 |  | 945 |  | 955 |  | 965 |  | 975 |  | 986 |  | 996 |
|  | 935 |  | 945 |  | 955 |  | 965 |  | 976 |  | 986 |  | 996 |
|  | 935 |  | 945 |  | 955 |  | 966 |  | 976 |  | 986 |  | 996 |
|  | 935 |  | 945 |  | 956 |  | 966 |  | 976 |  | 986 |  | 997 |
|  | 935 |  | 946 |  | 956 |  | 966 |  | 976 |  | 987 |  | 997 |
|  | 936 |  | 946 |  | 956 |  | 966 |  | 977 |  | 987 |  | 997 |
|  | 936 |  | 946 |  | 956 |  | 967 |  | 977 |  | 987 |  | 997 |
|  | 936 |  | 946 |  | 957 |  | 967 |  | 977 |  | 987 |  | 998 |
|  | 936 |  | 947 |  | 957 |  | 967 |  | 977 |  | 988 |  | 998 |
|  | 937 |  | 947 |  | 957 |  | 967 |  | 978 |  | 988 |  | 998 |
|  | 937 |  | 947 |  | 957 |  | 968 |  | 978 |  | 988 |  | 998 |
|  | 937 |  | 947 |  | 958 |  | 968 |  | 978 |  | 988 |  | 999 |
|  | 937 |  | 948 |  | 958 |  | 968 |  | 978 |  | 989 |  | 999 |
|  | 938 |  | 948 |  | 958 |  | 968 |  | 979 |  | 989 |  | 999 |
|  | 938 |  | 948 |  | 958 |  | 969 |  | 979 |  | 989 |  | 999 |
|  | 938 |  | 948 |  | 959 |  | 969 |  | 979 |  | 989 |  | 1000 |
|  | 938 |  | 949 |  | 959 |  | 969 |  | 979 |  | 990 |  | 1000 |
|  | 939 |  | 949 |  | 959 |  | 969 |  | 980 |  | 990 |  | 1000 |
|  | 939 |  | 949 |  | 959 |  | 970 |  | 980 |  | 990 |  | 1000 |
|  | 939 |  | 949 |  | 960 |  | 970 |  | 980 |  | 990 |  | 1001 |
|  | 939 |  | 950 |  | 960 |  | 970 |  | 980 |  | 991 |  | 1001 |
|  | 940 |  | 950 |  | 960 |  | 970 |  | 981 |  | 991 |  | 1001 |
|  | 940 |  | 950 |  | 960 |  | 971 |  | 981 |  | 991 |  | 1001 |
|  | 940 |  | 950 |  | 961 |  | 971 |  | 981 |  | 991 |  | 1002 |
|  | 940 |  | 951 |  | 961 |  | 971 |  | 981 |  | 992 |  | 1002 |
|  | 941 |  | 951 |  | 961 |  | 971 |  | 982 |  | 992 |  | 1002 |
|  | 941 |  | 951 |  | 961 |  | 972 |  | 982 |  | 992 |  | 1002 |
|  | 941 |  | 951 |  | 962 |  | 972 |  | 982 |  | 992 |  | 1003 |
|  | 941 |  | 952 |  | 962 |  | 972 |  | 982 |  | 993 |  | 1003 |
|  | 942 |  | 952 |  | 962 |  | 972 |  | 983 |  | 993 |  | 1003 |
|  | 942 |  | 952 |  | 962 |  | 973 |  | 983 |  | 993 |  | 1003 |
|  | 942 |  | 952 |  | 963 |  | 973 |  | 983 |  | 993 |  | 1004 |
|  | 942 |  | 953 |  | 963 |  | 973 |  | 983 |  | 994 |  | 1004 |
|  | 943 |  | 953 |  | 963 |  | 973 |  | 984 |  | 994 |  | 1004 |
|  | 943 |  | 953 |  | 963 |  | 974 |  | 984 |  | 994 |  | 1004 |
|  | 943 |  | 953 |  | 964 |  | 974 |  | 984 |  | 994 |  | 1005 |
|  | 943 |  | 954 |  | 964 |  | 974 |  | 984 |  | 995 |  | 1005 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1005 | PPD | 1015 | PPD | 1026 | PPD | 1036 | PPD | 1046 | PPD | 1056 | PPD | 1067 |
|  | 1005 |  | 1016 |  | 1026 |  | 1036 |  | 1046 |  | 1057 |  | 1067 |
|  | 1006 |  | 1016 |  | 1026 |  | 1036 |  | 1047 |  | 1057 |  | 1067 |
|  | 1006 |  | 1016 |  | 1026 |  | 1037 |  | 1047 |  | 1057 |  | 1067 |
|  | 1006 |  | 1016 |  | 1027 |  | 1037 |  | 1047 |  | 1057 |  | 1068 |
|  | 1006 |  | 1017 |  | 1027 |  | 1037 |  | 1047 |  | 1058 |  | 1068 |
|  | 1007 |  | 1017 |  | 1027 |  | 1037 |  | 1048 |  | 1058 |  | 1068 |
|  | 1007 |  | 1017 |  | 1027 |  | 1038 |  | 1048 |  | 1058 |  | 1068 |
|  | 1007 |  | 1017 |  | 1028 |  | 1038 |  | 1048 |  | 1058 |  | 1069 |
|  | 1007 |  | 1018 |  | 1028 |  | 1038 |  | 1048 |  | 1059 |  | 1069 |
|  | 1008 |  | 1018 |  | 1028 |  | 1038 |  | 1049 |  | 1059 |  | 1069 |
|  | 1008 |  | 1018 |  | 1028 |  | 1039 |  | 1049 |  | 1059 |  | 1069 |
|  | 1008 |  | 1018 |  | 1029 |  | 1039 |  | 1049 |  | 1059 |  | 1070 |
|  | 1008 |  | 1019 |  | 1029 |  | 1039 |  | 1049 |  | 1060 |  | 1070 |
|  | 1009 |  | 1019 |  | 1029 |  | 1039 |  | 1050 |  | 1060 |  | 1070 |
|  | 1009 |  | 1019 |  | 1029 |  | 1040 |  | 1050 |  | 1060 |  | 1070 |
|  | 1009 |  | 1019 |  | 1030 |  | 1040 |  | 1050 |  | 1060 |  | 1071 |
|  | 1009 |  | 1020 |  | 1030 |  | 1040 |  | 1050 |  | 1061 |  | 1071 |
|  | 1010 |  | 1020 |  | 1030 |  | 1040 |  | 1051 |  | 1061 |  | 1071 |
|  | 1010 |  | 1020 |  | 1030 |  | 1041 |  | 1051 |  | 1061 |  | 1071 |
|  | 1010 |  | 1020 |  | 1031 |  | 1041 |  | 1051 |  | 1061 |  | 1072 |
|  | 1010 |  | 1021 |  | 1031 |  | 1041 |  | 1051 |  | 1062 |  | 1072 |
|  | 1011 |  | 1021 |  | 1031 |  | 1041 |  | 1052 |  | 1062 |  | 1072 |
|  | 1011 |  | 1021 |  | 1031 |  | 1042 |  | 1052 |  | 1062 |  | 1072 |
|  | 1011 |  | 1021 |  | 1032 |  | 1042 |  | 1052 |  | 1062 |  | 1073 |
|  | 1011 |  | 1022 |  | 1032 |  | 1042 |  | 1052 |  | 1063 |  | 1073 |
|  | 1012 |  | 1022 |  | 1032 |  | 1042 |  | 1053 |  | 1063 |  | 1073 |
|  | 1012 |  | 1022 |  | 1032 |  | 1043 |  | 1053 |  | 1063 |  | 1073 |
|  | 1012 |  | 1022 |  | 1033 |  | 1043 |  | 1053 |  | 1063 |  | 1074 |
|  | 1012 |  | 1023 |  | 1033 |  | 1043 |  | 1053 |  | 1064 |  | 1074 |
|  | 1013 |  | 1023 |  | 1033 |  | 1043 |  | 1054 |  | 1064 |  | 1074 |
|  | 1013 |  | 1023 |  | 1033 |  | 1044 |  | 1054 |  | 1064 |  | 1074 |
|  | 1013 |  | 1023 |  | 1034 |  | 1044 |  | 1054 |  | 1064 |  | 1075 |
|  | 1013 |  | 1024 |  | 1034 |  | 1044 |  | 1054 |  | 1065 |  | 1075 |
|  | 1014 |  | 1024 |  | 1034 |  | 1044 |  | 1055 |  | 1065 |  | 1075 |
|  | 1014 |  | 1024 |  | 1034 |  | 1045 |  | 1055 |  | 1065 |  | 1075 |
|  | 1014 |  | 1024 |  | 1035 |  | 1045 |  | 1055 |  | 1065 |  | 1076 |
|  | 1014 |  | 1025 |  | 1035 |  | 1045 |  | 1055 |  | 1066 |  | 1076 |
|  | 1015 |  | 1025 |  | 1035 |  | 1045 |  | 1056 |  | 1066 |  | 1076 |
|  | 1015 |  | 1025 |  | 1035 |  | 1046 |  | 1056 |  | 1066 |  | 1076 |
|  | 1015 |  | 1025 |  | 1036 |  | 1046 |  | 1056 |  | 1066 |  | 1077 |

Treatment number associated to material : Hz/su-PreChemo


SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  |  |  | Bl nb |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1149 | PPD | 1159 | PPD | 1169 | PPD | 1179 | PPD | 1190 | PPD | 1200 | PPD | 1210 |
|  | 1149 |  | 1159 |  | 1169 |  | 1180 |  | 1190 |  | 1200 |  | 1210 |
|  | 1149 |  | 1159 |  | 1170 |  | 1180 |  | 1190 |  | 1200 |  | 1211 |
|  | 1149 |  | 1160 |  | 1170 |  | 1180 |  | 1190 |  | 1201 |  | 1211 |
|  | 1150 |  | 1160 |  | 1170 |  | 1180 |  | 1191 |  | 1201 |  | 1211 |
|  | 1150 |  | 1160 |  | 1170 |  | 1181 |  | 1191 |  | 1201 |  | 1211 |
|  | 1150 |  | 1160 |  | 1171 |  | 1181 |  | 1191 |  | 1201 |  | 1212 |
|  | 1150 |  | 1161 |  | 1171 |  | 1181 |  | 1191 |  | 1202 |  | 1212 |
|  | 1151 |  | 1161 |  | 1171 |  | 1181 |  | 1192 |  | 1202 |  | 1212 |
|  | 1151 |  | 1161 |  | 1171 |  | 1182 |  | 1192 |  | 1202 |  | 1212 |
|  | 1151 |  | 1161 |  | 1172 |  | 1182 |  | 1192 |  | 1202 |  | 1213 |
|  | 1151 |  | 1162 |  | 1172 |  | 1182 |  | 1192 |  | 1203 |  | 1213 |
|  | 1152 |  | 1162 |  | 1172 |  | 1182 |  | 1193 |  | 1203 |  | 1213 |
|  | 1152 |  | 1162 |  | 1172 |  | 1183 |  | 1193 |  | 1203 |  | 1213 |
|  | 1152 |  | 1162 |  | 1173 |  | 1183 |  | 1193 |  | 1203 |  | 1214 |
|  | 1152 |  | 1163 |  | 1173 |  | 1183 |  | 1193 |  | 1204 |  | 1214 |
|  | 1153 |  | 1163 |  | 1173 |  | 1183 |  | 1194 |  | 1204 |  | 1214 |
|  | 1153 |  | 1163 |  | 1173 |  | 1184 |  | 1194 |  | 1204 |  | 1214 |
|  | 1153 |  | 1163 |  | 1174 |  | 1184 |  | 1194 |  | 1204 |  | 1215 |
|  | 1153 |  | 1164 |  | 1174 |  | 1184 |  | 1194 |  | 1205 |  | 1215 |
|  | 1154 |  | 1164 |  | 1174 |  | 1184 |  | 1195 |  | 1205 |  | 1215 |
|  | 1154 |  | 1164 |  | 1174 |  | 1185 |  | 1195 |  | 1205 |  | 1215 |
|  | 1154 |  | 1164 |  | 1175 |  | 1185 |  | 1195 |  | 1205 |  | 1216 |
|  | 1154 |  | 1165 |  | 1175 |  | 1185 |  | 1195 |  | 1206 |  | 1216 |
|  | 1155 |  | 1165 |  | 1175 |  | 1185 |  | 1196 |  | 1206 |  | 1216 |
|  | 1155 |  | 1165 |  | 1175 |  | 1186 |  | 1196 |  | 1206 |  | 1216 |
|  | 1155 |  | 1165 |  | 1176 |  | 1186 |  | 1196 |  | 1206 |  | 1217 |
|  | 1155 |  | 1166 |  | 1176 |  | 1186 |  | 1196 |  | 1207 |  | 1217 |
|  | 1156 |  | 1166 |  | 1176 |  | 1186 |  | 1197 |  | 1207 |  | 1217 |
|  | 1156 |  | 1166 |  | 1176 |  | 1187 |  | 1197 |  | 1207 |  | 1217 |
|  | 1156 |  | 1166 |  | 1177 |  | 1187 |  | 1197 |  | 1207 |  | 1218 |
|  | 1156 |  | 1167 |  | 1177 |  | 1187 |  | 1197 |  | 1208 |  | 1218 |
|  | 1157 |  | 1167 |  | 1177 |  | 1187 |  | 1198 |  | 1208 |  | 1218 |
|  | 1157 |  | 1167 |  | 1177 |  | 1188 |  | 1198 |  | 1208 |  | 1218 |
|  | 1157 |  | 1167 |  | 1178 |  | 1188 |  | 1198 |  | 1208 |  | 1219 |
|  | 1157 |  | 1168 |  | 1178 |  | 1188 |  | 1198 |  | 1209 |  | 1219 |
|  | 1158 |  | 1168 |  | 1178 |  | 1188 |  | 1199 |  | 1209 |  | 1219 |
|  | 1158 |  | 1168 |  | 1178 |  | 1189 |  | 1199 |  | 1209 |  | 1219 |
|  | 1158 |  | 1168 |  | 1179 |  | 1189 |  | 1199 |  | 1209 |  | 1220 |
|  | 1158 |  | 1169 |  | 1179 |  | 1189 |  | 1199 |  | 1210 |  | 1220 |
|  | 1159 |  | 1169 |  | 1179 |  | 1189 |  | 1200 |  | 1210 |  | 1220 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| Trt. | Bl nb |  | Bl. | Trt | Bl . |  | Bl nb |  | Bl nb | Trt | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1220 | PPD | 1231 | PPD | 1241 | PPD | 1251 | PPD | 1261 | PPD | 1272 | PPD | 1282 |
|  | 1221 |  | 1231 |  | 1241 |  | 1251 |  | 1262 |  | 1272 |  | 1282 |
|  | 1221 |  | 1231 |  | 1241 |  | 1252 |  | 1262 |  | 1272 |  | 1282 |
|  | 1221 |  | 1231 |  | 1242 |  | 1252 |  | 1262 |  | 1272 |  | 1283 |
|  | 1221 |  | 1232 |  | 1242 |  | 1252 |  | 1262 |  | 1273 |  | 1283 |
|  | 1222 |  | 1232 |  | 1242 |  | 1252 |  | 1263 |  | 1273 |  | 1283 |
|  | 1222 |  | 1232 |  | 1242 |  | 1253 |  | 1263 |  | 1273 |  | 1283 |
|  | 1222 |  | 1232 |  | 1243 |  | 1253 |  | 1263 |  | 1273 |  | 1284 |
|  | 1222 |  | 1233 |  | 1243 |  | 1253 |  | 1263 |  | 1274 |  | 1284 |
|  | 1223 |  | 1233 |  | 1243 |  | 1253 |  | 1264 |  | 1274 |  | 1284 |
|  | 1223 |  | 1233 |  | 1243 |  | 1254 |  | 1264 |  | 1274 |  | 1284 |
|  | 1223 |  | 1233 |  | 1244 |  | 1254 |  | 1264 |  | 1274 |  | 1285 |
|  | 1223 |  | 1234 |  | 1244 |  | 1254 |  | 1264 |  | 1275 |  | 1285 |
|  | 1224 |  | 1234 |  | 1244 |  | 1254 |  | 1265 |  | 1275 |  | 1285 |
|  | 1224 |  | 1234 |  | 1244 |  | 1255 |  | 1265 |  | 1275 |  | 1285 |
|  | 1224 |  | 1234 |  | 1245 |  | 1255 |  | 1265 |  | 1275 |  | 1286 |
|  | 1224 |  | 1235 |  | 1245 |  | 1255 |  | 1265 |  | 1276 |  | 1286 |
|  | 1225 |  | 1235 |  | 1245 |  | 1255 |  | 1266 |  | 1276 |  | 1286 |
|  | 1225 |  | 1235 |  | 1245 |  | 1256 |  | 1266 |  | 1276 |  | 1286 |
|  | 1225 |  | 1235 |  | 1246 |  | 1256 |  | 1266 |  | 1276 |  | 1287 |
|  | 1225 |  | 1236 |  | 1246 |  | 1256 |  | 1266 |  | 1277 |  | 1287 |
|  | 1226 |  | 1236 |  | 1246 |  | 1256 |  | 1267 |  | 1277 |  | 1287 |
|  | 1226 |  | 1236 |  | 1246 |  | 1257 |  | 1267 |  | 1277 |  | 1287 |
|  | 1226 |  | 1236 |  | 1247 |  | 1257 |  | 1267 |  | 1277 |  | 1288 |
|  | 1226 |  | 1237 |  | 1247 |  | 1257 |  | 1267 |  | 1278 |  | 1288 |
|  | 1227 |  | 1237 |  | 1247 |  | 1257 |  | 1268 |  | 1278 |  | 1288 |
|  | 1227 |  | 1237 |  | 1247 |  | 1258 |  | 1268 |  | 1278 |  | 1288 |
|  | 1227 |  | 1237 |  | 1248 |  | 1258 |  | 1268 |  | 1278 |  | 1289 |
|  | 1227 |  | 1238 |  | 1248 |  | 1258 |  | 1268 |  | 1279 |  | 1289 |
|  | 1228 |  | 1238 |  | 1248 |  | 1258 |  | 1269 |  | 1279 |  | 1289 |
|  | 1228 |  | 1238 |  | 1248 |  | 1259 |  | 1269 |  | 1279 |  | 1289 |
|  | 1228 |  | 1238 |  | 1249 |  | 1259 |  | 1269 |  | 1279 |  | 1290 |
|  | 1228 |  | 1239 |  | 1249 |  | 1259 |  | 1269 |  | 1280 |  | 1290 |
|  | 1229 |  | 1239 |  | 1249 |  | 1259 |  | 1270 |  | 1280 |  | 1290 |
|  | 1229 |  | 1239 |  | 1249 |  | 1260 |  | 1270 |  | 1280 |  | 1290 |
|  | 1229 |  | 1239 |  | 1250 |  | 1260 |  | 1270 |  | 1280 |  | 1291 |
|  | 1229 |  | 1240 |  | 1250 |  | 1260 |  | 1270 |  | 1281 |  | 1291 |
|  | 1230 |  | 1240 |  | 1250 |  | 1260 |  | 1271 |  | 1281 |  | 1291 |
|  | 1230 |  | 1240 |  | 1250 |  | 1261 |  | 1271 |  | 1281 |  | 1291 |
|  | 1230 |  | 1240 |  | 1251 |  | 1261 |  | 1271 |  | 1281 |  | 1292 |
|  | 1230 |  | 1241 |  | 1251 |  | 1261 |  | 1271 |  | 1282 |  | 1292 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl n | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1292 | PPD | 1302 | PPD | 1313 | PPD | 1323 | PPD | 1333 | PPD | 1343 | PPD | 1354 |
|  | 1292 | PPD | 1303 |  | 1313 |  | 1323 |  | 1333 |  | 1344 |  | 1354 |
|  | 1293 |  | 1303 |  | 1313 |  | 1323 |  | 1334 |  | 1344 |  | 1354 |
|  | 1293 |  | 1303 |  | 1313 |  | 1324 |  | 1334 |  | 1344 |  | 1354 |
|  | 1293 |  | 1303 |  | 1314 |  | 1324 |  | 1334 |  | 1344 |  | 1355 |
|  | 1293 |  | 1304 |  | 1314 |  | 1324 |  | 1334 |  | 1345 |  | 1355 |
|  | 1294 |  | 1304 |  | 1314 |  | 1324 |  | 1335 |  | 1345 |  | 1355 |
|  | 1294 |  | 1304 |  | 1314 |  | 1325 |  | 1335 |  | 1345 |  | 1355 |
|  | 1294 |  | 1304 |  | 1315 |  | 1325 |  | 1335 |  | 1345 |  | 1356 |
|  | 1294 |  | 1305 |  | 1315 |  | 1325 |  | 1335 |  | 1346 |  | 1356 |
|  | 1295 |  | 1305 |  | 1315 |  | 1325 |  | 1336 |  | 1346 |  | 1356 |
|  | 1295 |  | 1305 |  | 1315 |  | 1326 |  | 1336 |  | 1346 |  | 1356 |
|  | 1295 |  | 1305 |  | 1316 |  | 1326 |  | 1336 |  | 1346 |  | 1357 |
|  | 1295 |  | 1306 |  | 1316 |  | 1326 |  | 1336 |  | 1347 |  | 1357 |
|  | 1296 |  | 1306 |  | 1316 |  | 1326 |  | 1337 |  | 1347 |  | 1357 |
|  | 1296 |  | 1306 |  | 1316 |  | 1327 |  | 1337 |  | 1347 |  | 1357 |
|  | 1296 |  | 1306 |  | 1317 |  | 1327 |  | 1337 |  | 1347 |  | 1358 |
|  | 1296 |  | 1307 |  | 1317 |  | 1327 |  | 1337 |  | 1348 |  | 1358 |
|  | 1297 |  | 1307 |  | 1317 |  | 1327 |  | 1338 |  | 1348 |  | 1358 |
|  | 1297 |  | 1307 |  | 1317 |  | 1328 |  | 1338 |  | 1348 |  | 1358 |
|  | 1297 |  | 1307 |  | 1318 |  | 1328 |  | 1338 |  | 1348 |  | 1359 |
|  | 1297 |  | 1308 |  | 1318 |  | 1328 |  | 1338 |  | 1349 |  | 1359 |
|  | 1298 |  | 1308 |  | 1318 |  | 1328 |  | 1339 |  | 1349 |  | 1359 |
|  | 1298 |  | 1308 |  | 1318 |  | 1329 |  | 1339 |  | 1349 |  | 1359 |
|  | 1298 |  | 1308 |  | 1319 |  | 1329 |  | 1339 |  | 1349 |  | 1360 |
|  | 1298 |  | 1309 |  | 1319 |  | 1329 |  | 1339 |  | 1350 |  | 1360 |
|  | 1299 |  | 1309 |  | 1319 |  | 1329 |  | 1340 |  | 1350 |  | 1360 |
|  | 1299 |  | 1309 |  | 1319 |  | 1330 |  | 1340 |  | 1350 |  | 1360 |
|  | 1299 |  | 1309 |  | 1320 |  | 1330 |  | 1340 |  | 1350 |  | 1361 |
|  | 1299 |  | 1310 |  | 1320 |  | 1330 |  | 1340 |  | 1351 |  | 1361 |
|  | 1300 |  | 1310 |  | 1320 |  | 1330 |  | 1341 |  | 1351 |  | 1361 |
|  | 1300 |  | 1310 |  | 1320 |  | 1331 |  | 1341 |  | 1351 |  | 1361 |
|  | 1300 |  | 1310 |  | 1321 |  | 1331 |  | 1341 |  | 1351 |  | 1362 |
|  | 1300 |  | 1311 |  | 1321 |  | 1331 |  | 1341 |  | 1352 |  | 1362 |
|  | 1301 |  | 1311 |  | 1321 |  | 1331 |  | 1342 |  | 1352 |  | 1362 |
|  | 1301 |  | 1311 |  | 1321 |  | 1332 |  | 1342 |  | 1352 |  | 1362 |
|  | 1301 |  | 1311 |  | 1322 |  | 1332 |  | 1342 |  | 1352 |  | 1363 |
|  | 1301 |  | 1312 |  | 1322 |  | 1332 |  | 1342 |  | 1353 |  | 1363 |
|  | 1302 |  | 1312 |  | 1322 |  | 1332 |  | 1343 |  | 1353 |  | 1363 |
|  | 1302 |  | 1312 |  | 1322 |  | 1333 |  | 1343 |  | 1353 |  | 1363 |
|  | 1302 |  | 1312 |  | 1323 |  | 1333 |  | 1343 |  | 1353 |  | 1364 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  | Bl. |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1364 | PPD | 1374 | PPD | 1384 | PPD | 1395 | PPD | 1405 | PPD | 1415 | PPD | 1425 |
|  | 1364 |  | 1374 |  | 1385 |  | 1395 |  | 1405 |  | 1415 |  | 1426 |
|  | 1364 |  | 1375 |  | 1385 |  | 1395 |  | 1405 |  | 1416 |  | 1426 |
|  | 1365 |  | 1375 |  | 1385 |  | 1395 |  | 1406 |  | 1416 |  | 1426 |
|  | 1365 |  | 1375 |  | 1385 |  | 1396 |  | 1406 |  | 1416 |  | 1426 |
|  | 1365 |  | 1375 |  | 1386 |  | 1396 |  | 1406 |  | 1416 |  | 1427 |
|  | 1365 |  | 1376 |  | 1386 |  | 1396 |  | 1406 |  | 1417 |  | 1427 |
|  | 1366 |  | 1376 |  | 1386 |  | 1396 |  | 1407 |  | 1417 |  | 1427 |
|  | 1366 |  | 1376 |  | 1386 |  | 1397 |  | 1407 |  | 1417 |  | 1427 |
|  | 1366 |  | 1376 |  | 1387 |  | 1397 |  | 1407 |  | 1417 |  | 1428 |
|  | 1366 |  | 1377 |  | 1387 |  | 1397 |  | 1407 |  | 1418 |  | 1428 |
|  | 1367 |  | 1377 |  | 1387 |  | 1397 |  | 1408 |  | 1418 |  | 1428 |
|  | 1367 |  | 1377 |  | 1387 |  | 1398 |  | 1408 |  | 1418 |  | 1428 |
|  | 1367 |  | 1377 |  | 1388 |  | 1398 |  | 1408 |  | 1418 |  | 1429 |
|  | 1367 |  | 1378 |  | 1388 |  | 1398 |  | 1408 |  | 1419 |  | 1429 |
|  | 1368 |  | 1378 |  | 1388 |  | 1398 |  | 1409 |  | 1419 |  | 1429 |
|  | 1368 |  | 1378 |  | 1388 |  | 1399 |  | 1409 |  | 1419 |  | 1429 |
|  | 1368 |  | 1378 |  | 1389 |  | 1399 |  | 1409 |  | 1419 |  | 1430 |
|  | 1368 |  | 1379 |  | 1389 |  | 1399 |  | 1409 |  | 1420 |  | 1430 |
|  | 1369 |  | 1379 |  | 1389 |  | 1399 |  | 1410 |  | 1420 |  | 1430 |
|  | 1369 |  | 1379 |  | 1389 |  | 1400 |  | 1410 |  | 1420 |  | 1430 |
|  | 1369 |  | 1379 |  | 1390 |  | 1400 |  | 1410 |  | 1420 |  | 1431 |
|  | 1369 |  | 1380 |  | 1390 |  | 1400 |  | 1410 |  | 1421 |  | 1431 |
|  | 1370 |  | 1380 |  | 1390 |  | 1400 |  | 1411 |  | 1421 |  | 1431 |
|  | 1370 |  | 1380 |  | 1390 |  | 1401 |  | 1411 |  | 1421 |  | 1431 |
|  | 1370 |  | 1380 |  | 1391 |  | 1401 |  | 1411 |  | 1421 |  | 1432 |
|  | 1370 |  | 1381 |  | 1391 |  | 1401 |  | 1411 |  | 1422 |  | 1432 |
|  | 1371 |  | 1381 |  | 1391 |  | 1401 |  | 1412 |  | 1422 |  | 1432 |
|  | 1371 |  | 1381 |  | 1391 |  | 1402 |  | 1412 |  | 1422 |  | 1432 |
|  | 1371 |  | 1381 |  | 1392 |  | 1402 |  | 1412 |  | 1422 |  | 1433 |
|  | 1371 |  | 1382 |  | 1392 |  | 1402 |  | 1412 |  | 1423 |  | 1433 |
|  | 1372 |  | 1382 |  | 1392 |  | 1402 |  | 1413 |  | 1423 |  | 1433 |
|  | 1372 |  | 1382 |  | 1392 |  | 1403 |  | 1413 |  | 1423 |  | 1433 |
|  | 1372 |  | 1382 |  | 1393 |  | 1403 |  | 1413 |  | 1423 |  | 1434 |
|  | 1372 |  | 1383 |  | 1393 |  | 1403 |  | 1413 |  | 1424 |  | 1434 |
|  | 1373 |  | 1383 |  | 1393 |  | 1403 |  | 1414 |  | 1424 |  | 1434 |
|  | 1373 |  | 1383 |  | 1393 |  | 1404 |  | 1414 |  | 1424 |  | 1434 |
|  | 1373 |  | 1383 |  | 1394 |  | 1404 |  | 1414 |  | 1424 |  | 1435 |
|  | 1373 |  | 1384 |  | 1394 |  | 1404 |  | 1414 |  | 1425 |  | 1435 |
|  | 1374 |  | 1384 |  | 1394 |  | 1404 |  | 1415 |  | 1425 |  | 1435 |
|  | 1374 |  | 1384 |  | 1394 |  | 1405 |  | 1415 |  | 1425 |  | 1435 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  |  |  | Bl nb |  | Bl nb |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1436 | PPD | 1446 | PPD | 1456 | PPD | 1466 | PPD | 1477 | PPD | 1487 | PPD | 1497 |
|  | 1436 |  | 1446 |  | 1456 |  | 1467 |  | 1477 |  | 1487 |  | 1497 |
|  | 1436 |  | 1446 |  | 1457 |  | 1467 |  | 1477 |  | 1487 |  | 1498 |
|  | 1436 |  | 1447 |  | 1457 |  | 1467 |  | 1477 |  | 1488 |  | 1498 |
|  | 1437 |  | 1447 |  | 1457 |  | 1467 |  | 1478 |  | 1488 |  | 1498 |
|  | 1437 |  | 1447 |  | 1457 |  | 1468 |  | 1478 |  | 1488 |  | 1498 |
|  | 1437 |  | 1447 |  | 1458 |  | 1468 |  | 1478 |  | 1488 |  | 1499 |
|  | 1437 |  | 1448 |  | 1458 |  | 1468 |  | 1478 |  | 1489 |  | 1499 |
|  | 1438 |  | 1448 |  | 1458 |  | 1468 |  | 1479 |  | 1489 |  | 1499 |
|  | 1438 |  | 1448 |  | 1458 |  | 1469 |  | 1479 |  | 1489 |  | 1499 |
|  | 1438 |  | 1448 |  | 1459 |  | 1469 |  | 1479 |  | 1489 |  | 1500 |
|  | 1438 |  | 1449 |  | 1459 |  | 1469 |  | 1479 |  | 1490 |  | 1500 |
|  | 1439 |  | 1449 |  | 1459 |  | 1469 |  | 1480 |  | 1490 |  | 1500 |
|  | 1439 |  | 1449 |  | 1459 |  | 1470 |  | 1480 |  | 1490 |  | 1500 |
|  | 1439 |  | 1449 |  | 1460 |  | 1470 |  | 1480 |  | 1490 |  | 1501 |
|  | 1439 |  | 1450 |  | 1460 |  | 1470 |  | 1480 |  | 1491 |  | 1501 |
|  | 1440 |  | 1450 |  | 1460 |  | 1470 |  | 1481 |  | 1491 |  | 1501 |
|  | 1440 |  | 1450 |  | 1460 |  | 1471 |  | 1481 |  | 1491 |  | 1501 |
|  | 1440 |  | 1450 |  | 1461 |  | 1471 |  | 1481 |  | 1491 |  | 1502 |
|  | 1440 |  | 1451 |  | 1461 |  | 1471 |  | 1481 |  | 1492 |  | 1502 |
|  | 1441 |  | 1451 |  | 1461 |  | 1471 |  | 1482 |  | 1492 |  | 1502 |
|  | 1441 |  | 1451 |  | 1461 |  | 1472 |  | 1482 |  | 1492 |  | 1502 |
|  | 1441 |  | 1451 |  | 1462 |  | 1472 |  | 1482 |  | 1492 |  | 1503 |
|  | 1441 |  | 1452 |  | 1462 |  | 1472 |  | 1482 |  | 1493 |  | 1503 |
|  | 1442 |  | 1452 |  | 1462 |  | 1472 |  | 1483 |  | 1493 |  | 1503 |
|  | 1442 |  | 1452 |  | 1462 |  | 1473 |  | 1483 |  | 1493 |  | 1503 |
|  | 1442 |  | 1452 |  | 1463 |  | 1473 |  | 1483 |  | 1493 |  | 1504 |
|  | 1442 |  | 1453 |  | 1463 |  | 1473 |  | 1483 |  | 1494 |  | 1504 |
|  | 1443 |  | 1453 |  | 1463 |  | 1473 |  | 1484 |  | 1494 |  | 1504 |
|  | 1443 |  | 1453 |  | 1463 |  | 1474 |  | 1484 |  | 1494 |  | 1504 |
|  | 1443 |  | 1453 |  | 1464 |  | 1474 |  | 1484 |  | 1494 |  | 1505 |
|  | 1443 |  | 1454 |  | 1464 |  | 1474 |  | 1484 |  | 1495 |  | 1505 |
|  | 1444 |  | 1454 |  | 1464 |  | 1474 |  | 1485 |  | 1495 |  | 1505 |
|  | 1444 |  | 1454 |  | 1464 |  | 1475 |  | 1485 |  | 1495 |  | 1505 |
|  | 1444 |  | 1454 |  | 1465 |  | 1475 |  | 1485 |  | 1495 |  | 1506 |
|  | 1444 |  | 1455 |  | 1465 |  | 1475 |  | 1485 |  | 1496 |  | 1506 |
|  | 1445 |  | 1455 |  | 1465 |  | 1475 |  | 1486 |  | 1496 |  | 1506 |
|  | 1445 |  | 1455 |  | 1465 |  | 1476 |  | 1486 |  | 1496 |  | 1506 |
|  | 1445 |  | 1455 |  | 1466 |  | 1476 |  | 1486 |  | 1496 |  | 1507 |
|  | 1445 |  | 1456 |  | 1466 |  | 1476 |  | 1486 |  | 1497 |  | 1507 |
|  | 1446 |  | 1456 |  | 1466 |  | 1476 |  | 1487 |  | 1497 |  | 1507 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| Trt. |  |  |  |  | Bl nb |  | Bl nb |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1507 | PPD | 1518 | PPD | 1528 | PPD | 1538 | PPD | 1548 | PPD | 1559 | PPD | 1569 |
|  | 1508 |  | 1518 |  | 1528 |  | 1538 |  | 1549 |  | 1559 |  | 1569 |
|  | 1508 |  | 1518 |  | 1528 |  | 1539 |  | 1549 |  | 1559 |  | 1569 |
|  | 1508 |  | 1518 |  | 1529 |  | 1539 |  | 1549 |  | 1559 |  | 1570 |
|  | 1508 |  | 1519 |  | 1529 |  | 1539 |  | 1549 |  | 1560 |  | 1570 |
|  | 1509 |  | 1519 |  | 1529 |  | 1539 |  | 1550 |  | 1560 |  | 1570 |
|  | 1509 |  | 1519 |  | 1529 |  | 1540 |  | 1550 |  | 1560 |  | 1570 |
|  | 1509 |  | 1519 |  | 1530 |  | 1540 |  | 1550 |  | 1560 |  | 1571 |
|  | 1509 |  | 1520 |  | 1530 |  | 1540 |  | 1550 |  | 1561 |  | 1571 |
|  | 1510 |  | 1520 |  | 1530 |  | 1540 |  | 1551 |  | 1561 |  | 1571 |
|  | 1510 |  | 1520 |  | 1530 |  | 1541 |  | 1551 |  | 1561 |  | 1571 |
|  | 1510 |  | 1520 |  | 1531 |  | 1541 |  | 1551 |  | 1561 |  | 1572 |
|  | 1510 |  | 1521 |  | 1531 |  | 1541 |  | 1551 |  | 1562 |  | 1572 |
|  | 1511 |  | 1521 |  | 1531 |  | 1541 |  | 1552 |  | 1562 |  | 1572 |
|  | 1511 |  | 1521 |  | 1531 |  | 1542 |  | 1552 |  | 1562 |  | 1572 |
|  | 1511 |  | 1521 |  | 1532 |  | 1542 |  | 1552 |  | 1562 |  | 1573 |
|  | 1511 |  | 1522 |  | 1532 |  | 1542 |  | 1552 |  | 1563 |  | 1573 |
|  | 1512 |  | 1522 |  | 1532 |  | 1542 |  | 1553 |  | 1563 |  | 1573 |
|  | 1512 |  | 1522 |  | 1532 |  | 1543 |  | 1553 |  | 1563 |  | 1573 |
|  | 1512 |  | 1522 |  | 1533 |  | 1543 |  | 1553 |  | 1563 |  | 1574 |
|  | 1512 |  | 1523 |  | 1533 |  | 1543 |  | 1553 |  | 1564 |  | 1574 |
|  | 1513 |  | 1523 |  | 1533 |  | 1543 |  | 1554 |  | 1564 |  | 1574 |
|  | 1513 |  | 1523 |  | 1533 |  | 1544 |  | 1554 |  | 1564 |  | 1574 |
|  | 1513 |  | 1523 |  | 1534 |  | 1544 |  | 1554 |  | 1564 |  | 1575 |
|  | 1513 |  | 1524 |  | 1534 |  | 1544 |  | 1554 |  | 1565 |  | 1575 |
|  | 1514 |  | 1524 |  | 1534 |  | 1544 |  | 1555 |  | 1565 |  | 1575 |
|  | 1514 |  | 1524 |  | 1534 |  | 1545 |  | 1555 |  | 1565 |  | 1575 |
|  | 1514 |  | 1524 |  | 1535 |  | 1545 |  | 1555 |  | 1565 |  | 1576 |
|  | 1514 |  | 1525 |  | 1535 |  | 1545 |  | 1555 |  | 1566 |  | 1576 |
|  | 1515 |  | 1525 |  | 1535 |  | 1545 |  | 1556 |  | 1566 |  | 1576 |
|  | 1515 |  | 1525 |  | 1535 |  | 1546 |  | 1556 |  | 1566 |  | 1576 |
|  | 1515 |  | 1525 |  | 1536 |  | 1546 |  | 1556 |  | 1566 |  | 1577 |
|  | 1515 |  | 1526 |  | 1536 |  | 1546 |  | 1556 |  | 1567 |  | 1577 |
|  | 1516 |  | 1526 |  | 1536 |  | 1546 |  | 1557 |  | 1567 |  | 1577 |
|  | 1516 |  | 1526 |  | 1536 |  | 1547 |  | 1557 |  | 1567 |  | 1577 |
|  | 1516 |  | 1526 |  | 1537 |  | 1547 |  | 1557 |  | 1567 |  | 1578 |
|  | 1516 |  | 1527 |  | 1537 |  | 1547 |  | 1557 |  | 1568 |  | 1578 |
|  | 1517 |  | 1527 |  | 1537 |  | 1547 |  | 1558 |  | 1568 |  | 1578 |
|  | 1517 |  | 1527 |  | 1537 |  | 1548 |  | 1558 |  | 1568 |  | 1578 |
|  | 1517 |  | 1527 |  | 1538 |  | 1548 |  | 1558 |  | 1568 |  | 1579 |
|  | 1517 |  | 1528 |  | 1538 |  | 1548 |  | 1558 |  | 1569 |  | 1579 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  | Bl nb |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1579 | PPD | 1589 | PPD | 1600 | PPD | 1610 | PPD | 1620 | PPD | 1630 | PPD | 1641 |
|  | 1579 |  | 1590 |  | 1600 |  | 1610 |  | 1620 |  | 1631 |  | 1641 |
|  | 1580 |  | 1590 |  | 1600 |  | 1610 |  | 1621 |  | 1631 |  | 1641 |
|  | 1580 |  | 1590 |  | 1600 |  | 1611 |  | 1621 |  | 1631 |  | 1641 |
|  | 1580 |  | 1590 |  | 1601 |  | 1611 |  | 1621 |  | 1631 |  | 1642 |
|  | 1580 |  | 1591 |  | 1601 |  | 1611 |  | 1621 |  | 1632 |  | 1642 |
|  | 1581 |  | 1591 |  | 1601 |  | 1611 |  | 1622 |  | 1632 |  | 1642 |
|  | 1581 |  | 1591 |  | 1601 |  | 1612 |  | 1622 |  | 1632 |  | 1642 |
|  | 1581 |  | 1591 |  | 1602 |  | 1612 |  | 1622 |  | 1632 |  | 1643 |
|  | 1581 |  | 1592 |  | 1602 |  | 1612 |  | 1622 |  | 1633 |  | 1643 |
|  | 1582 |  | 1592 |  | 1602 |  | 1612 |  | 1623 |  | 1633 |  | 1643 |
|  | 1582 |  | 1592 |  | 1602 |  | 1613 |  | 1623 |  | 1633 |  | 1643 |
|  | 1582 |  | 1592 |  | 1603 |  | 1613 |  | 1623 |  | 1633 |  | 1644 |
|  | 1582 |  | 1593 |  | 1603 |  | 1613 |  | 1623 |  | 1634 |  | 1644 |
|  | 1583 |  | 1593 |  | 1603 |  | 1613 |  | 1624 |  | 1634 |  | 1644 |
|  | 1583 |  | 1593 |  | 1603 |  | 1614 |  | 1624 |  | 1634 |  | 1644 |
|  | 1583 |  | 1593 |  | 1604 |  | 1614 |  | 1624 |  | 1634 |  | 1645 |
|  | 1583 |  | 1594 |  | 1604 |  | 1614 |  | 1624 |  | 1635 |  | 1645 |
|  | 1584 |  | 1594 |  | 1604 |  | 1614 |  | 1625 |  | 1635 |  | 1645 |
|  | 1584 |  | 1594 |  | 1604 |  | 1615 |  | 1625 |  | 1635 |  | 1645 |
|  | 1584 |  | 1594 |  | 1605 |  | 1615 |  | 1625 |  | 1635 |  | 1646 |
|  | 1584 |  | 1595 |  | 1605 |  | 1615 |  | 1625 |  | 1636 |  | 1646 |
|  | 1585 |  | 1595 |  | 1605 |  | 1615 |  | 1626 |  | 1636 |  | 1646 |
|  | 1585 |  | 1595 |  | 1605 |  | 1616 |  | 1626 |  | 1636 |  | 1646 |
|  | 1585 |  | 1595 |  | 1606 |  | 1616 |  | 1626 |  | 1636 |  | 1647 |
|  | 1585 |  | 1596 |  | 1606 |  | 1616 |  | 1626 |  | 1637 |  | 1647 |
|  | 1586 |  | 1596 |  | 1606 |  | 1616 |  | 1627 |  | 1637 |  | 1647 |
|  | 1586 |  | 1596 |  | 1606 |  | 1617 |  | 1627 |  | 1637 |  | 1647 |
|  | 1586 |  | 1596 |  | 1607 |  | 1617 |  | 1627 |  | 1637 |  | 1648 |
|  | 1586 |  | 1597 |  | 1607 |  | 1617 |  | 1627 |  | 1638 |  | 1648 |
|  | 1587 |  | 1597 |  | 1607 |  | 1617 |  | 1628 |  | 1638 |  | 1648 |
|  | 1587 |  | 1597 |  | 1607 |  | 1618 |  | 1628 |  | 1638 |  | 1648 |
|  | 1587 |  | 1597 |  | 1608 |  | 1618 |  | 1628 |  | 1638 |  | 1649 |
|  | 1587 |  | 1598 |  | 1608 |  | 1618 |  | 1628 |  | 1639 |  | 1649 |
|  | 1588 |  | 1598 |  | 1608 |  | 1618 |  | 1629 |  | 1639 |  | 1649 |
|  | 1588 |  | 1598 |  | 1608 |  | 1619 |  | 1629 |  | 1639 |  | 1649 |
|  | 1588 |  | 1598 |  | 1609 |  | 1619 |  | 1629 |  | 1639 |  | 1650 |
|  | 1588 |  | 1599 |  | 1609 |  | 1619 |  | 1629 |  | 1640 |  | 1650 |
|  | 1589 |  | 1599 |  | 1609 |  | 1619 |  | 1630 |  | 1640 |  | 1650 |
|  | 1589 |  | 1599 |  | 1609 |  | 1620 |  | 1630 |  | 1640 |  | 1650 |
|  | 1589 |  | 1599 |  | 1610 |  | 1620 |  | 1630 |  | 1640 |  | 1651 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl nb |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} . \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1651 | PPD | 1661 | PPD | 1671 | PPD | 1682 | PPD | 1692 | PPD | 1702 | PPD | 1712 |
|  | 1651 |  | 1661 |  | 1672 |  | 1682 |  | 1692 |  | 1702 |  | 1713 |
|  | 1651 |  | 1662 |  | 1672 |  | 1682 |  | 1692 |  | 1703 |  | 1713 |
|  | 1652 |  | 1662 |  | 1672 |  | 1682 |  | 1693 |  | 1703 |  | 1713 |
|  | 1652 |  | 1662 |  | 1672 |  | 1683 |  | 1693 |  | 1703 |  | 1713 |
|  | 1652 |  | 1662 |  | 1673 |  | 1683 |  | 1693 |  | 1703 |  | 1714 |
|  | 1652 |  | 1663 |  | 1673 |  | 1683 |  | 1693 |  | 1704 |  | 1714 |
|  | 1653 |  | 1663 |  | 1673 |  | 1683 |  | 1694 |  | 1704 |  | 1714 |
|  | 1653 |  | 1663 |  | 1673 |  | 1684 |  | 1694 |  | 1704 |  | 1714 |
|  | 1653 |  | 1663 |  | 1674 |  | 1684 |  | 1694 |  | 1704 |  | 1715 |
|  | 1653 |  | 1664 |  | 1674 |  | 1684 |  | 1694 |  | 1705 |  | 1715 |
|  | 1654 |  | 1664 |  | 1674 |  | 1684 |  | 1695 |  | 1705 |  | 1715 |
|  | 1654 |  | 1664 |  | 1674 |  | 1685 |  | 1695 |  | 1705 |  | 1715 |
|  | 1654 |  | 1664 |  | 1675 |  | 1685 |  | 1695 |  | 1705 |  | 1716 |
|  | 1654 |  | 1665 |  | 1675 |  | 1685 |  | 1695 |  | 1706 |  | 1716 |
|  | 1655 |  | 1665 |  | 1675 |  | 1685 |  | 1696 |  | 1706 |  | 1716 |
|  | 1655 |  | 1665 |  | 1675 |  | 1686 |  | 1696 |  | 1706 |  | 1716 |
|  | 1655 |  | 1665 |  | 1676 |  | 1686 |  | 1696 |  | 1706 |  | 1717 |
|  | 1655 |  | 1666 |  | 1676 |  | 1686 |  | 1696 |  | 1707 |  | 1717 |
|  | 1656 |  | 1666 |  | 1676 |  | 1686 |  | 1697 |  | 1707 |  | 1717 |
|  | 1656 |  | 1666 |  | 1676 |  | 1687 |  | 1697 |  | 1707 |  | 1717 |
|  | 1656 |  | 1666 |  | 1677 |  | 1687 |  | 1697 |  | 1707 |  | 1718 |
|  | 1656 |  | 1667 |  | 1677 |  | 1687 |  | 1697 |  | 1708 |  | 1718 |
|  | 1657 |  | 1667 |  | 1677 |  | 1687 |  | 1698 |  | 1708 |  | 1718 |
|  | 1657 |  | 1667 |  | 1677 |  | 1688 |  | 1698 |  | 1708 |  | 1718 |
|  | 1657 |  | 1667 |  | 1678 |  | 1688 |  | 1698 |  | 1708 |  | 1719 |
|  | 1657 |  | 1668 |  | 1678 |  | 1688 |  | 1698 |  | 1709 |  | 1719 |
|  | 1658 |  | 1668 |  | 1678 |  | 1688 |  | 1699 |  | 1709 |  | 1719 |
|  | 1658 |  | 1668 |  | 1678 |  | 1689 |  | 1699 |  | 1709 |  | 1719 |
|  | 1658 |  | 1668 |  | 1679 |  | 1689 |  | 1699 |  | 1709 |  | 1720 |
|  | 1658 |  | 1669 |  | 1679 |  | 1689 |  | 1699 |  | 1710 |  | 1720 |
|  | 1659 |  | 1669 |  | 1679 |  | 1689 |  | 1700 |  | 1710 |  | 1720 |
|  | 1659 |  | 1669 |  | 1679 |  | 1690 |  | 1700 |  | 1710 |  | 1720 |
|  | 1659 |  | 1669 |  | 1680 |  | 1690 |  | 1700 |  | 1710 |  | 1721 |
|  | 1659 |  | 1670 |  | 1680 |  | 1690 |  | 1700 |  | 1711 |  | 1721 |
|  | 1660 |  | 1670 |  | 1680 |  | 1690 |  | 1701 |  | 1711 |  | 1721 |
|  | 1660 |  | 1670 |  | 1680 |  | 1691 |  | 1701 |  | 1711 |  | 1721 |
|  | 1660 |  | 1670 |  | 1681 |  | 1691 |  | 1701 |  | 1711 |  | 1722 |
|  | 1660 |  | 1671 |  | 1681 |  | 1691 |  | 1701 |  | 1712 |  | 1722 |
|  | 1661 |  | 1671 |  | 1681 |  | 1691 |  | 1702 |  | 1712 |  | 1722 |
|  | 1661 |  | 1671 |  | 1681 |  | 1692 |  | 1702 |  | 1712 |  | 1722 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl n | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Tret. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1723 | PPD | 1733 | PPD | 1743 | PPD | 1753 | PPD | 1764 | PPD | 1774 | PPD | 1784 |
|  | 1723 | PPD | 1733 |  | 1743 |  | 1754 |  | 1764 |  | 1774 |  | 1784 |
|  | 1723 |  | 1733 |  | 1744 |  | 1754 |  | 1764 |  | 1774 |  | 1785 |
|  | 1723 |  | 1734 |  | 1744 |  | 1754 |  | 1764 |  | 1775 |  | 1785 |
|  | 1724 |  | 1734 |  | 1744 |  | 1754 |  | 1765 |  | 1775 |  | 1785 |
|  | 1724 |  | 1734 |  | 1744 |  | 1755 |  | 1765 |  | 1775 |  | 1785 |
|  | 1724 |  | 1734 |  | 1745 |  | 1755 |  | 1765 |  | 1775 |  | 1786 |
|  | 1724 |  | 1735 |  | 1745 |  | 1755 |  | 1765 |  | 1776 |  | 1786 |
|  | 1725 |  | 1735 |  | 1745 |  | 1755 |  | 1766 |  | 1776 |  | 1786 |
|  | 1725 |  | 1735 |  | 1745 |  | 1756 |  | 1766 |  | 1776 |  | 1786 |
|  | 1725 |  | 1735 |  | 1746 |  | 1756 |  | 1766 |  | 1776 |  | 1787 |
|  | 1725 |  | 1736 |  | 1746 |  | 1756 |  | 1766 |  | 1777 |  | 1787 |
|  | 1726 |  | 1736 |  | 1746 |  | 1756 |  | 1767 |  | 1777 |  | 1787 |
|  | 1726 |  | 1736 |  | 1746 |  | 1757 |  | 1767 |  | 1777 |  | 1787 |
|  | 1726 |  | 1736 |  | 1747 |  | 1757 |  | 1767 |  | 1777 |  | 1788 |
|  | 1726 |  | 1737 |  | 1747 |  | 1757 |  | 1767 |  | 1778 |  | 1788 |
|  | 1727 |  | 1737 |  | 1747 |  | 1757 |  | 1768 |  | 1778 |  | 1788 |
|  | 1727 |  | 1737 |  | 1747 |  | 1758 |  | 1768 |  | 1778 |  | 1788 |
|  | 1727 |  | 1737 |  | 1748 |  | 1758 |  | 1768 |  | 1778 |  | 1789 |
|  | 1727 |  | 1738 |  | 1748 |  | 1758 |  | 1768 |  | 1779 |  | 1789 |
|  | 1728 |  | 1738 |  | 1748 |  | 1758 |  | 1769 |  | 1779 |  | 1789 |
|  | 1728 |  | 1738 |  | 1748 |  | 1759 |  | 1769 |  | 1779 |  | 1789 |
|  | 1728 |  | 1738 |  | 1749 |  | 1759 |  | 1769 |  | 1779 |  | 1790 |
|  | 1728 |  | 1739 |  | 1749 |  | 1759 |  | 1769 |  | 1780 |  | 1790 |
|  | 1729 |  | 1739 |  | 1749 |  | 1759 |  | 1770 |  | 1780 |  | 1790 |
|  | 1729 |  | 1739 |  | 1749 |  | 1760 |  | 1770 |  | 1780 |  | 1790 |
|  | 1729 |  | 1739 |  | 1750 |  | 1760 |  | 1770 |  | 1780 |  | 1791 |
|  | 1729 |  | 1740 |  | 1750 |  | 1760 |  | 1770 |  | 1781 |  | 1791 |
|  | 1730 |  | 1740 |  | 1750 |  | 1760 |  | 1771 |  | 1781 |  | 1791 |
|  | 1730 |  | 1740 |  | 1750 |  | 1761 |  | 1771 |  | 1781 |  | 1791 |
|  | 1730 |  | 1740 |  | 1751 |  | 1761 |  | 1771 |  | 1781 |  | 1792 |
|  | 1730 |  | 1741 |  | 1751 |  | 1761 |  | 1771 |  | 1782 |  | 1792 |
|  | 1731 |  | 1741 |  | 1751 |  | 1761 |  | 1772 |  | 1782 |  | 1792 |
|  | 1731 |  | 1741 |  | 1751 |  | 1762 |  | 1772 |  | 1782 |  | 1792 |
|  | 1731 |  | 1741 |  | 1752 |  | 1762 |  | 1772 |  | 1782 |  | 1793 |
|  | 1731 |  | 1742 |  | 1752 |  | 1762 |  | 1772 |  | 1783 |  | 1793 |
|  | 1732 |  | 1742 |  | 1752 |  | 1762 |  | 1773 |  | 1783 |  | 1793 |
|  | 1732 |  | 1742 |  | 1752 |  | 1763 |  | 1773 |  | 1783 |  | 1793 |
|  | 1732 |  | 1742 |  | 1753 |  | 1763 |  | 1773 |  | 1783 |  | 1794 |
|  | 1732 |  | 1743 |  | 1753 |  | 1763 |  | 1773 |  | 1784 |  | 1794 |
|  | 1733 |  | 1743 |  | 1753 |  | 1763 |  | 1774 |  | 1784 |  | 1794 |

Treatment number associated to material : Hz/su-PreChemo

| Trt. | Bl nb | Trt. Bl.No nb |  | Trt. Bl. <br> No nb |  | Trt. Bl. |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1794 | PPD | 1805 | PPD | 1815 | PPD | 1825 | PPD | 1835 | PPD | 1846 | PPD | 1856 |
|  | 1795 |  | 1805 |  | 1815 |  | 1825 |  | 1836 |  | 1846 |  | 1856 |
|  | 1795 |  | 1805 |  | 1815 |  | 1826 |  | 1836 |  | 1846 |  | 1856 |
|  | 1795 |  | 1805 |  | 1816 |  | 1826 |  | 1836 |  | 1846 |  | 1857 |
|  | 1795 |  | 1806 |  | 1816 |  | 1826 |  | 1836 |  | 1847 |  | 1857 |
|  | 1796 |  | 1806 |  | 1816 |  | 1826 |  | 1837 |  | 1847 |  | 1857 |
|  | 1796 |  | 1806 |  | 1816 |  | 1827 |  | 1837 |  | 1847 |  | 1857 |
|  | 1796 |  | 1806 |  | 1817 |  | 1827 |  | 1837 |  | 1847 |  | 1858 |
|  | 1796 |  | 1807 |  | 1817 |  | 1827 |  | 1837 |  | 1848 |  | 1858 |
|  | 1797 |  | 1807 |  | 1817 |  | 1827 |  | 1838 |  | 1848 |  | 1858 |
|  | 1797 |  | 1807 |  | 1817 |  | 1828 |  | 1838 |  | 1848 |  | 1858 |
|  | 1797 |  | 1807 |  | 1818 |  | 1828 |  | 1838 |  | 1848 |  | 1859 |
|  | 1797 |  | 1808 |  | 1818 |  | 1828 |  | 1838 |  | 1849 |  | 1859 |
|  | 1798 |  | 1808 |  | 1818 |  | 1828 |  | 1839 |  | 1849 |  | 1859 |
|  | 1798 |  | 1808 |  | 1818 |  | 1829 |  | 1839 |  | 1849 |  | 1859 |
|  | 1798 |  | 1808 |  | 1819 |  | 1829 |  | 1839 |  | 1849 |  | 1860 |
|  | 1798 |  | 1809 |  | 1819 |  | 1829 |  | 1839 |  | 1850 |  | 1860 |
|  | 1799 |  | 1809 |  | 1819 |  | 1829 |  | 1840 |  | 1850 |  | 1860 |
|  | 1799 |  | 1809 |  | 1819 |  | 1830 |  | 1840 |  | 1850 |  | 1860 |
|  | 1799 |  | 1809 |  | 1820 |  | 1830 |  | 1840 |  | 1850 |  | 1861 |
|  | 1799 |  | 1810 |  | 1820 |  | 1830 |  | 1840 |  | 1851 |  | 1861 |
|  | 1800 |  | 1810 |  | 1820 |  | 1830 |  | 1841 |  | 1851 |  | 1861 |
|  | 1800 |  | 1810 |  | 1820 |  | 1831 |  | 1841 |  | 1851 |  | 1861 |
|  | 1800 |  | 1810 |  | 1821 |  | 1831 |  | 1841 |  | 1851 |  | 1862 |
|  | 1800 |  | 1811 |  | 1821 |  | 1831 |  | 1841 |  | 1852 |  | 1862 |
|  | 1801 |  | 1811 |  | 1821 |  | 1831 |  | 1842 |  | 1852 |  | 1862 |
|  | 1801 |  | 1811 |  | 1821 |  | 1832 |  | 1842 |  | 1852 |  | 1862 |
|  | 1801 |  | 1811 |  | 1822 |  | 1832 |  | 1842 |  | 1852 |  | 1863 |
|  | 1801 |  | 1812 |  | 1822 |  | 1832 |  | 1842 |  | 1853 |  | 1863 |
|  | 1802 |  | 1812 |  | 1822 |  | 1832 |  | 1843 |  | 1853 |  | 1863 |
|  | 1802 |  | 1812 |  | 1822 |  | 1833 |  | 1843 |  | 1853 |  | 1863 |
|  | 1802 |  | 1812 |  | 1823 |  | 1833 |  | 1843 |  | 1853 |  | 1864 |
|  | 1802 |  | 1813 |  | 1823 |  | 1833 |  | 1843 |  | 1854 |  | 1864 |
|  | 1803 |  | 1813 |  | 1823 |  | 1833 |  | 1844 |  | 1854 |  | 1864 |
|  | 1803 |  | 1813 |  | 1823 |  | 1834 |  | 1844 |  | 1854 |  | 1864 |
|  | 1803 |  | 1813 |  | 1824 |  | 1834 |  | 1844 |  | 1854 |  | 1865 |
|  | 1803 |  | 1814 |  | 1824 |  | 1834 |  | 1844 |  | 1855 |  | 1865 |
|  | 1804 |  | 1814 |  | 1824 |  | 1834 |  | 1845 |  | 1855 |  | 1865 |
|  | 1804 |  | 1814 |  | 1824 |  | 1835 |  | 1845 |  | 1855 |  | 1865 |
|  | 1804 |  | 1814 |  | 1825 |  | 1835 |  | 1845 |  | 1855 |  | 1866 |
|  | 1804 |  | 1815 |  | 1825 |  | 1835 |  | 1845 |  | 1856 |  | 1866 |

Treatment number associated to material : Hz/su-PreChemo

| $\begin{array}{r} \operatorname{Trt} \\ \mathrm{N} \end{array}$ | Bl. |  | Bl. |  |  | Trt | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1866 | PPD | 1876 | PPD | 1887 | PPD | 1897 | PPD | 1907 | PPD | 1917 | PPD | 1928 |
|  | 1866 |  | 1877 |  | 1887 |  | 1897 |  | 1907 |  | 1918 |  | 1928 |
|  | 1867 |  | 1877 |  | 1887 |  | 1897 |  | 1908 |  | 1918 |  | 1928 |
|  | 1867 |  | 1877 |  | 1887 |  | 1898 |  | 1908 |  | 1918 |  | 1928 |
|  | 1867 |  | 1877 |  | 1888 |  | 1898 |  | 1908 |  | 1918 |  | 1929 |
|  | 1867 |  | 1878 |  | 1888 |  | 1898 |  | 1908 |  | 1919 |  | 1929 |
|  | 1868 |  | 1878 |  | 1888 |  | 1898 |  | 1909 |  | 1919 |  | 1929 |
|  | 1868 |  | 1878 |  | 1888 |  | 1899 |  | 1909 |  | 1919 |  | 1929 |
|  | 1868 |  | 1878 |  | 1889 |  | 1899 |  | 1909 |  | 1919 |  | 1930 |
|  | 1868 |  | 1879 |  | 1889 |  | 1899 |  | 1909 |  | 1920 |  | 1930 |
|  | 1869 |  | 1879 |  | 1889 |  | 1899 |  | 1910 |  | 1920 |  | 1930 |
|  | 1869 |  | 1879 |  | 1889 |  | 1900 |  | 1910 |  | 1920 |  | 1930 |
|  | 1869 |  | 1879 |  | 1890 |  | 1900 |  | 1910 |  | 1920 |  | 1931 |
|  | 1869 |  | 1880 |  | 1890 |  | 1900 |  | 1910 |  | 1921 |  | 1931 |
|  | 1870 |  | 1880 |  | 1890 |  | 1900 |  | 1911 |  | 1921 |  | 1931 |
|  | 1870 |  | 1880 |  | 1890 |  | 1901 |  | 1911 |  | 1921 |  | 1931 |
|  | 1870 |  | 1880 |  | 1891 |  | 1901 |  | 1911 |  | 1921 |  | 1932 |
|  | 1870 |  | 1881 |  | 1891 |  | 1901 |  | 1911 |  | 1922 |  | 1932 |
|  | 1871 |  | 1881 |  | 1891 |  | 1901 |  | 1912 |  | 1922 |  | 1932 |
|  | 1871 |  | 1881 |  | 1891 |  | 1902 |  | 1912 |  | 1922 |  | 1932 |
|  | 1871 |  | 1881 |  | 1892 |  | 1902 |  | 1912 |  | 1922 |  | 1933 |
|  | 1871 |  | 1882 |  | 1892 |  | 1902 |  | 1912 |  | 1923 |  | 1933 |
|  | 1872 |  | 1882 |  | 1892 |  | 1902 |  | 1913 |  | 1923 |  | 1933 |
|  | 1872 |  | 1882 |  | 1892 |  | 1903 |  | 1913 |  | 1923 |  | 1933 |
|  | 1872 |  | 1882 |  | 1893 |  | 1903 |  | 1913 |  | 1923 |  | 1934 |
|  | 1872 |  | 1883 |  | 1893 |  | 1903 |  | 1913 |  | 1924 |  | 1934 |
|  | 1873 |  | 1883 |  | 1893 |  | 1903 |  | 1914 |  | 1924 |  | 1934 |
|  | 1873 |  | 1883 |  | 1893 |  | 1904 |  | 1914 |  | 1924 |  | 1934 |
|  | 1873 |  | 1883 |  | 1894 |  | 1904 |  | 1914 |  | 1924 |  | 1935 |
|  | 1873 |  | 1884 |  | 1894 |  | 1904 |  | 1914 |  | 1925 |  | 1935 |
|  | 1874 |  | 1884 |  | 1894 |  | 1904 |  | 1915 |  | 1925 |  | 1935 |
|  | 1874 |  | 1884 |  | 1894 |  | 1905 |  | 1915 |  | 1925 |  | 1935 |
|  | 1874 |  | 1884 |  | 1895 |  | 1905 |  | 1915 |  | 1925 |  | 1936 |
|  | 1874 |  | 1885 |  | 1895 |  | 1905 |  | 1915 |  | 1926 |  | 1936 |
|  | 1875 |  | 1885 |  | 1895 |  | 1905 |  | 1916 |  | 1926 |  | 1936 |
|  | 1875 |  | 1885 |  | 1895 |  | 1906 |  | 1916 |  | 1926 |  | 1936 |
|  | 1875 |  | 1885 |  | 1896 |  | 1906 |  | 1916 |  | 1926 |  | 1937 |
|  | 1875 |  | 1886 |  | 1896 |  | 1906 |  | 1916 |  | 1927 |  | 1937 |
|  | 1876 |  | 1886 |  | 1896 |  | 1906 |  | 1917 |  | 1927 |  | 1937 |
|  | 1876 |  | 1886 |  | 1896 |  | 1907 |  | 1917 |  | 1927 |  | 1937 |
|  | 1876 |  | 1886 |  | 1897 |  | 1907 |  | 1917 |  | 1927 |  | 1938 |

SD4 4 RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl. | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No n. } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1938 | PPD | 1948 | PPD | 1958 | PPD | 1969 | PPD | 1979 | PPD | 1989 | PPD | 1999 |
|  | 1938 |  | 1948 |  | 1959 |  | 1969 |  | 1979 |  | 1989 |  | 2000 |
|  | 1938 |  | 1949 |  | 1959 |  | 1969 |  | 1979 |  | 1990 |  | 2000 |
|  | 1939 |  | 1949 |  | 1959 |  | 1969 |  | 1980 |  | 1990 |  | 2000 |
|  | 1939 |  | 1949 |  | 1959 |  | 1970 |  | 1980 |  | 1990 |  | 2000 |
|  | 1939 |  | 1949 |  | 1960 |  | 1970 |  | 1980 |  | 1990 |  | 2001 |
|  | 1939 |  | 1950 |  | 1960 |  | 1970 |  | 1980 |  | 1991 |  | 2001 |
|  | 1940 |  | 1950 |  | 1960 |  | 1970 |  | 1981 |  | 1991 |  | 2001 |
|  | 1940 |  | 1950 |  | 1960 |  | 1971 |  | 1981 |  | 1991 |  | 2001 |
|  | 1940 |  | 1950 |  | 1961 |  | 1971 |  | 1981 |  | 1991 |  | 2002 |
|  | 1940 |  | 1951 |  | 1961 |  | 1971 |  | 1981 |  | 1992 |  | 2002 |
|  | 1941 |  | 1951 |  | 1961 |  | 1971 |  | 1982 |  | 1992 |  | 2002 |
|  | 1941 |  | 1951 |  | 1961 |  | 1972 |  | 1982 |  | 1992 |  | 2002 |
|  | 1941 |  | 1951 |  | 1962 |  | 1972 |  | 1982 |  | 1992 |  | 2003 |
|  | 1941 |  | 1952 |  | 1962 |  | 1972 |  | 1982 |  | 1993 |  | 2003 |
|  | 1942 |  | 1952 |  | 1962 |  | 1972 |  | 1983 |  | 1993 |  | 2003 |
|  | 1942 |  | 1952 |  | 1962 |  | 1973 |  | 1983 |  | 1993 |  | 2003 |
|  | 1942 |  | 1952 |  | 1963 |  | 1973 |  | 1983 |  | 1993 |  | 2004 |
|  | 1942 |  | 1953 |  | 1963 |  | 1973 |  | 1983 |  | 1994 |  | 2004 |
|  | 1943 |  | 1953 |  | 1963 |  | 1973 |  | 1984 |  | 1994 |  | 2004 |
|  | 1943 |  | 1953 |  | 1963 |  | 1974 |  | 1984 |  | 1994 |  | 2004 |
|  | 1943 |  | 1953 |  | 1964 |  | 1974 |  | 1984 |  | 1994 |  | 2005 |
|  | 1943 |  | 1954 |  | 1964 |  | 1974 |  | 1984 |  | 1995 |  | 2005 |
|  | 1944 |  | 1954 |  | 1964 |  | 1974 |  | 1985 |  | 1995 |  | 2005 |
|  | 1944 |  | 1954 |  | 1964 |  | 1975 |  | 1985 |  | 1995 |  | 2005 |
|  | 1944 |  | 1954 |  | 1965 |  | 1975 |  | 1985 |  | 1995 |  | 2006 |
|  | 1944 |  | 1955 |  | 1965 |  | 1975 |  | 1985 |  | 1996 |  | 2006 |
|  | 1945 |  | 1955 |  | 1965 |  | 1975 |  | 1986 |  | 1996 |  | 2006 |
|  | 1945 |  | 1955 |  | 1965 |  | 1976 |  | 1986 |  | 1996 |  | 2006 |
|  | 1945 |  | 1955 |  | 1966 |  | 1976 |  | 1986 |  | 1996 |  | 2007 |
|  | 1945 |  | 1956 |  | 1966 |  | 1976 |  | 1986 |  | 1997 |  | 2007 |
|  | 1946 |  | 1956 |  | 1966 |  | 1976 |  | 1987 |  | 1997 |  | 2007 |
|  | 1946 |  | 1956 |  | 1966 |  | 1977 |  | 1987 |  | 1997 |  | 2007 |
|  | 1946 |  | 1956 |  | 1967 |  | 1977 |  | 1987 |  | 1997 |  | 2008 |
|  | 1946 |  | 1957 |  | 1967 |  | 1977 |  | 1987 |  | 1998 |  | 2008 |
|  | 1947 |  | 1957 |  | 1967 |  | 1977 |  | 1988 |  | 1998 |  | 2008 |
|  | 1947 |  | 1957 |  | 1967 |  | 1978 |  | 1988 |  | 1998 |  | 2008 |
|  | 1947 |  | 1957 |  | 1968 |  | 1978 |  | 1988 |  | 1998 |  | 2009 |
|  | 1947 |  | 1958 |  | 1968 |  | 1978 |  | 1988 |  | 1999 |  | 2009 |
|  | 1948 |  | 1958 |  | 1968 |  | 1978 |  | 1989 |  | 1999 |  | 2009 |
|  | 1948 |  | 1958 |  | 1968 |  | 1979 |  | 1989 |  | 1999 |  | 2009 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | Trt. |  |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2010 | PPD | 2020 | PPD | 2030 | PPD | 2040 | PPD | 2051 | PPD | 2061 | PPD | 2071 |
|  | 2010 |  | 2020 |  | 2030 |  | 2041 |  | 2051 |  | 2061 |  | 2071 |
|  | 2010 |  | 2020 |  | 2031 |  | 2041 |  | 2051 |  | 2061 |  | 2072 |
|  | 2010 |  | 2021 |  | 2031 |  | 2041 |  | 2051 |  | 2062 |  | 2072 |
|  | 2011 |  | 2021 |  | 2031 |  | 2041 |  | 2052 |  | 2062 |  | 2072 |
|  | 2011 |  | 2021 |  | 2031 |  | 2042 |  | 2052 |  | 2062 |  | 2072 |
|  | 2011 |  | 2021 |  | 2032 |  | 2042 |  | 2052 |  | 2062 |  | 2073 |
|  | 2011 |  | 2022 |  | 2032 |  | 2042 |  | 2052 |  | 2063 |  | 2073 |
|  | 2012 |  | 2022 |  | 2032 |  | 2042 |  | 2053 |  | 2063 |  | 2073 |
|  | 2012 |  | 2022 |  | 2032 |  | 2043 |  | 2053 |  | 2063 |  | 2073 |
|  | 2012 |  | 2022 |  | 2033 |  | 2043 |  | 2053 |  | 2063 |  | 2074 |
|  | 2012 |  | 2023 |  | 2033 |  | 2043 |  | 2053 |  | 2064 |  | 2074 |
|  | 2013 |  | 2023 |  | 2033 |  | 2043 |  | 2054 |  | 2064 |  | 2074 |
|  | 2013 |  | 2023 |  | 2033 |  | 2044 |  | 2054 |  | 2064 |  | 2074 |
|  | 2013 |  | 2023 |  | 2034 |  | 2044 |  | 2054 |  | 2064 |  | 2075 |
|  | 2013 |  | 2024 |  | 2034 |  | 2044 |  | 2054 |  | 2065 |  | 2075 |
|  | 2014 |  | 2024 |  | 2034 |  | 2044 |  | 2055 |  | 2065 |  | 2075 |
|  | 2014 |  | 2024 |  | 2034 |  | 2045 |  | 2055 |  | 2065 |  | 2075 |
|  | 2014 |  | 2024 |  | 2035 |  | 2045 |  | 2055 |  | 2065 |  | 2076 |
|  | 2014 |  | 2025 |  | 2035 |  | 2045 |  | 2055 |  | 2066 |  | 2076 |
|  | 2015 |  | 2025 |  | 2035 |  | 2045 |  | 2056 |  | 2066 |  | 2076 |
|  | 2015 |  | 2025 |  | 2035 |  | 2046 |  | 2056 |  | 2066 |  | 2076 |
|  | 2015 |  | 2025 |  | 2036 |  | 2046 |  | 2056 |  | 2066 |  | 2077 |
|  | 2015 |  | 2026 |  | 2036 |  | 2046 |  | 2056 |  | 2067 |  | 2077 |
|  | 2016 |  | 2026 |  | 2036 |  | 2046 |  | 2057 |  | 2067 |  | 2077 |
|  | 2016 |  | 2026 |  | 2036 |  | 2047 |  | 2057 |  | 2067 |  | 2077 |
|  | 2016 |  | 2026 |  | 2037 |  | 2047 |  | 2057 |  | 2067 |  | 2078 |
|  | 2016 |  | 2027 |  | 2037 |  | 2047 |  | 2057 |  | 2068 |  | 2078 |
|  | 2017 |  | 2027 |  | 2037 |  | 2047 |  | 2058 |  | 2068 |  | 2078 |
|  | 2017 |  | 2027 |  | 2037 |  | 2048 |  | 2058 |  | 2068 |  | 2078 |
|  | 2017 |  | 2027 |  | 2038 |  | 2048 |  | 2058 |  | 2068 |  | 2079 |
|  | 2017 |  | 2028 |  | 2038 |  | 2048 |  | 2058 |  | 2069 |  | 2079 |
|  | 2018 |  | 2028 |  | 2038 |  | 2048 |  | 2059 |  | 2069 |  | 2079 |
|  | 2018 |  | 2028 |  | 2038 |  | 2049 |  | 2059 |  | 2069 |  | 2079 |
|  | 2018 |  | 2028 |  | 2039 |  | 2049 |  | 2059 |  | 2069 |  | 2080 |
|  | 2018 |  | 2029 |  | 2039 |  | 2049 |  | 2059 |  | 2070 |  | 2080 |
|  | 2019 |  | 2029 |  | 2039 |  | 2049 |  | 2060 |  | 2070 |  | 2080 |
|  | 2019 |  | 2029 |  | 2039 |  | 2050 |  | 2060 |  | 2070 |  | 2080 |
|  | 2019 |  | 2029 |  | 2040 |  | 2050 |  | 2060 |  | 2070 |  | 2081 |
|  | 2019 |  | 2030 |  | 2040 |  | 2050 |  | 2060 |  | 2071 |  | 2081 |
|  | 2020 |  | 2030 |  | 2040 |  | 2050 |  | 2061 |  | 2071 |  | 2081 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ | Bl nb |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. } \\ & \text { No nl. } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2081 | PPD | 2092 | PPD | 2102 | PPD | 2112 | PPD | 2122 | PPD | 2133 | PPD | 2143 |
|  | 2082 |  | 2092 |  | 2102 |  | 2112 |  | 2123 |  | 2133 |  | 2143 |
|  | 2082 |  | 2092 |  | 2102 |  | 2113 |  | 2123 |  | 2133 |  | 2143 |
|  | 2082 |  | 2092 |  | 2103 |  | 2113 |  | 2123 |  | 2133 |  | 2144 |
|  | 2082 |  | 2093 |  | 2103 |  | 2113 |  | 2123 |  | 2134 |  | 2144 |
|  | 2083 |  | 2093 |  | 2103 |  | 2113 |  | 2124 |  | 2134 |  | 2144 |
|  | 2083 |  | 2093 |  | 2103 |  | 2114 |  | 2124 |  | 2134 |  | 2144 |
|  | 2083 |  | 2093 |  | 2104 |  | 2114 |  | 2124 |  | 2134 |  | 2145 |
|  | 2083 |  | 2094 |  | 2104 |  | 2114 |  | 2124 |  | 2135 |  | 2145 |
|  | 2084 |  | 2094 |  | 2104 |  | 2114 |  | 2125 |  | 2135 |  | 2145 |
|  | 2084 |  | 2094 |  | 2104 |  | 2115 |  | 2125 |  | 2135 |  | 2145 |
|  | 2084 |  | 2094 |  | 2105 |  | 2115 |  | 2125 |  | 2135 |  | 2146 |
|  | 2084 |  | 2095 |  | 2105 |  | 2115 |  | 2125 |  | 2136 |  | 2146 |
|  | 2085 |  | 2095 |  | 2105 |  | 2115 |  | 2126 |  | 2136 |  | 2146 |
|  | 2085 |  | 2095 |  | 2105 |  | 2116 |  | 2126 |  | 2136 |  | 2146 |
|  | 2085 |  | 2095 |  | 2106 |  | 2116 |  | 2126 |  | 2136 |  | 2147 |
|  | 2085 |  | 2096 |  | 2106 |  | 2116 |  | 2126 |  | 2137 |  | 2147 |
|  | 2086 |  | 2096 |  | 2106 |  | 2116 |  | 2127 |  | 2137 |  | 2147 |
|  | 2086 |  | 2096 |  | 2106 |  | 2117 |  | 2127 |  | 2137 |  | 2147 |
|  | 2086 |  | 2096 |  | 2107 |  | 2117 |  | 2127 |  | 2137 |  | 2148 |
|  | 2086 |  | 2097 |  | 2107 |  | 2117 |  | 2127 |  | 2138 |  | 2148 |
|  | 2087 |  | 2097 |  | 2107 |  | 2117 |  | 2128 |  | 2138 |  | 2148 |
|  | 2087 |  | 2097 |  | 2107 |  | 2118 |  | 2128 |  | 2138 |  | 2148 |
|  | 2087 |  | 2097 |  | 2108 |  | 2118 |  | 2128 |  | 2138 |  | 2149 |
|  | 2087 |  | 2098 |  | 2108 |  | 2118 |  | 2128 |  | 2139 |  | 2149 |
|  | 2088 |  | 2098 |  | 2108 |  | 2118 |  | 2129 |  | 2139 |  | 2149 |
|  | 2088 |  | 2098 |  | 2108 |  | 2119 |  | 2129 |  | 2139 |  | 2149 |
|  | 2088 |  | 2098 |  | 2109 |  | 2119 |  | 2129 |  | 2139 |  | 2150 |
|  | 2088 |  | 2099 |  | 2109 |  | 2119 |  | 2129 |  | 2140 |  | 2150 |
|  | 2089 |  | 2099 |  | 2109 |  | 2119 |  | 2130 |  | 2140 |  | 2150 |
|  | 2089 |  | 2099 |  | 2109 |  | 2120 |  | 2130 |  | 2140 |  | 2150 |
|  | 2089 |  | 2099 |  | 2110 |  | 2120 |  | 2130 |  | 2140 |  | 2151 |
|  | 2089 |  | 2100 |  | 2110 |  | 2120 |  | 2130 |  | 2141 |  | 2151 |
|  | 2090 |  | 2100 |  | 2110 |  | 2120 |  | 2131 |  | 2141 |  | 2151 |
|  | 2090 |  | 2100 |  | 2110 |  | 2121 |  | 2131 |  | 2141 |  | 2151 |
|  | 2090 |  | 2100 |  | 2111 |  | 2121 |  | 2131 |  | 2141 |  | 2152 |
|  | 2090 |  | 2101 |  | 2111 |  | 2121 |  | 2131 |  | 2142 |  | 2152 |
|  | 2091 |  | 2101 |  | 2111 |  | 2121 |  | 2132 |  | 2142 |  | 2152 |
|  | 2091 |  | 2101 |  | 2111 |  | 2122 |  | 2132 |  | 2142 |  | 2152 |
|  | 2091 |  | 2101 |  | 2112 |  | 2122 |  | 2132 |  | 2142 |  | 2153 |
|  | 2091 |  | 2102 |  | 2112 |  | 2122 |  | 2132 |  | 2143 |  | 2153 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. |  | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2153 | PPD | 2163 | PPD | 2174 | PPD | 2184 | PPD | 2194 | PPD | 2204 | PPD | 2215 |
|  | 2153 |  | 2164 |  | 2174 |  | 2184 |  | 2194 |  | 2205 |  | 2215 |
|  | 2154 |  | 2164 |  | 2174 |  | 2184 |  | 2195 |  | 2205 |  | 2215 |
|  | 2154 |  | 2164 |  | 2174 |  | 2185 |  | 2195 |  | 2205 |  | 2215 |
|  | 2154 |  | 2164 |  | 2175 |  | 2185 |  | 2195 |  | 2205 |  | 2216 |
|  | 2154 |  | 2165 |  | 2175 |  | 2185 |  | 2195 |  | 2206 |  | 2216 |
|  | 2155 |  | 2165 |  | 2175 |  | 2185 |  | 2196 |  | 2206 |  | 2216 |
|  | 2155 |  | 2165 |  | 2175 |  | 2186 |  | 2196 |  | 2206 |  | 2216 |
|  | 2155 |  | 2165 |  | 2176 |  | 2186 |  | 2196 |  | 2206 |  | 2217 |
|  | 2155 |  | 2166 |  | 2176 |  | 2186 |  | 2196 |  | 2207 |  | 2217 |
|  | 2156 |  | 2166 |  | 2176 |  | 2186 |  | 2197 |  | 2207 |  | 2217 |
|  | 2156 |  | 2166 |  | 2176 |  | 2187 |  | 2197 |  | 2207 |  | 2217 |
|  | 2156 |  | 2166 |  | 2177 |  | 2187 |  | 2197 |  | 2207 |  | 2218 |
|  | 2156 |  | 2167 |  | 2177 |  | 2187 |  | 2197 |  | 2208 |  | 2218 |
|  | 2157 |  | 2167 |  | 2177 |  | 2187 |  | 2198 |  | 2208 |  | 2218 |
|  | 2157 |  | 2167 |  | 2177 |  | 2188 |  | 2198 |  | 2208 |  | 2218 |
|  | 2157 |  | 2167 |  | 2178 |  | 2188 |  | 2198 |  | 2208 |  | 2219 |
|  | 2157 |  | 2168 |  | 2178 |  | 2188 |  | 2198 |  | 2209 |  | 2219 |
|  | 2158 |  | 2168 |  | 2178 |  | 2188 |  | 2199 |  | 2209 |  | 2219 |
|  | 2158 |  | 2168 |  | 2178 |  | 2189 |  | 2199 |  | 2209 |  | 2219 |
|  | 2158 |  | 2168 |  | 2179 |  | 2189 |  | 2199 |  | 2209 |  | 2220 |
|  | 2158 |  | 2169 |  | 2179 |  | 2189 |  | 2199 |  | 2210 |  | 2220 |
|  | 2159 |  | 2169 |  | 2179 |  | 2189 |  | 2200 |  | 2210 |  | 2220 |
|  | 2159 |  | 2169 |  | 2179 |  | 2190 |  | 2200 |  | 2210 |  | 2220 |
|  | 2159 |  | 2169 |  | 2180 |  | 2190 |  | 2200 |  | 2210 |  | 2221 |
|  | 2159 |  | 2170 |  | 2180 |  | 2190 |  | 2200 |  | 2211 |  | 2221 |
|  | 2160 |  | 2170 |  | 2180 |  | 2190 |  | 2201 |  | 2211 |  | 2221 |
|  | 2160 |  | 2170 |  | 2180 |  | 2191 |  | 2201 |  | 2211 |  | 2221 |
|  | 2160 |  | 2170 |  | 2181 |  | 2191 |  | 2201 |  | 2211 |  | 2222 |
|  | 2160 |  | 2171 |  | 2181 |  | 2191 |  | 2201 |  | 2212 |  | 2222 |
|  | 2161 |  | 2171 |  | 2181 |  | 2191 |  | 2202 |  | 2212 |  | 2222 |
|  | 2161 |  | 2171 |  | 2181 |  | 2192 |  | 2202 |  | 2212 |  | 2222 |
|  | 2161 |  | 2171 |  | 2182 |  | 2192 |  | 2202 |  | 2212 |  | 2223 |
|  | 2161 |  | 2172 |  | 2182 |  | 2192 |  | 2202 |  | 2213 |  | 2223 |
|  | 2162 |  | 2172 |  | 2182 |  | 2192 |  | 2203 |  | 2213 |  | 2223 |
|  | 2162 |  | 2172 |  | 2182 |  | 2193 |  | 2203 |  | 2213 |  | 2223 |
|  | 2162 |  | 2172 |  | 2183 |  | 2193 |  | 2203 |  | 2213 |  | 2224 |
|  | 2162 |  | 2173 |  | 2183 |  | 2193 |  | 2203 |  | 2214 |  | 2224 |
|  | 2163 |  | 2173 |  | 2183 |  | 2193 |  | 2204 |  | 2214 |  | 2224 |
|  | 2163 |  | 2173 |  | 2183 |  | 2194 |  | 2204 |  | 2214 |  | 2224 |
|  | 2163 |  | 2173 |  | 2184 |  | 2194 |  | 2204 |  | 2214 |  | 2225 |

SD4 4 RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl. |  | Bl. |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2225 | PPD | 2235 | PPD | 2245 | PPD | 2256 | PPD | 2266 | PPD | 2276 | PPD | 2286 |
|  | 2225 |  | 2235 |  | 2246 |  | 2256 |  | 2266 |  | 2276 |  | 2287 |
|  | 2225 |  | 2236 |  | 2246 |  | 2256 |  | 2266 |  | 2277 |  | 2287 |
|  | 2226 |  | 2236 |  | 2246 |  | 2256 |  | 2267 |  | 2277 |  | 2287 |
|  | 2226 |  | 2236 |  | 2246 |  | 2257 |  | 2267 |  | 2277 |  | 2287 |
|  | 2226 |  | 2236 |  | 2247 |  | 2257 |  | 2267 |  | 2277 |  | 2288 |
|  | 2226 |  | 2237 |  | 2247 |  | 2257 |  | 2267 |  | 2278 |  | 2288 |
|  | 2227 |  | 2237 |  | 2247 |  | 2257 |  | 2268 |  | 2278 |  | 2288 |
|  | 2227 |  | 2237 |  | 2247 |  | 2258 |  | 2268 |  | 2278 |  | 2288 |
|  | 2227 |  | 2237 |  | 2248 |  | 2258 |  | 2268 |  | 2278 |  | 2289 |
|  | 2227 |  | 2238 |  | 2248 |  | 2258 |  | 2268 |  | 2279 |  | 2289 |
|  | 2228 |  | 2238 |  | 2248 |  | 2258 |  | 2269 |  | 2279 |  | 2289 |
|  | 2228 |  | 2238 |  | 2248 |  | 2259 |  | 2269 |  | 2279 |  | 2289 |
|  | 2228 |  | 2238 |  | 2249 |  | 2259 |  | 2269 |  | 2279 |  | 2290 |
|  | 2228 |  | 2239 |  | 2249 |  | 2259 |  | 2269 |  | 2280 |  | 2290 |
|  | 2229 |  | 2239 |  | 2249 |  | 2259 |  | 2270 |  | 2280 |  | 2290 |
|  | 2229 |  | 2239 |  | 2249 |  | 2260 |  | 2270 |  | 2280 |  | 2290 |
|  | 2229 |  | 2239 |  | 2250 |  | 2260 |  | 2270 |  | 2280 |  | 2291 |
|  | 2229 |  | 2240 |  | 2250 |  | 2260 |  | 2270 |  | 2281 |  | 2291 |
|  | 2230 |  | 2240 |  | 2250 |  | 2260 |  | 2271 |  | 2281 |  | 2291 |
|  | 2230 |  | 2240 |  | 2250 |  | 2261 |  | 2271 |  | 2281 |  | 2291 |
|  | 2230 |  | 2240 |  | 2251 |  | 2261 |  | 2271 |  | 2281 |  | 2292 |
|  | 2230 |  | 2241 |  | 2251 |  | 2261 |  | 2271 |  | 2282 |  | 2292 |
|  | 2231 |  | 2241 |  | 2251 |  | 2261 |  | 2272 |  | 2282 |  | 2292 |
|  | 2231 |  | 2241 |  | 2251 |  | 2262 |  | 2272 |  | 2282 |  | 2292 |
|  | 2231 |  | 2241 |  | 2252 |  | 2262 |  | 2272 |  | 2282 |  | 2293 |
|  | 2231 |  | 2242 |  | 2252 |  | 2262 |  | 2272 |  | 2283 |  | 2293 |
|  | 2232 |  | 2242 |  | 2252 |  | 2262 |  | 2273 |  | 2283 |  | 2293 |
|  | 2232 |  | 2242 |  | 2252 |  | 2263 |  | 2273 |  | 2283 |  | 2293 |
|  | 2232 |  | 2242 |  | 2253 |  | 2263 |  | 2273 |  | 2283 |  | 2294 |
|  | 2232 |  | 2243 |  | 2253 |  | 2263 |  | 2273 |  | 2284 |  | 2294 |
|  | 2233 |  | 2243 |  | 2253 |  | 2263 |  | 2274 |  | 2284 |  | 2294 |
|  | 2233 |  | 2243 |  | 2253 |  | 2264 |  | 2274 |  | 2284 |  | 2294 |
|  | 2233 |  | 2243 |  | 2254 |  | 2264 |  | 2274 |  | 2284 |  | 2295 |
|  | 2233 |  | 2244 |  | 2254 |  | 2264 |  | 2274 |  | 2285 |  | 2295 |
|  | 2234 |  | 2244 |  | 2254 |  | 2264 |  | 2275 |  | 2285 |  | 2295 |
|  | 2234 |  | 2244 |  | 2254 |  | 2265 |  | 2275 |  | 2285 |  | 2295 |
|  | 2234 |  | 2244 |  | 2255 |  | 2265 |  | 2275 |  | 2285 |  | 2296 |
|  | 2234 |  | 2245 |  | 2255 |  | 2265 |  | 2275 |  | 2286 |  | 2296 |
|  | 2235 |  | 2245 |  | 2255 |  | 2265 |  | 2276 |  | 2286 |  | 2296 |
|  | 2235 |  | 2245 |  | 2255 |  | 2266 |  | 2276 |  | 2286 |  | 2296 |

Treatment number associated to material : Hz/su-PreChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ | $\mathrm{Bl}_{\mathrm{Bl}} \mathrm{C}$ |  |  | Trt |  |  | Bl. | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2297 | PPD | 2307 | PPD | 2317 | PPD | 2327 | PPD | 2338 | PPD | 2348 | PPD | 2358 |
|  | 2297 |  | 2307 |  | 2317 |  | 2328 |  | 2338 |  | 2348 |  | 2358 |
|  | 2297 |  | 2307 |  | 2318 |  | 2328 |  | 2338 |  | 2348 |  | 2359 |
|  | 2297 |  | 2308 |  | 2318 |  | 2328 |  | 2338 |  | 2349 |  | 2359 |
|  | 2298 |  | 2308 |  | 2318 |  | 2328 |  | 2339 |  | 2349 |  | 2359 |
|  | 2298 |  | 2308 |  | 2318 |  | 2329 |  | 2339 |  | 2349 |  | 2359 |
|  | 2298 |  | 2308 |  | 2319 |  | 2329 |  | 2339 |  | 2349 |  | 2360 |
|  | 2298 |  | 2309 |  | 2319 |  | 2329 |  | 2339 |  | 2350 |  | 2360 |
|  | 2299 |  | 2309 |  | 2319 |  | 2329 |  | 2340 |  | 2350 |  | 2360 |
|  | 2299 |  | 2309 |  | 2319 |  | 2330 |  | 2340 |  | 2350 |  | 2360 |
|  | 2299 |  | 2309 |  | 2320 |  | 2330 |  | 2340 |  | 2350 |  | 2361 |
|  | 2299 |  | 2310 |  | 2320 |  | 2330 |  | 2340 |  | 2351 |  | 2361 |
|  | 2300 |  | 2310 |  | 2320 |  | 2330 |  | 2341 |  | 2351 |  | 2361 |
|  | 2300 |  | 2310 |  | 2320 |  | 2331 |  | 2341 |  | 2351 |  | 2361 |
|  | 2300 |  | 2310 |  | 2321 |  | 2331 |  | 2341 |  | 2351 |  | 2362 |
|  | 2300 |  | 2311 |  | 2321 |  | 2331 |  | 2341 |  | 2352 |  | 2362 |
|  | 2301 |  | 2311 |  | 2321 |  | 2331 |  | 2342 |  | 2352 |  | 2362 |
|  | 2301 |  | 2311 |  | 2321 |  | 2332 |  | 2342 |  | 2352 |  | 2362 |
|  | 2301 |  | 2311 |  | 2322 |  | 2332 |  | 2342 |  | 2352 |  | 2363 |
|  | 2301 |  | 2312 |  | 2322 |  | 2332 |  | 2342 |  | 2353 |  | 2363 |
|  | 2302 |  | 2312 |  | 2322 |  | 2332 |  | 2343 |  | 2353 |  | 2363 |
|  | 2302 |  | 2312 |  | 2322 |  | 2333 |  | 2343 |  | 2353 |  | 2363 |
|  | 2302 |  | 2312 |  | 2323 |  | 2333 |  | 2343 |  | 2353 |  | 2364 |
|  | 2302 |  | 2313 |  | 2323 |  | 2333 |  | 2343 |  | 2354 |  | 2364 |
|  | 2303 |  | 2313 |  | 2323 |  | 2333 |  | 2344 |  | 2354 |  | 2364 |
|  | 2303 |  | 2313 |  | 2323 |  | 2334 |  | 2344 |  | 2354 |  | 2364 |
|  | 2303 |  | 2313 |  | 2324 |  | 2334 |  | 2344 |  | 2354 |  | 2365 |
|  | 2303 |  | 2314 |  | 2324 |  | 2334 |  | 2344 |  | 2355 |  | 2365 |
|  | 2304 |  | 2314 |  | 2324 |  | 2334 |  | 2345 |  | 2355 |  | 2365 |
|  | 2304 |  | 2314 |  | 2324 |  | 2335 |  | 2345 |  | 2355 |  | 2365 |
|  | 2304 |  | 2314 |  | 2325 |  | 2335 |  | 2345 |  | 2355 |  | 2366 |
|  | 2304 |  | 2315 |  | 2325 |  | 2335 |  | 2345 |  | 2356 |  | 2366 |
|  | 2305 |  | 2315 |  | 2325 |  | 2335 |  | 2346 |  | 2356 |  | 2366 |
|  | 2305 |  | 2315 |  | 2325 |  | 2336 |  | 2346 |  | 2356 |  | 2366 |
|  | 2305 |  | 2315 |  | 2326 |  | 2336 |  | 2346 |  | 2356 |  | 2367 |
|  | 2305 |  | 2316 |  | 2326 |  | 2336 |  | 2346 |  | 2357 |  | 2367 |
|  | 2306 |  | 2316 |  | 2326 |  | 2336 |  | 2347 |  | 2357 |  | 2367 |
|  | 2306 |  | 2316 |  | 2326 |  | 2337 |  | 2347 |  | 2357 |  | 2367 |
|  | 2306 |  | 2316 |  | 2327 |  | 2337 |  | 2347 |  | 2357 |  | 2368 |
|  | 2306 |  | 2317 |  | 2327 |  | 2337 |  | 2347 |  | 2358 |  | 2368 |
|  | 2307 |  | 2317 |  | 2327 |  | 2337 |  | 2348 |  | 2358 |  | 2368 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | Trt | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2368 | PPD | 2379 | PPD | 2389 | PPD | 2399 | PPD | 2409 | PPD | 2420 | PPD | 2430 |
|  | 2369 |  | 2379 |  | 2389 |  | 2399 |  | 2410 |  | 2420 |  | 2430 |
|  | 2369 |  | 2379 |  | 2389 |  | 2400 |  | 2410 |  | 2420 |  | 2430 |
|  | 2369 |  | 2379 |  | 2390 |  | 2400 |  | 2410 |  | 2420 |  | 2431 |
|  | 2369 |  | 2380 |  | 2390 |  | 2400 |  | 2410 |  | 2421 |  | 2431 |
|  | 2370 |  | 2380 |  | 2390 |  | 2400 |  | 2411 |  | 2421 |  | 2431 |
|  | 2370 |  | 2380 |  | 2390 |  | 2401 |  | 2411 |  | 2421 |  | 2431 |
|  | 2370 |  | 2380 |  | 2391 |  | 2401 |  | 2411 |  | 2421 |  | 2432 |
|  | 2370 |  | 2381 |  | 2391 |  | 2401 |  | 2411 |  | 2422 |  | 2432 |
|  | 2371 |  | 2381 |  | 2391 |  | 2401 |  | 2412 |  | 2422 |  | 2432 |
|  | 2371 |  | 2381 |  | 2391 |  | 2402 |  | 2412 |  | 2422 |  | 2432 |
|  | 2371 |  | 2381 |  | 2392 |  | 2402 |  | 2412 |  | 2422 |  | 2433 |
|  | 2371 |  | 2382 |  | 2392 |  | 2402 |  | 2412 |  | 2423 |  | 2433 |
|  | 2372 |  | 2382 |  | 2392 |  | 2402 |  | 2413 |  | 2423 |  | 2433 |
|  | 2372 |  | 2382 |  | 2392 |  | 2403 |  | 2413 |  | 2423 |  | 2433 |
|  | 2372 |  | 2382 |  | 2393 |  | 2403 |  | 2413 |  | 2423 |  | 2434 |
|  | 2372 |  | 2383 |  | 2393 |  | 2403 |  | 2413 |  | 2424 |  | 2434 |
|  | 2373 |  | 2383 |  | 2393 |  | 2403 |  | 2414 |  | 2424 |  | 2434 |
|  | 2373 |  | 2383 |  | 2393 |  | 2404 |  | 2414 |  | 2424 |  | 2434 |
|  | 2373 |  | 2383 |  | 2394 |  | 2404 |  | 2414 |  | 2424 |  | 2435 |
|  | 2373 |  | 2384 |  | 2394 |  | 2404 |  | 2414 |  | 2425 |  | 2435 |
|  | 2374 |  | 2384 |  | 2394 |  | 2404 |  | 2415 |  | 2425 |  | 2435 |
|  | 2374 |  | 2384 |  | 2394 |  | 2405 |  | 2415 |  | 2425 |  | 2435 |
|  | 2374 |  | 2384 |  | 2395 |  | 2405 |  | 2415 |  | 2425 |  | 2436 |
|  | 2374 |  | 2385 |  | 2395 |  | 2405 |  | 2415 |  | 2426 |  | 2436 |
|  | 2375 |  | 2385 |  | 2395 |  | 2405 |  | 2416 |  | 2426 |  | 2436 |
|  | 2375 |  | 2385 |  | 2395 |  | 2406 |  | 2416 |  | 2426 |  | 2436 |
|  | 2375 |  | 2385 |  | 2396 |  | 2406 |  | 2416 |  | 2426 |  | 2437 |
|  | 2375 |  | 2386 |  | 2396 |  | 2406 |  | 2416 |  | 2427 |  | 2437 |
|  | 2376 |  | 2386 |  | 2396 |  | 2406 |  | 2417 |  | 2427 |  | 2437 |
|  | 2376 |  | 2386 |  | 2396 |  | 2407 |  | 2417 |  | 2427 |  | 2437 |
|  | 2376 |  | 2386 |  | 2397 |  | 2407 |  | 2417 |  | 2427 |  | 2438 |
|  | 2376 |  | 2387 |  | 2397 |  | 2407 |  | 2417 |  | 2428 |  | 2438 |
|  | 2377 |  | 2387 |  | 2397 |  | 2407 |  | 2418 |  | 2428 |  | 2438 |
|  | 2377 |  | 2387 |  | 2397 |  | 2408 |  | 2418 |  | 2428 |  | 2438 |
|  | 2377 |  | 2387 |  | 2398 |  | 2408 |  | 2418 |  | 2428 |  | 2439 |
|  | 2377 |  | 2388 |  | 2398 |  | 2408 |  | 2418 |  | 2429 |  | 2439 |
|  | 2378 |  | 2388 |  | 2398 |  | 2408 |  | 2419 |  | 2429 |  | 2439 |
|  | 2378 |  | 2388 |  | 2398 |  | 2409 |  | 2419 |  | 2429 |  | 2439 |
|  | 2378 |  | 2388 |  | 2399 |  | 2409 |  | 2419 |  | 2429 |  | 2440 |
|  | 2378 |  | 2389 |  | 2399 |  | 2409 |  | 2419 |  | 2430 |  | 2440 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl. |  | Bl. |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2440 | PPD | 2450 | PPD | 2461 | PPD | 2471 | PPD | 2481 | PPD | 2491 | PPD | 2502 |
|  | 2440 |  | 2451 |  | 2461 |  | 2471 |  | 2481 |  | 2492 |  | 2502 |
|  | 2441 |  | 2451 |  | 2461 |  | 2471 |  | 2482 |  | 2492 |  | 2502 |
|  | 2441 |  | 2451 |  | 2461 |  | 2472 |  | 2482 |  | 2492 |  | 2502 |
|  | 2441 |  | 2451 |  | 2462 |  | 2472 |  | 2482 |  | 2492 |  | 2503 |
|  | 2441 |  | 2452 |  | 2462 |  | 2472 |  | 2482 |  | 2493 |  | 2503 |
|  | 2442 |  | 2452 |  | 2462 |  | 2472 |  | 2483 |  | 2493 |  | 2503 |
|  | 2442 |  | 2452 |  | 2462 |  | 2473 |  | 2483 |  | 2493 |  | 2503 |
|  | 2442 |  | 2452 |  | 2463 |  | 2473 |  | 2483 |  | 2493 |  | 2504 |
|  | 2442 |  | 2453 |  | 2463 |  | 2473 |  | 2483 |  | 2494 |  | 2504 |
|  | 2443 |  | 2453 |  | 2463 |  | 2473 |  | 2484 |  | 2494 |  | 2504 |
|  | 2443 |  | 2453 |  | 2463 |  | 2474 |  | 2484 |  | 2494 |  | 2504 |
|  | 2443 |  | 2453 |  | 2464 |  | 2474 |  | 2484 |  | 2494 |  | 2505 |
|  | 2443 |  | 2454 |  | 2464 |  | 2474 |  | 2484 |  | 2495 |  | 2505 |
|  | 2444 |  | 2454 |  | 2464 |  | 2474 |  | 2485 |  | 2495 |  | 2505 |
|  | 2444 |  | 2454 |  | 2464 |  | 2475 |  | 2485 |  | 2495 |  | 2505 |
|  | 2444 |  | 2454 |  | 2465 |  | 2475 |  | 2485 |  | 2495 |  | 2506 |
|  | 2444 |  | 2455 |  | 2465 |  | 2475 |  | 2485 |  | 2496 |  | 2506 |
|  | 2445 |  | 2455 |  | 2465 |  | 2475 |  | 2486 |  | 2496 |  | 2506 |
|  | 2445 |  | 2455 |  | 2465 |  | 2476 |  | 2486 |  | 2496 |  | 2506 |
|  | 2445 |  | 2455 |  | 2466 |  | 2476 |  | 2486 |  | 2496 |  | 2507 |
|  | 2445 |  | 2456 |  | 2466 |  | 2476 |  | 2486 |  | 2497 |  | 2507 |
|  | 2446 |  | 2456 |  | 2466 |  | 2476 |  | 2487 |  | 2497 |  | 2507 |
|  | 2446 |  | 2456 |  | 2466 |  | 2477 |  | 2487 |  | 2497 |  | 2507 |
|  | 2446 |  | 2456 |  | 2467 |  | 2477 |  | 2487 |  | 2497 |  | 2508 |
|  | 2446 |  | 2457 |  | 2467 |  | 2477 |  | 2487 |  | 2498 |  | 2508 |
|  | 2447 |  | 2457 |  | 2467 |  | 2477 |  | 2488 |  | 2498 |  | 2508 |
|  | 2447 |  | 2457 |  | 2467 |  | 2478 |  | 2488 |  | 2498 |  | 2508 |
|  | 2447 |  | 2457 |  | 2468 |  | 2478 |  | 2488 |  | 2498 |  | 2509 |
|  | 2447 |  | 2458 |  | 2468 |  | 2478 |  | 2488 |  | 2499 |  | 2509 |
|  | 2448 |  | 2458 |  | 2468 |  | 2478 |  | 2489 |  | 2499 |  | 2509 |
|  | 2448 |  | 2458 |  | 2468 |  | 2479 |  | 2489 |  | 2499 |  | 2509 |
|  | 2448 |  | 2458 |  | 2469 |  | 2479 |  | 2489 |  | 2499 |  | 2510 |
|  | 2448 |  | 2459 |  | 2469 |  | 2479 |  | 2489 |  | 2500 |  | 2510 |
|  | 2449 |  | 2459 |  | 2469 |  | 2479 |  | 2490 |  | 2500 |  | 2510 |
|  | 2449 |  | 2459 |  | 2469 |  | 2480 |  | 2490 |  | 2500 |  | 2510 |
|  | 2449 |  | 2459 |  | 2470 |  | 2480 |  | 2490 |  | 2500 |  | 2511 |
|  | 2449 |  | 2460 |  | 2470 |  | 2480 |  | 2490 |  | 2501 |  | 2511 |
|  | 2450 |  | 2460 |  | 2470 |  | 2480 |  | 2491 |  | 2501 |  | 2511 |
|  | 2450 |  | 2460 |  | 2470 |  | 2481 |  | 2491 |  | 2501 |  | 2511 |
|  | 2450 |  | 2460 |  | 2471 |  | 2481 |  | 2491 |  | 2501 |  | 2512 |

SD4 4 RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ | Bl nb |  | Bl. |  | Bl nb |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} . \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2512 | PPD | 2522 | PPD | 2532 | PPD | 2543 | PPD | 2553 | PPD | 2563 | PPD | 2573 |
|  | 2512 |  | 2522 |  | 2533 |  | 2543 |  | 2553 |  | 2563 |  | 2574 |
|  | 2512 |  | 2523 |  | 2533 |  | 2543 |  | 2553 |  | 2564 |  | 2574 |
|  | 2513 |  | 2523 |  | 2533 |  | 2543 |  | 2554 |  | 2564 |  | 2574 |
|  | 2513 |  | 2523 |  | 2533 |  | 2544 |  | 2554 |  | 2564 |  | 2574 |
|  | 2513 |  | 2523 |  | 2534 |  | 2544 |  | 2554 |  | 2564 |  | 2575 |
|  | 2513 |  | 2524 |  | 2534 |  | 2544 |  | 2554 |  | 2565 |  | 2575 |
|  | 2514 |  | 2524 |  | 2534 |  | 2544 |  | 2555 |  | 2565 |  | 2575 |
|  | 2514 |  | 2524 |  | 2534 |  | 2545 |  | 2555 |  | 2565 |  | 2575 |
|  | 2514 |  | 2524 |  | 2535 |  | 2545 |  | 2555 |  | 2565 |  | 2576 |
|  | 2514 |  | 2525 |  | 2535 |  | 2545 |  | 2555 |  | 2566 |  | 2576 |
|  | 2515 |  | 2525 |  | 2535 |  | 2545 |  | 2556 |  | 2566 |  | 2576 |
|  | 2515 |  | 2525 |  | 2535 |  | 2546 |  | 2556 |  | 2566 |  | 2576 |
|  | 2515 |  | 2525 |  | 2536 |  | 2546 |  | 2556 |  | 2566 |  | 2577 |
|  | 2515 |  | 2526 |  | 2536 |  | 2546 |  | 2556 |  | 2567 |  | 2577 |
|  | 2516 |  | 2526 |  | 2536 |  | 2546 |  | 2557 |  | 2567 |  | 2577 |
|  | 2516 |  | 2526 |  | 2536 |  | 2547 |  | 2557 |  | 2567 |  | 2577 |
|  | 2516 |  | 2526 |  | 2537 |  | 2547 |  | 2557 |  | 2567 |  | 2578 |
|  | 2516 |  | 2527 |  | 2537 |  | 2547 |  | 2557 |  | 2568 |  | 2578 |
|  | 2517 |  | 2527 |  | 2537 |  | 2547 |  | 2558 |  | 2568 |  | 2578 |
|  | 2517 |  | 2527 |  | 2537 |  | 2548 |  | 2558 |  | 2568 |  | 2578 |
|  | 2517 |  | 2527 |  | 2538 |  | 2548 |  | 2558 |  | 2568 |  | 2579 |
|  | 2517 |  | 2528 |  | 2538 |  | 2548 |  | 2558 |  | 2569 |  | 2579 |
|  | 2518 |  | 2528 |  | 2538 |  | 2548 |  | 2559 |  | 2569 |  | 2579 |
|  | 2518 |  | 2528 |  | 2538 |  | 2549 |  | 2559 |  | 2569 |  | 2579 |
|  | 2518 |  | 2528 |  | 2539 |  | 2549 |  | 2559 |  | 2569 |  | 2580 |
|  | 2518 |  | 2529 |  | 2539 |  | 2549 |  | 2559 |  | 2570 |  | 2580 |
|  | 2519 |  | 2529 |  | 2539 |  | 2549 |  | 2560 |  | 2570 |  | 2580 |
|  | 2519 |  | 2529 |  | 2539 |  | 2550 |  | 2560 |  | 2570 |  | 2580 |
|  | 2519 |  | 2529 |  | 2540 |  | 2550 |  | 2560 |  | 2570 |  | 2581 |
|  | 2519 |  | 2530 |  | 2540 |  | 2550 |  | 2560 |  | 2571 |  | 2581 |
|  | 2520 |  | 2530 |  | 2540 |  | 2550 |  | 2561 |  | 2571 |  | 2581 |
|  | 2520 |  | 2530 |  | 2540 |  | 2551 |  | 2561 |  | 2571 |  | 2581 |
|  | 2520 |  | 2530 |  | 2541 |  | 2551 |  | 2561 |  | 2571 |  | 2582 |
|  | 2520 |  | 2531 |  | 2541 |  | 2551 |  | 2561 |  | 2572 |  | 2582 |
|  | 2521 |  | 2531 |  | 2541 |  | 2551 |  | 2562 |  | 2572 |  | 2582 |
|  | 2521 |  | 2531 |  | 2541 |  | 2552 |  | 2562 |  | 2572 |  | 2582 |
|  | 2521 |  | 2531 |  | 2542 |  | 2552 |  | 2562 |  | 2572 |  | 2583 |
|  | 2521 |  | 2532 |  | 2542 |  | 2552 |  | 2562 |  | 2573 |  | 2583 |
|  | 2522 |  | 2532 |  | 2542 |  | 2552 |  | 2563 |  | 2573 |  | 2583 |
|  | 2522 |  | 2532 |  | 2542 |  | 2553 |  | 2563 |  | 2573 |  | 2583 |

SD4 \RDE $\backslash$ ENABLE
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Treatment number associated to material : HZ/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2584 | PPD | 2594 | PPD | 2604 | PPD | 2614 | PPD | 2625 | PPD | 2635 | PPD | 2645 |
|  | 2584 |  | 2594 |  | 2604 |  | 2615 |  | 2625 |  | 2635 |  | 2645 |
|  | 2584 |  | 2594 |  | 2605 |  | 2615 |  | 2625 |  | 2635 |  | 2646 |
|  | 2584 |  | 2595 |  | 2605 |  | 2615 |  | 2625 |  | 2636 |  | 2646 |
|  | 2585 |  | 2595 |  | 2605 |  | 2615 |  | 2626 |  | 2636 |  | 2646 |
|  | 2585 |  | 2595 |  | 2605 |  | 2616 |  | 2626 |  | 2636 |  | 2646 |
|  | 2585 |  | 2595 |  | 2606 |  | 2616 |  | 2626 |  | 2636 |  | 2647 |
|  | 2585 |  | 2596 |  | 2606 |  | 2616 |  | 2626 |  | 2637 |  | 2647 |
|  | 2586 |  | 2596 |  | 2606 |  | 2616 |  | 2627 |  | 2637 |  | 2647 |
|  | 2586 |  | 2596 |  | 2606 |  | 2617 |  | 2627 |  | 2637 |  | 2647 |
|  | 2586 |  | 2596 |  | 2607 |  | 2617 |  | 2627 |  | 2637 |  | 2648 |
|  | 2586 |  | 2597 |  | 2607 |  | 2617 |  | 2627 |  | 2638 |  | 2648 |
|  | 2587 |  | 2597 |  | 2607 |  | 2617 |  | 2628 |  | 2638 |  | 2648 |
|  | 2587 |  | 2597 |  | 2607 |  | 2618 |  | 2628 |  | 2638 |  | 2648 |
|  | 2587 |  | 2597 |  | 2608 |  | 2618 |  | 2628 |  | 2638 |  | 2649 |
|  | 2587 |  | 2598 |  | 2608 |  | 2618 |  | 2628 |  | 2639 |  | 2649 |
|  | 2588 |  | 2598 |  | 2608 |  | 2618 |  | 2629 |  | 2639 |  | 2649 |
|  | 2588 |  | 2598 |  | 2608 |  | 2619 |  | 2629 |  | 2639 |  | 2649 |
|  | 2588 |  | 2598 |  | 2609 |  | 2619 |  | 2629 |  | 2639 |  | 2650 |
|  | 2588 |  | 2599 |  | 2609 |  | 2619 |  | 2629 |  | 2640 |  | 2650 |
|  | 2589 |  | 2599 |  | 2609 |  | 2619 |  | 2630 |  | 2640 |  | 2650 |
|  | 2589 |  | 2599 |  | 2609 |  | 2620 |  | 2630 |  | 2640 |  | 2650 |
|  | 2589 |  | 2599 |  | 2610 |  | 2620 |  | 2630 |  | 2640 |  | 2651 |
|  | 2589 |  | 2600 |  | 2610 |  | 2620 |  | 2630 |  | 2641 |  | 2651 |
|  | 2590 |  | 2600 |  | 2610 |  | 2620 |  | 2631 |  | 2641 |  | 2651 |
|  | 2590 |  | 2600 |  | 2610 |  | 2621 |  | 2631 |  | 2641 |  | 2651 |
|  | 2590 |  | 2600 |  | 2611 |  | 2621 |  | 2631 |  | 2641 |  | 2652 |
|  | 2590 |  | 2601 |  | 2611 |  | 2621 |  | 2631 |  | 2642 |  | 2652 |
|  | 2591 |  | 2601 |  | 2611 |  | 2621 |  | 2632 |  | 2642 |  | 2652 |
|  | 2591 |  | 2601 |  | 2611 |  | 2622 |  | 2632 |  | 2642 |  | 2652 |
|  | 2591 |  | 2601 |  | 2612 |  | 2622 |  | 2632 |  | 2642 |  | 2653 |
|  | 2591 |  | 2602 |  | 2612 |  | 2622 |  | 2632 |  | 2643 |  | 2653 |
|  | 2592 |  | 2602 |  | 2612 |  | 2622 |  | 2633 |  | 2643 |  | 2653 |
|  | 2592 |  | 2602 |  | 2612 |  | 2623 |  | 2633 |  | 2643 |  | 2653 |
|  | 2592 |  | 2602 |  | 2613 |  | 2623 |  | 2633 |  | 2643 |  | 2654 |
|  | 2592 |  | 2603 |  | 2613 |  | 2623 |  | 2633 |  | 2644 |  | 2654 |
|  | 2593 |  | 2603 |  | 2613 |  | 2623 |  | 2634 |  | 2644 |  | 2654 |
|  | 2593 |  | 2603 |  | 2613 |  | 2624 |  | 2634 |  | 2644 |  | 2654 |
|  | 2593 |  | 2603 |  | 2614 |  | 2624 |  | 2634 |  | 2644 |  | 2655 |
|  | 2593 |  | 2604 |  | 2614 |  | 2624 |  | 2634 |  | 2645 |  | 2655 |
|  | 2594 |  | 2604 |  | 2614 |  | 2624 |  | 2635 |  | 2645 |  | 2655 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl nb |  |  |  | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. } \mathrm{Bl} . \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2655 | PPD | 2666 | PPD | 2676 | PPD | 2686 | PPD | 2696 | PPD | 2707 | PPD | 2717 |
|  | 2656 |  | 2666 |  | 2676 |  | 2686 |  | 2697 |  | 2707 |  | 2717 |
|  | 2656 |  | 2666 |  | 2676 |  | 2687 |  | 2697 |  | 2707 |  | 2717 |
|  | 2656 |  | 2666 |  | 2677 |  | 2687 |  | 2697 |  | 2707 |  | 2718 |
|  | 2656 |  | 2667 |  | 2677 |  | 2687 |  | 2697 |  | 2708 |  | 2718 |
|  | 2657 |  | 2667 |  | 2677 |  | 2687 |  | 2698 |  | 2708 |  | 2718 |
|  | 2657 |  | 2667 |  | 2677 |  | 2688 |  | 2698 |  | 2708 |  | 2718 |
|  | 2657 |  | 2667 |  | 2678 |  | 2688 |  | 2698 |  | 2708 |  | 2719 |
|  | 2657 |  | 2668 |  | 2678 |  | 2688 |  | 2698 |  | 2709 |  | 2719 |
|  | 2658 |  | 2668 |  | 2678 |  | 2688 |  | 2699 |  | 2709 |  | 2719 |
|  | 2658 |  | 2668 |  | 2678 |  | 2689 |  | 2699 |  | 2709 |  | 2719 |
|  | 2658 |  | 2668 |  | 2679 |  | 2689 |  | 2699 |  | 2709 |  | 2720 |
|  | 2658 |  | 2669 |  | 2679 |  | 2689 |  | 2699 |  | 2710 |  | 2720 |
|  | 2659 |  | 2669 |  | 2679 |  | 2689 |  | 2700 |  | 2710 |  | 2720 |
|  | 2659 |  | 2669 |  | 2679 |  | 2690 |  | 2700 |  | 2710 |  | 2720 |
|  | 2659 |  | 2669 |  | 2680 |  | 2690 |  | 2700 |  | 2710 |  | 2721 |
|  | 2659 |  | 2670 |  | 2680 |  | 2690 |  | 2700 |  | 2711 |  | 2721 |
|  | 2660 |  | 2670 |  | 2680 |  | 2690 |  | 2701 |  | 2711 |  | 2721 |
|  | 2660 |  | 2670 |  | 2680 |  | 2691 |  | 2701 |  | 2711 |  | 2721 |
|  | 2660 |  | 2670 |  | 2681 |  | 2691 |  | 2701 |  | 2711 |  | 2722 |
|  | 2660 |  | 2671 |  | 2681 |  | 2691 |  | 2701 |  | 2712 |  | 2722 |
|  | 2661 |  | 2671 |  | 2681 |  | 2691 |  | 2702 |  | 2712 |  | 2722 |
|  | 2661 |  | 2671 |  | 2681 |  | 2692 |  | 2702 |  | 2712 |  | 2722 |
|  | 2661 |  | 2671 |  | 2682 |  | 2692 |  | 2702 |  | 2712 |  | 2723 |
|  | 2661 |  | 2672 |  | 2682 |  | 2692 |  | 2702 |  | 2713 |  | 2723 |
|  | 2662 |  | 2672 |  | 2682 |  | 2692 |  | 2703 |  | 2713 |  | 2723 |
|  | 2662 |  | 2672 |  | 2682 |  | 2693 |  | 2703 |  | 2713 |  | 2723 |
|  | 2662 |  | 2672 |  | 2683 |  | 2693 |  | 2703 |  | 2713 |  | 2724 |
|  | 2662 |  | 2673 |  | 2683 |  | 2693 |  | 2703 |  | 2714 |  | 2724 |
|  | 2663 |  | 2673 |  | 2683 |  | 2693 |  | 2704 |  | 2714 |  | 2724 |
|  | 2663 |  | 2673 |  | 2683 |  | 2694 |  | 2704 |  | 2714 |  | 2724 |
|  | 2663 |  | 2673 |  | 2684 |  | 2694 |  | 2704 |  | 2714 |  | 2725 |
|  | 2663 |  | 2674 |  | 2684 |  | 2694 |  | 2704 |  | 2715 |  | 2725 |
|  | 2664 |  | 2674 |  | 2684 |  | 2694 |  | 2705 |  | 2715 |  | 2725 |
|  | 2664 |  | 2674 |  | 2684 |  | 2695 |  | 2705 |  | 2715 |  | 2725 |
|  | 2664 |  | 2674 |  | 2685 |  | 2695 |  | 2705 |  | 2715 |  | 2726 |
|  | 2664 |  | 2675 |  | 2685 |  | 2695 |  | 2705 |  | 2716 |  | 2726 |
|  | 2665 |  | 2675 |  | 2685 |  | 2695 |  | 2706 |  | 2716 |  | 2726 |
|  | 2665 |  | 2675 |  | 2685 |  | 2696 |  | 2706 |  | 2716 |  | 2726 |
|  | 2665 |  | 2675 |  | 2686 |  | 2696 |  | 2706 |  | 2716 |  | 2727 |
|  | 2665 |  | 2676 |  | 2686 |  | 2696 |  | 2706 |  | 2717 |  | 2727 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  |  |  |  |  |  |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2727 | PPD | 2737 | PPD | 2748 | PPD | 2758 | PPD | 2768 | PPD | 2778 | PPD | 2789 |
|  | 2727 |  | 2738 |  | 2748 |  | 2758 |  | 2768 |  | 2779 |  | 2789 |
|  | 2728 |  | 2738 |  | 2748 |  | 2758 |  | 2769 |  | 2779 |  | 2789 |
|  | 2728 |  | 2738 |  | 2748 |  | 2759 |  | 2769 |  | 2779 |  | 2789 |
|  | 2728 |  | 2738 |  | 2749 |  | 2759 |  | 2769 |  | 2779 |  | 2790 |
|  | 2728 |  | 2739 |  | 2749 |  | 2759 |  | 2769 |  | 2780 |  | 2790 |
|  | 2729 |  | 2739 |  | 2749 |  | 2759 |  | 2770 |  | 2780 |  | 2790 |
|  | 2729 |  | 2739 |  | 2749 |  | 2760 |  | 2770 |  | 2780 |  | 2790 |
|  | 2729 |  | 2739 |  | 2750 |  | 2760 |  | 2770 |  | 2780 |  | 2791 |
|  | 2729 |  | 2740 |  | 2750 |  | 2760 |  | 2770 |  | 2781 |  | 2791 |
|  | 2730 |  | 2740 |  | 2750 |  | 2760 |  | 2771 |  | 2781 |  | 2791 |
|  | 2730 |  | 2740 |  | 2750 |  | 2761 |  | 2771 |  | 2781 |  | 2791 |
|  | 2730 |  | 2740 |  | 2751 |  | 2761 |  | 2771 |  | 2781 |  | 2792 |
|  | 2730 |  | 2741 |  | 2751 |  | 2761 |  | 2771 |  | 2782 |  | 2792 |
|  | 2731 |  | 2741 |  | 2751 |  | 2761 |  | 2772 |  | 2782 |  | 2792 |
|  | 2731 |  | 2741 |  | 2751 |  | 2762 |  | 2772 |  | 2782 |  | 2792 |
|  | 2731 |  | 2741 |  | 2752 |  | 2762 |  | 2772 |  | 2782 |  | 2793 |
|  | 2731 |  | 2742 |  | 2752 |  | 2762 |  | 2772 |  | 2783 |  | 2793 |
|  | 2732 |  | 2742 |  | 2752 |  | 2762 |  | 2773 |  | 2783 |  | 2793 |
|  | 2732 |  | 2742 |  | 2752 |  | 2763 |  | 2773 |  | 2783 |  | 2793 |
|  | 2732 |  | 2742 |  | 2753 |  | 2763 |  | 2773 |  | 2783 |  | 2794 |
|  | 2732 |  | 2743 |  | 2753 |  | 2763 |  | 2773 |  | 2784 |  | 2794 |
|  | 2733 |  | 2743 |  | 2753 |  | 2763 |  | 2774 |  | 2784 |  | 2794 |
|  | 2733 |  | 2743 |  | 2753 |  | 2764 |  | 2774 |  | 2784 |  | 2794 |
|  | 2733 |  | 2743 |  | 2754 |  | 2764 |  | 2774 |  | 2784 |  | 2795 |
|  | 2733 |  | 2744 |  | 2754 |  | 2764 |  | 2774 |  | 2785 |  | 2795 |
|  | 2734 |  | 2744 |  | 2754 |  | 2764 |  | 2775 |  | 2785 |  | 2795 |
|  | 2734 |  | 2744 |  | 2754 |  | 2765 |  | 2775 |  | 2785 |  | 2795 |
|  | 2734 |  | 2744 |  | 2755 |  | 2765 |  | 2775 |  | 2785 |  | 2796 |
|  | 2734 |  | 2745 |  | 2755 |  | 2765 |  | 2775 |  | 2786 |  | 2796 |
|  | 2735 |  | 2745 |  | 2755 |  | 2765 |  | 2776 |  | 2786 |  | 2796 |
|  | 2735 |  | 2745 |  | 2755 |  | 2766 |  | 2776 |  | 2786 |  | 2796 |
|  | 2735 |  | 2745 |  | 2756 |  | 2766 |  | 2776 |  | 2786 |  | 2797 |
|  | 2735 |  | 2746 |  | 2756 |  | 2766 |  | 2776 |  | 2787 |  | 2797 |
|  | 2736 |  | 2746 |  | 2756 |  | 2766 |  | 2777 |  | 2787 |  | 2797 |
|  | 2736 |  | 2746 |  | 2756 |  | 2767 |  | 2777 |  | 2787 |  | 2797 |
|  | 2736 |  | 2746 |  | 2757 |  | 2767 |  | 2777 |  | 2787 |  | 2798 |
|  | 2736 |  | 2747 |  | 2757 |  | 2767 |  | 2777 |  | 2788 |  | 2798 |
|  | 2737 |  | 2747 |  | 2757 |  | 2767 |  | 2778 |  | 2788 |  | 2798 |
|  | 2737 |  | 2747 |  | 2757 |  | 2768 |  | 2778 |  | 2788 |  | 2798 |
|  | 2737 |  | 2747 |  | 2758 |  | 2768 |  | 2778 |  | 2788 |  | 2799 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2799 | PPD | 2809 | PPD | 2819 | PPD | 2830 | PPD | 2840 | PPD | 2850 | PPD | 2860 |
|  | 2799 |  | 2809 |  | 2820 |  | 2830 |  | 2840 |  | 2850 |  | 2861 |
|  | 2799 |  | 2810 |  | 2820 |  | 2830 |  | 2840 |  | 2851 |  | 2861 |
|  | 2800 |  | 2810 |  | 2820 |  | 2830 |  | 2841 |  | 2851 |  | 2861 |
|  | 2800 |  | 2810 |  | 2820 |  | 2831 |  | 2841 |  | 2851 |  | 2861 |
|  | 2800 |  | 2810 |  | 2821 |  | 2831 |  | 2841 |  | 2851 |  | 2862 |
|  | 2800 |  | 2811 |  | 2821 |  | 2831 |  | 2841 |  | 2852 |  | 2862 |
|  | 2801 |  | 2811 |  | 2821 |  | 2831 |  | 2842 |  | 2852 |  | 2862 |
|  | 2801 |  | 2811 |  | 2821 |  | 2832 |  | 2842 |  | 2852 |  | 2862 |
|  | 2801 |  | 2811 |  | 2822 |  | 2832 |  | 2842 |  | 2852 |  | 2863 |
|  | 2801 |  | 2812 |  | 2822 |  | 2832 |  | 2842 |  | 2853 |  | 2863 |
|  | 2802 |  | 2812 |  | 2822 |  | 2832 |  | 2843 |  | 2853 |  | 2863 |
|  | 2802 |  | 2812 |  | 2822 |  | 2833 |  | 2843 |  | 2853 |  | 2863 |
|  | 2802 |  | 2812 |  | 2823 |  | 2833 |  | 2843 |  | 2853 |  | 2864 |
|  | 2802 |  | 2813 |  | 2823 |  | 2833 |  | 2843 |  | 2854 |  | 2864 |
|  | 2803 |  | 2813 |  | 2823 |  | 2833 |  | 2844 |  | 2854 |  | 2864 |
|  | 2803 |  | 2813 |  | 2823 |  | 2834 |  | 2844 |  | 2854 |  | 2864 |
|  | 2803 |  | 2813 |  | 2824 |  | 2834 |  | 2844 |  | 2854 |  | 2865 |
|  | 2803 |  | 2814 |  | 2824 |  | 2834 |  | 2844 |  | 2855 |  | 2865 |
|  | 2804 |  | 2814 |  | 2824 |  | 2834 |  | 2845 |  | 2855 |  | 2865 |
|  | 2804 |  | 2814 |  | 2824 |  | 2835 |  | 2845 |  | 2855 |  | 2865 |
|  | 2804 |  | 2814 |  | 2825 |  | 2835 |  | 2845 |  | 2855 |  | 2866 |
|  | 2804 |  | 2815 |  | 2825 |  | 2835 |  | 2845 |  | 2856 |  | 2866 |
|  | 2805 |  | 2815 |  | 2825 |  | 2835 |  | 2846 |  | 2856 |  | 2866 |
|  | 2805 |  | 2815 |  | 2825 |  | 2836 |  | 2846 |  | 2856 |  | 2866 |
|  | 2805 |  | 2815 |  | 2826 |  | 2836 |  | 2846 |  | 2856 |  | 2867 |
|  | 2805 |  | 2816 |  | 2826 |  | 2836 |  | 2846 |  | 2857 |  | 2867 |
|  | 2806 |  | 2816 |  | 2826 |  | 2836 |  | 2847 |  | 2857 |  | 2867 |
|  | 2806 |  | 2816 |  | 2826 |  | 2837 |  | 2847 |  | 2857 |  | 2867 |
|  | 2806 |  | 2816 |  | 2827 |  | 2837 |  | 2847 |  | 2857 |  | 2868 |
|  | 2806 |  | 2817 |  | 2827 |  | 2837 |  | 2847 |  | 2858 |  | 2868 |
|  | 2807 |  | 2817 |  | 2827 |  | 2837 |  | 2848 |  | 2858 |  | 2868 |
|  | 2807 |  | 2817 |  | 2827 |  | 2838 |  | 2848 |  | 2858 |  | 2868 |
|  | 2807 |  | 2817 |  | 2828 |  | 2838 |  | 2848 |  | 2858 |  | 2869 |
|  | 2807 |  | 2818 |  | 2828 |  | 2838 |  | 2848 |  | 2859 |  | 2869 |
|  | 2808 |  | 2818 |  | 2828 |  | 2838 |  | 2849 |  | 2859 |  | 2869 |
|  | 2808 |  | 2818 |  | 2828 |  | 2839 |  | 2849 |  | 2859 |  | 2869 |
|  | 2808 |  | 2818 |  | 2829 |  | 2839 |  | 2849 |  | 2859 |  | 2870 |
|  | 2808 |  | 2819 |  | 2829 |  | 2839 |  | 2849 |  | 2860 |  | 2870 |
|  | 2809 |  | 2819 |  | 2829 |  | 2839 |  | 2850 |  | 2860 |  | 2870 |
|  | 2809 |  | 2819 |  | 2829 |  | 2840 |  | 2850 |  | 2860 |  | 2870 |

SD4 4 RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | Trt | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. } . \text { Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2871 | PPD | 2881 | PPD | 2891 | PPD | 2901 | PPD | 2912 | PPD | 2922 | PPD | 2932 |
|  | 2871 |  | 2881 |  | 2891 |  | 2902 |  | 2912 |  | 2922 |  | 2932 |
|  | 2871 |  | 2881 |  | 2892 |  | 2902 |  | 2912 |  | 2922 |  | 2933 |
|  | 2871 |  | 2882 |  | 2892 |  | 2902 |  | 2912 |  | 2923 |  | 2933 |
|  | 2872 |  | 2882 |  | 2892 |  | 2902 |  | 2913 |  | 2923 |  | 2933 |
|  | 2872 |  | 2882 |  | 2892 |  | 2903 |  | 2913 |  | 2923 |  | 2933 |
|  | 2872 |  | 2882 |  | 2893 |  | 2903 |  | 2913 |  | 2923 |  | 2934 |
|  | 2872 |  | 2883 |  | 2893 |  | 2903 |  | 2913 |  | 2924 |  | 2934 |
|  | 2873 |  | 2883 |  | 2893 |  | 2903 |  | 2914 |  | 2924 |  | 2934 |
|  | 2873 |  | 2883 |  | 2893 |  | 2904 |  | 2914 |  | 2924 |  | 2934 |
|  | 2873 |  | 2883 |  | 2894 |  | 2904 |  | 2914 |  | 2924 |  | 2935 |
|  | 2873 |  | 2884 |  | 2894 |  | 2904 |  | 2914 |  | 2925 |  | 2935 |
|  | 2874 |  | 2884 |  | 2894 |  | 2904 |  | 2915 |  | 2925 |  | 2935 |
|  | 2874 |  | 2884 |  | 2894 |  | 2905 |  | 2915 |  | 2925 |  | 2935 |
|  | 2874 |  | 2884 |  | 2895 |  | 2905 |  | 2915 |  | 2925 |  | 2936 |
|  | 2874 |  | 2885 |  | 2895 |  | 2905 |  | 2915 |  | 2926 |  | 2936 |
|  | 2875 |  | 2885 |  | 2895 |  | 2905 |  | 2916 |  | 2926 |  | 2936 |
|  | 2875 |  | 2885 |  | 2895 |  | 2906 |  | 2916 |  | 2926 |  | 2936 |
|  | 2875 |  | 2885 |  | 2896 |  | 2906 |  | 2916 |  | 2926 |  | 2937 |
|  | 2875 |  | 2886 |  | 2896 |  | 2906 |  | 2916 |  | 2927 |  | 2937 |
|  | 2876 |  | 2886 |  | 2896 |  | 2906 |  | 2917 |  | 2927 |  | 2937 |
|  | 2876 |  | 2886 |  | 2896 |  | 2907 |  | 2917 |  | 2927 |  | 2937 |
|  | 2876 |  | 2886 |  | 2897 |  | 2907 |  | 2917 |  | 2927 |  | 2938 |
|  | 2876 |  | 2887 |  | 2897 |  | 2907 |  | 2917 |  | 2928 |  | 2938 |
|  | 2877 |  | 2887 |  | 2897 |  | 2907 |  | 2918 |  | 2928 |  | 2938 |
|  | 2877 |  | 2887 |  | 2897 |  | 2908 |  | 2918 |  | 2928 |  | 2938 |
|  | 2877 |  | 2887 |  | 2898 |  | 2908 |  | 2918 |  | 2928 |  | 2939 |
|  | 2877 |  | 2888 |  | 2898 |  | 2908 |  | 2918 |  | 2929 |  | 2939 |
|  | 2878 |  | 2888 |  | 2898 |  | 2908 |  | 2919 |  | 2929 |  | 2939 |
|  | 2878 |  | 2888 |  | 2898 |  | 2909 |  | 2919 |  | 2929 |  | 2939 |
|  | 2878 |  | 2888 |  | 2899 |  | 2909 |  | 2919 |  | 2929 |  | 2940 |
|  | 2878 |  | 2889 |  | 2899 |  | 2909 |  | 2919 |  | 2930 |  | 2940 |
|  | 2879 |  | 2889 |  | 2899 |  | 2909 |  | 2920 |  | 2930 |  | 2940 |
|  | 2879 |  | 2889 |  | 2899 |  | 2910 |  | 2920 |  | 2930 |  | 2940 |
|  | 2879 |  | 2889 |  | 2900 |  | 2910 |  | 2920 |  | 2930 |  | 2941 |
|  | 2879 |  | 2890 |  | 2900 |  | 2910 |  | 2920 |  | 2931 |  | 2941 |
|  | 2880 |  | 2890 |  | 2900 |  | 2910 |  | 2921 |  | 2931 |  | 2941 |
|  | 2880 |  | 2890 |  | 2900 |  | 2911 |  | 2921 |  | 2931 |  | 2941 |
|  | 2880 |  | 2890 |  | 2901 |  | 2911 |  | 2921 |  | 2931 |  | 2942 |
|  | 2880 |  | 2891 |  | 2901 |  | 2911 |  | 2921 |  | 2932 |  | 2942 |
|  | 2881 |  | 2891 |  | 2901 |  | 2911 |  | 2922 |  | 2932 |  | 2942 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2942 | PPD | 2953 | PPD | 2963 | PPD | 2973 | PPD | 2983 | PPD | 2994 | PPD | 3004 |
|  | 2943 |  | 2953 |  | 2963 |  | 2973 |  | 2984 |  | 2994 |  | 3004 |
|  | 2943 |  | 2953 |  | 2963 |  | 2974 |  | 2984 |  | 2994 |  | 3004 |
|  | 2943 |  | 2953 |  | 2964 |  | 2974 |  | 2984 |  | 2994 |  | 3005 |
|  | 2943 |  | 2954 |  | 2964 |  | 2974 |  | 2984 |  | 2995 |  | 3005 |
|  | 2944 |  | 2954 |  | 2964 |  | 2974 |  | 2985 |  | 2995 |  | 3005 |
|  | 2944 |  | 2954 |  | 2964 |  | 2975 |  | 2985 |  | 2995 |  | 3005 |
|  | 2944 |  | 2954 |  | 2965 |  | 2975 |  | 2985 |  | 2995 |  | 3006 |
|  | 2944 |  | 2955 |  | 2965 |  | 2975 |  | 2985 |  | 2996 |  | 3006 |
|  | 2945 |  | 2955 |  | 2965 |  | 2975 |  | 2986 |  | 2996 |  | 3006 |
|  | 2945 |  | 2955 |  | 2965 |  | 2976 |  | 2986 |  | 2996 |  | 3006 |
|  | 2945 |  | 2955 |  | 2966 |  | 2976 |  | 2986 |  | 2996 |  | 3007 |
|  | 2945 |  | 2956 |  | 2966 |  | 2976 |  | 2986 |  | 2997 |  | 3007 |
|  | 2946 |  | 2956 |  | 2966 |  | 2976 |  | 2987 |  | 2997 |  | 3007 |
|  | 2946 |  | 2956 |  | 2966 |  | 2977 |  | 2987 |  | 2997 |  | 3007 |
|  | 2946 |  | 2956 |  | 2967 |  | 2977 |  | 2987 |  | 2997 |  | 3008 |
|  | 2946 |  | 2957 |  | 2967 |  | 2977 |  | 2987 |  | 2998 |  | 3008 |
|  | 2947 |  | 2957 |  | 2967 |  | 2977 |  | 2988 |  | 2998 |  | 3008 |
|  | 2947 |  | 2957 |  | 2967 |  | 2978 |  | 2988 |  | 2998 |  | 3008 |
|  | 2947 |  | 2957 |  | 2968 |  | 2978 |  | 2988 |  | 2998 |  | 3009 |
|  | 2947 |  | 2958 |  | 2968 |  | 2978 |  | 2988 |  | 2999 |  | 3009 |
|  | 2948 |  | 2958 |  | 2968 |  | 2978 |  | 2989 |  | 2999 |  | 3009 |
|  | 2948 |  | 2958 |  | 2968 |  | 2979 |  | 2989 |  | 2999 |  | 3009 |
|  | 2948 |  | 2958 |  | 2969 |  | 2979 |  | 2989 |  | 2999 |  | 3010 |
|  | 2948 |  | 2959 |  | 2969 |  | 2979 |  | 2989 |  | 3000 |  | 3010 |
|  | 2949 |  | 2959 |  | 2969 |  | 2979 |  | 2990 |  | 3000 |  | 3010 |
|  | 2949 |  | 2959 |  | 2969 |  | 2980 |  | 2990 |  | 3000 |  | 3010 |
|  | 2949 |  | 2959 |  | 2970 |  | 2980 |  | 2990 |  | 3000 |  | 3011 |
|  | 2949 |  | 2960 |  | 2970 |  | 2980 |  | 2990 |  | 3001 |  | 3011 |
|  | 2950 |  | 2960 |  | 2970 |  | 2980 |  | 2991 |  | 3001 |  | 3011 |
|  | 2950 |  | 2960 |  | 2970 |  | 2981 |  | 2991 |  | 3001 |  | 3011 |
|  | 2950 |  | 2960 |  | 2971 |  | 2981 |  | 2991 |  | 3001 |  | 3012 |
|  | 2950 |  | 2961 |  | 2971 |  | 2981 |  | 2991 |  | 3002 |  | 3012 |
|  | 2951 |  | 2961 |  | 2971 |  | 2981 |  | 2992 |  | 3002 |  | 3012 |
|  | 2951 |  | 2961 |  | 2971 |  | 2982 |  | 2992 |  | 3002 |  | 3012 |
|  | 2951 |  | 2961 |  | 2972 |  | 2982 |  | 2992 |  | 3002 |  | 3013 |
|  | 2951 |  | 2962 |  | 2972 |  | 2982 |  | 2992 |  | 3003 |  | 3013 |
|  | 2952 |  | 2962 |  | 2972 |  | 2982 |  | 2993 |  | 3003 |  | 3013 |
|  | 2952 |  | 2962 |  | 2972 |  | 2983 |  | 2993 |  | 3003 |  | 3013 |
|  | 2952 |  | 2962 |  | 2973 |  | 2983 |  | 2993 |  | 3003 |  | 3014 |
|  | 2952 |  | 2963 |  | 2973 |  | 2983 |  | 2993 |  | 3004 |  | 3014 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| Trt. |  |  | Bl. |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3014 | PPD | 3024 | PPD | 3035 | PPD | 3045 | PPD | 3055 | PPD | 3065 | PPD | 3076 |
|  | 3014 |  | 3025 |  | 3035 |  | 3045 |  | 3055 |  | 3066 |  | 3076 |
|  | 3015 |  | 3025 |  | 3035 |  | 3045 |  | 3056 |  | 3066 |  | 3076 |
|  | 3015 |  | 3025 |  | 3035 |  | 3046 |  | 3056 |  | 3066 |  | 3076 |
|  | 3015 |  | 3025 |  | 3036 |  | 3046 |  | 3056 |  | 3066 |  | 3077 |
|  | 3015 |  | 3026 |  | 3036 |  | 3046 |  | 3056 |  | 3067 |  | 3077 |
|  | 3016 |  | 3026 |  | 3036 |  | 3046 |  | 3057 |  | 3067 |  | 3077 |
|  | 3016 |  | 3026 |  | 3036 |  | 3047 |  | 3057 |  | 3067 |  | 3077 |
|  | 3016 |  | 3026 |  | 3037 |  | 3047 |  | 3057 |  | 3067 |  | 3078 |
|  | 3016 |  | 3027 |  | 3037 |  | 3047 |  | 3057 |  | 3068 |  | 3078 |
|  | 3017 |  | 3027 |  | 3037 |  | 3047 |  | 3058 |  | 3068 |  | 3078 |
|  | 3017 |  | 3027 |  | 3037 |  | 3048 |  | 3058 |  | 3068 |  | 3078 |
|  | 3017 |  | 3027 |  | 3038 |  | 3048 |  | 3058 |  | 3068 |  | 3079 |
|  | 3017 |  | 3028 |  | 3038 |  | 3048 |  | 3058 |  | 3069 |  | 3079 |
|  | 3018 |  | 3028 |  | 3038 |  | 3048 |  | 3059 |  | 3069 |  | 3079 |
|  | 3018 |  | 3028 |  | 3038 |  | 3049 |  | 3059 |  | 3069 |  | 3079 |
|  | 3018 |  | 3028 |  | 3039 |  | 3049 |  | 3059 |  | 3069 |  | 3080 |
|  | 3018 |  | 3029 |  | 3039 |  | 3049 |  | 3059 |  | 3070 |  | 3080 |
|  | 3019 |  | 3029 |  | 3039 |  | 3049 |  | 3060 |  | 3070 |  | 3080 |
|  | 3019 |  | 3029 |  | 3039 |  | 3050 |  | 3060 |  | 3070 |  | 3080 |
|  | 3019 |  | 3029 |  | 3040 |  | 3050 |  | 3060 |  | 3070 |  | 3081 |
|  | 3019 |  | 3030 |  | 3040 |  | 3050 |  | 3060 |  | 3071 |  | 3081 |
|  | 3020 |  | 3030 |  | 3040 |  | 3050 |  | 3061 |  | 3071 |  | 3081 |
|  | 3020 |  | 3030 |  | 3040 |  | 3051 |  | 3061 |  | 3071 |  | 3081 |
|  | 3020 |  | 3030 |  | 3041 |  | 3051 |  | 3061 |  | 3071 |  | 3082 |
|  | 3020 |  | 3031 |  | 3041 |  | 3051 |  | 3061 |  | 3072 |  | 3082 |
|  | 3021 |  | 3031 |  | 3041 |  | 3051 |  | 3062 |  | 3072 |  | 3082 |
|  | 3021 |  | 3031 |  | 3041 |  | 3052 |  | 3062 |  | 3072 |  | 3082 |
|  | 3021 |  | 3031 |  | 3042 |  | 3052 |  | 3062 |  | 3072 |  | 3083 |
|  | 3021 |  | 3032 |  | 3042 |  | 3052 |  | 3062 |  | 3073 |  | 3083 |
|  | 3022 |  | 3032 |  | 3042 |  | 3052 |  | 3063 |  | 3073 |  | 3083 |
|  | 3022 |  | 3032 |  | 3042 |  | 3053 |  | 3063 |  | 3073 |  | 3083 |
|  | 3022 |  | 3032 |  | 3043 |  | 3053 |  | 3063 |  | 3073 |  | 3084 |
|  | 3022 |  | 3033 |  | 3043 |  | 3053 |  | 3063 |  | 3074 |  | 3084 |
|  | 3023 |  | 3033 |  | 3043 |  | 3053 |  | 3064 |  | 3074 |  | 3084 |
|  | 3023 |  | 3033 |  | 3043 |  | 3054 |  | 3064 |  | 3074 |  | 3084 |
|  | 3023 |  | 3033 |  | 3044 |  | 3054 |  | 3064 |  | 3074 |  | 3085 |
|  | 3023 |  | 3034 |  | 3044 |  | 3054 |  | 3064 |  | 3075 |  | 3085 |
|  | 3024 |  | 3034 |  | 3044 |  | 3054 |  | 3065 |  | 3075 |  | 3085 |
|  | 3024 |  | 3034 |  | 3044 |  | 3055 |  | 3065 |  | 3075 |  | 3085 |
|  | 3024 |  | 3034 |  | 3045 |  | 3055 |  | 3065 |  | 3075 |  | 3086 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. | Trt | Bl nb | Trt | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{n} . \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3086 | PPD | 3096 | PPD | 3106 | PPD | 3117 | PPD | 3127 | PPD | 3137 | PPD | 3147 |
|  | 3086 |  | 3096 |  | 3107 |  | 3117 |  | 3127 |  | 3137 |  | 3148 |
|  | 3086 |  | 3097 |  | 3107 |  | 3117 |  | 3127 |  | 3138 |  | 3148 |
|  | 3087 |  | 3097 |  | 3107 |  | 3117 |  | 3128 |  | 3138 |  | 3148 |
|  | 3087 |  | 3097 |  | 3107 |  | 3118 |  | 3128 |  | 3138 |  | 3148 |
|  | 3087 |  | 3097 |  | 3108 |  | 3118 |  | 3128 |  | 3138 |  | 3149 |
|  | 3087 |  | 3098 |  | 3108 |  | 3118 |  | 3128 |  | 3139 |  | 3149 |
|  | 3088 |  | 3098 |  | 3108 |  | 3118 |  | 3129 |  | 3139 |  | 3149 |
|  | 3088 |  | 3098 |  | 3108 |  | 3119 |  | 3129 |  | 3139 |  | 3149 |
|  | 3088 |  | 3098 |  | 3109 |  | 3119 |  | 3129 |  | 3139 |  | 3150 |
|  | 3088 |  | 3099 |  | 3109 |  | 3119 |  | 3129 |  | 3140 |  | 3150 |
|  | 3089 |  | 3099 |  | 3109 |  | 3119 |  | 3130 |  | 3140 |  | 3150 |
|  | 3089 |  | 3099 |  | 3109 |  | 3120 |  | 3130 |  | 3140 |  | 3150 |
|  | 3089 |  | 3099 |  | 3110 |  | 3120 |  | 3130 |  | 3140 |  | 3151 |
|  | 3089 |  | 3100 |  | 3110 |  | 3120 |  | 3130 |  | 3141 |  | 3151 |
|  | 3090 |  | 3100 |  | 3110 |  | 3120 |  | 3131 |  | 3141 |  | 3151 |
|  | 3090 |  | 3100 |  | 3110 |  | 3121 |  | 3131 |  | 3141 |  | 3151 |
|  | 3090 |  | 3100 |  | 3111 |  | 3121 |  | 3131 |  | 3141 |  | 3152 |
|  | 3090 |  | 3101 |  | 3111 |  | 3121 |  | 3131 |  | 3142 |  | 3152 |
|  | 3091 |  | 3101 |  | 3111 |  | 3121 |  | 3132 |  | 3142 |  | 3152 |
|  | 3091 |  | 3101 |  | 3111 |  | 3122 |  | 3132 |  | 3142 |  | 3152 |
|  | 3091 |  | 3101 |  | 3112 |  | 3122 |  | 3132 |  | 3142 |  | 3153 |
|  | 3091 |  | 3102 |  | 3112 |  | 3122 |  | 3132 |  | 3143 |  | 3153 |
|  | 3092 |  | 3102 |  | 3112 |  | 3122 |  | 3133 |  | 3143 |  | 3153 |
|  | 3092 |  | 3102 |  | 3112 |  | 3123 |  | 3133 |  | 3143 |  | 3153 |
|  | 3092 |  | 3102 |  | 3113 |  | 3123 |  | 3133 |  | 3143 |  | 3154 |
|  | 3092 |  | 3103 |  | 3113 |  | 3123 |  | 3133 |  | 3144 |  | 3154 |
|  | 3093 |  | 3103 |  | 3113 |  | 3123 |  | 3134 |  | 3144 |  | 3154 |
|  | 3093 |  | 3103 |  | 3113 |  | 3124 |  | 3134 |  | 3144 |  | 3154 |
|  | 3093 |  | 3103 |  | 3114 |  | 3124 |  | 3134 |  | 3144 |  | 3155 |
|  | 3093 |  | 3104 |  | 3114 |  | 3124 |  | 3134 |  | 3145 |  | 3155 |
|  | 3094 |  | 3104 |  | 3114 |  | 3124 |  | 3135 |  | 3145 |  | 3155 |
|  | 3094 |  | 3104 |  | 3114 |  | 3125 |  | 3135 |  | 3145 |  | 3155 |
|  | 3094 |  | 3104 |  | 3115 |  | 3125 |  | 3135 |  | 3145 |  | 3156 |
|  | 3094 |  | 3105 |  | 3115 |  | 3125 |  | 3135 |  | 3146 |  | 3156 |
|  | 3095 |  | 3105 |  | 3115 |  | 3125 |  | 3136 |  | 3146 |  | 3156 |
|  | 3095 |  | 3105 |  | 3115 |  | 3126 |  | 3136 |  | 3146 |  | 3156 |
|  | 3095 |  | 3105 |  | 3116 |  | 3126 |  | 3136 |  | 3146 |  | 3157 |
|  | 3095 |  | 3106 |  | 3116 |  | 3126 |  | 3136 |  | 3147 |  | 3157 |
|  | 3096 |  | 3106 |  | 3116 |  | 3126 |  | 3137 |  | 3147 |  | 3157 |
|  | 3096 |  | 3106 |  | 3116 |  | 3127 |  | 3137 |  | 3147 |  | 3157 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3158 | PPD | 3168 | PPD | 3178 | PPD | 3188 | PPD | 3199 | PPD | 3209 | PPD | 3219 |
|  | 3158 |  | 3168 |  | 3178 |  | 3189 |  | 3199 |  | 3209 |  | 3219 |
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SD4 4 RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
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Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3301 | PPD | 3311 | PPD | 3322 | PPD | 3332 | PPD | 3342 | PPD | 3352 | PPD | 3363 |
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Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl. |  | Bl. |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
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SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
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|  | 3451 |  | 3461 |  | 3471 |  | 3482 |  | 3492 |  | 3502 |  | 3512 |
|  | 3451 |  | 3461 |  | 3472 |  | 3482 |  | 3492 |  | 3502 |  | 3513 |
|  | 3451 |  | 3462 |  | 3472 |  | 3482 |  | 3492 |  | 3503 |  | 3513 |
|  | 3452 |  | 3462 |  | 3472 |  | 3482 |  | 3493 |  | 3503 |  | 3513 |
|  | 3452 |  | 3462 |  | 3472 |  | 3483 |  | 3493 |  | 3503 |  | 3513 |
|  | 3452 |  | 3462 |  | 3473 |  | 3483 |  | 3493 |  | 3503 |  | 3514 |
|  | 3452 |  | 3463 |  | 3473 |  | 3483 |  | 3493 |  | 3504 |  | 3514 |
|  | 3453 |  | 3463 |  | 3473 |  | 3483 |  | 3494 |  | 3504 |  | 3514 |
|  | 3453 |  | 3463 |  | 3473 |  | 3484 |  | 3494 |  | 3504 |  | 3514 |
|  | 3453 |  | 3463 |  | 3474 |  | 3484 |  | 3494 |  | 3504 |  | 3515 |
|  | 3453 |  | 3464 |  | 3474 |  | 3484 |  | 3494 |  | 3505 |  | 3515 |
|  | 3454 |  | 3464 |  | 3474 |  | 3484 |  | 3495 |  | 3505 |  | 3515 |
|  | 3454 |  | 3464 |  | 3474 |  | 3485 |  | 3495 |  | 3505 |  | 3515 |
|  | 3454 |  | 3464 |  | 3475 |  | 3485 |  | 3495 |  | 3505 |  | 3516 |
|  | 3454 |  | 3465 |  | 3475 |  | 3485 |  | 3495 |  | 3506 |  | 3516 |
|  | 3455 |  | 3465 |  | 3475 |  | 3485 |  | 3496 |  | 3506 |  | 3516 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{gathered} \text { Trt. Bl. } \\ \text { No nb } \end{gathered}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3516 | PPD | 3527 | PPD | 3537 | PPD | 3547 | PPD | 3557 | PPD | 3568 | PPD | 3578 |
|  | 3517 |  | 3527 |  | 3537 |  | 3547 |  | 3558 |  | 3568 |  | 3578 |
|  | 3517 |  | 3527 |  | 3537 |  | 3548 |  | 3558 |  | 3568 |  | 3578 |
|  | 3517 |  | 3527 |  | 3538 |  | 3548 |  | 3558 |  | 3568 |  | 3579 |
|  | 3517 |  | 3528 |  | 3538 |  | 3548 |  | 3558 |  | 3569 |  | 3579 |
|  | 3518 |  | 3528 |  | 3538 |  | 3548 |  | 3559 |  | 3569 |  | 3579 |
|  | 3518 |  | 3528 |  | 3538 |  | 3549 |  | 3559 |  | 3569 |  | 3579 |
|  | 3518 |  | 3528 |  | 3539 |  | 3549 |  | 3559 |  | 3569 |  | 3580 |
|  | 3518 |  | 3529 |  | 3539 |  | 3549 |  | 3559 |  | 3570 |  | 3580 |
|  | 3519 |  | 3529 |  | 3539 |  | 3549 |  | 3560 |  | 3570 |  | 3580 |
|  | 3519 |  | 3529 |  | 3539 |  | 3550 |  | 3560 |  | 3570 |  | 3580 |
|  | 3519 |  | 3529 |  | 3540 |  | 3550 |  | 3560 |  | 3570 |  | 3581 |
|  | 3519 |  | 3530 |  | 3540 |  | 3550 |  | 3560 |  | 3571 |  | 3581 |
|  | 3520 |  | 3530 |  | 3540 |  | 3550 |  | 3561 |  | 3571 |  | 3581 |
|  | 3520 |  | 3530 |  | 3540 |  | 3551 |  | 3561 |  | 3571 |  | 3581 |
|  | 3520 |  | 3530 |  | 3541 |  | 3551 |  | 3561 |  | 3571 |  | 3582 |
|  | 3520 |  | 3531 |  | 3541 |  | 3551 |  | 3561 |  | 3572 |  | 3582 |
|  | 3521 |  | 3531 |  | 3541 |  | 3551 |  | 3562 |  | 3572 |  | 3582 |
|  | 3521 |  | 3531 |  | 3541 |  | 3552 |  | 3562 |  | 3572 |  | 3582 |
|  | 3521 |  | 3531 |  | 3542 |  | 3552 |  | 3562 |  | 3572 |  | 3583 |
|  | 3521 |  | 3532 |  | 3542 |  | 3552 |  | 3562 |  | 3573 |  | 3583 |
|  | 3522 |  | 3532 |  | 3542 |  | 3552 |  | 3563 |  | 3573 |  | 3583 |
|  | 3522 |  | 3532 |  | 3542 |  | 3553 |  | 3563 |  | 3573 |  | 3583 |
|  | 3522 |  | 3532 |  | 3543 |  | 3553 |  | 3563 |  | 3573 |  | 3584 |
|  | 3522 |  | 3533 |  | 3543 |  | 3553 |  | 3563 |  | 3574 |  | 3584 |
|  | 3523 |  | 3533 |  | 3543 |  | 3553 |  | 3564 |  | 3574 |  | 3584 |
|  | 3523 |  | 3533 |  | 3543 |  | 3554 |  | 3564 |  | 3574 |  | 3584 |
|  | 3523 |  | 3533 |  | 3544 |  | 3554 |  | 3564 |  | 3574 |  | 3585 |
|  | 3523 |  | 3534 |  | 3544 |  | 3554 |  | 3564 |  | 3575 |  | 3585 |
|  | 3524 |  | 3534 |  | 3544 |  | 3554 |  | 3565 |  | 3575 |  | 3585 |
|  | 3524 |  | 3534 |  | 3544 |  | 3555 |  | 3565 |  | 3575 |  | 3585 |
|  | 3524 |  | 3534 |  | 3545 |  | 3555 |  | 3565 |  | 3575 |  | 3586 |
|  | 3524 |  | 3535 |  | 3545 |  | 3555 |  | 3565 |  | 3576 |  | 3586 |
|  | 3525 |  | 3535 |  | 3545 |  | 3555 |  | 3566 |  | 3576 |  | 3586 |
|  | 3525 |  | 3535 |  | 3545 |  | 3556 |  | 3566 |  | 3576 |  | 3586 |
|  | 3525 |  | 3535 |  | 3546 |  | 3556 |  | 3566 |  | 3576 |  | 3587 |
|  | 3525 |  | 3536 |  | 3546 |  | 3556 |  | 3566 |  | 3577 |  | 3587 |
|  | 3526 |  | 3536 |  | 3546 |  | 3556 |  | 3567 |  | 3577 |  | 3587 |
|  | 3526 |  | 3536 |  | 3546 |  | 3557 |  | 3567 |  | 3577 |  | 3587 |
|  | 3526 |  | 3536 |  | 3547 |  | 3557 |  | 3567 |  | 3577 |  | 3588 |
|  | 3526 |  | 3537 |  | 3547 |  | 3557 |  | 3567 |  | 3578 |  | 3588 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl nb |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3588 | PPD | 3598 | PPD | 3609 | PPD | 3619 | PPD | 3629 | PPD | 3639 | PPD | 3650 |
|  | 3588 |  | 3599 |  | 3609 |  | 3619 |  | 3629 |  | 3640 |  | 3650 |
|  | 3589 |  | 3599 |  | 3609 |  | 3619 |  | 3630 |  | 3640 |  | 3650 |
|  | 3589 |  | 3599 |  | 3609 |  | 3620 |  | 3630 |  | 3640 |  | 3650 |
|  | 3589 |  | 3599 |  | 3610 |  | 3620 |  | 3630 |  | 3640 |  | 3651 |
|  | 3589 |  | 3600 |  | 3610 |  | 3620 |  | 3630 |  | 3641 |  | 3651 |
|  | 3590 |  | 3600 |  | 3610 |  | 3620 |  | 3631 |  | 3641 |  | 3651 |
|  | 3590 |  | 3600 |  | 3610 |  | 3621 |  | 3631 |  | 3641 |  | 3651 |
|  | 3590 |  | 3600 |  | 3611 |  | 3621 |  | 3631 |  | 3641 |  | 3652 |
|  | 3590 |  | 3601 |  | 3611 |  | 3621 |  | 3631 |  | 3642 |  | 3652 |
|  | 3591 |  | 3601 |  | 3611 |  | 3621 |  | 3632 |  | 3642 |  | 3652 |
|  | 3591 |  | 3601 |  | 3611 |  | 3622 |  | 3632 |  | 3642 |  | 3652 |
|  | 3591 |  | 3601 |  | 3612 |  | 3622 |  | 3632 |  | 3642 |  | 3653 |
|  | 3591 |  | 3602 |  | 3612 |  | 3622 |  | 3632 |  | 3643 |  | 3653 |
|  | 3592 |  | 3602 |  | 3612 |  | 3622 |  | 3633 |  | 3643 |  | 3653 |
|  | 3592 |  | 3602 |  | 3612 |  | 3623 |  | 3633 |  | 3643 |  | 3653 |
|  | 3592 |  | 3602 |  | 3613 |  | 3623 |  | 3633 |  | 3643 |  | 3654 |
|  | 3592 |  | 3603 |  | 3613 |  | 3623 |  | 3633 |  | 3644 |  | 3654 |
|  | 3593 |  | 3603 |  | 3613 |  | 3623 |  | 3634 |  | 3644 |  | 3654 |
|  | 3593 |  | 3603 |  | 3613 |  | 3624 |  | 3634 |  | 3644 |  | 3654 |
|  | 3593 |  | 3603 |  | 3614 |  | 3624 |  | 3634 |  | 3644 |  | 3655 |
|  | 3593 |  | 3604 |  | 3614 |  | 3624 |  | 3634 |  | 3645 |  | 3655 |
|  | 3594 |  | 3604 |  | 3614 |  | 3624 |  | 3635 |  | 3645 |  | 3655 |
|  | 3594 |  | 3604 |  | 3614 |  | 3625 |  | 3635 |  | 3645 |  | 3655 |
|  | 3594 |  | 3604 |  | 3615 |  | 3625 |  | 3635 |  | 3645 |  | 3656 |
|  | 3594 |  | 3605 |  | 3615 |  | 3625 |  | 3635 |  | 3646 |  | 3656 |
|  | 3595 |  | 3605 |  | 3615 |  | 3625 |  | 3636 |  | 3646 |  | 3656 |
|  | 3595 |  | 3605 |  | 3615 |  | 3626 |  | 3636 |  | 3646 |  | 3656 |
|  | 3595 |  | 3605 |  | 3616 |  | 3626 |  | 3636 |  | 3646 |  | 3657 |
|  | 3595 |  | 3606 |  | 3616 |  | 3626 |  | 3636 |  | 3647 |  | 3657 |
|  | 3596 |  | 3606 |  | 3616 |  | 3626 |  | 3637 |  | 3647 |  | 3657 |
|  | 3596 |  | 3606 |  | 3616 |  | 3627 |  | 3637 |  | 3647 |  | 3657 |
|  | 3596 |  | 3606 |  | 3617 |  | 3627 |  | 3637 |  | 3647 |  | 3658 |
|  | 3596 |  | 3607 |  | 3617 |  | 3627 |  | 3637 |  | 3648 |  | 3658 |
|  | 3597 |  | 3607 |  | 3617 |  | 3627 |  | 3638 |  | 3648 |  | 3658 |
|  | 3597 |  | 3607 |  | 3617 |  | 3628 |  | 3638 |  | 3648 |  | 3658 |
|  | 3597 |  | 3607 |  | 3618 |  | 3628 |  | 3638 |  | 3648 |  | 3659 |
|  | 3597 |  | 3608 |  | 3618 |  | 3628 |  | 3638 |  | 3649 |  | 3659 |
|  | 3598 |  | 3608 |  | 3618 |  | 3628 |  | 3639 |  | 3649 |  | 3659 |
|  | 3598 |  | 3608 |  | 3618 |  | 3629 |  | 3639 |  | 3649 |  | 3659 |
|  | 3598 |  | 3608 |  | 3619 |  | 3629 |  | 3639 |  | 3649 |  | 3660 |

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3660 | PPD | 3670 | PPD | 3680 | PPD | 3691 | PPD | 3701 | PPD | 3711 | PPD | 3721 |
|  | 3660 |  | 3670 |  | 3681 |  | 3691 |  | 3701 |  | 3711 |  | 3722 |
|  | 3660 |  | 3671 |  | 3681 |  | 3691 |  | 3701 |  | 3712 |  | 3722 |
|  | 3661 |  | 3671 |  | 3681 |  | 3691 |  | 3702 |  | 3712 |  | 3722 |
|  | 3661 |  | 3671 |  | 3681 |  | 3692 |  | 3702 |  | 3712 |  | 3722 |
|  | 3661 |  | 3671 |  | 3682 |  | 3692 |  | 3702 |  | 3712 |  | 3723 |
|  | 3661 |  | 3672 |  | 3682 |  | 3692 |  | 3702 |  | 3713 |  | 3723 |
|  | 3662 |  | 3672 |  | 3682 |  | 3692 |  | 3703 |  | 3713 |  | 3723 |
|  | 3662 |  | 3672 |  | 3682 |  | 3693 |  | 3703 |  | 3713 |  | 3723 |
|  | 3662 |  | 3672 |  | 3683 |  | 3693 |  | 3703 |  | 3713 |  | 3724 |
|  | 3662 |  | 3673 |  | 3683 |  | 3693 |  | 3703 |  | 3714 |  | 3724 |
|  | 3663 |  | 3673 |  | 3683 |  | 3693 |  | 3704 |  | 3714 |  | 3724 |
|  | 3663 |  | 3673 |  | 3683 |  | 3694 |  | 3704 |  | 3714 |  | 3724 |
|  | 3663 |  | 3673 |  | 3684 |  | 3694 |  | 3704 |  | 3714 |  | 3725 |
|  | 3663 |  | 3674 |  | 3684 |  | 3694 |  | 3704 |  | 3715 |  | 3725 |
|  | 3664 |  | 3674 |  | 3684 |  | 3694 |  | 3705 |  | 3715 |  | 3725 |
|  | 3664 |  | 3674 |  | 3684 |  | 3695 |  | 3705 |  | 3715 |  | 3725 |
|  | 3664 |  | 3674 |  | 3685 |  | 3695 |  | 3705 |  | 3715 |  | 3726 |
|  | 3664 |  | 3675 |  | 3685 |  | 3695 |  | 3705 |  | 3716 |  | 3726 |
|  | 3665 |  | 3675 |  | 3685 |  | 3695 |  | 3706 |  | 3716 |  | 3726 |
|  | 3665 |  | 3675 |  | 3685 |  | 3696 |  | 3706 |  | 3716 |  | 3726 |
|  | 3665 |  | 3675 |  | 3686 |  | 3696 |  | 3706 |  | 3716 |  | 3727 |
|  | 3665 |  | 3676 |  | 3686 |  | 3696 |  | 3706 |  | 3717 |  | 3727 |
|  | 3666 |  | 3676 |  | 3686 |  | 3696 |  | 3707 |  | 3717 |  | 3727 |
|  | 3666 |  | 3676 |  | 3686 |  | 3697 |  | 3707 |  | 3717 |  | 3727 |
|  | 3666 |  | 3676 |  | 3687 |  | 3697 |  | 3707 |  | 3717 |  | 3728 |
|  | 3666 |  | 3677 |  | 3687 |  | 3697 |  | 3707 |  | 3718 |  | 3728 |
|  | 3667 |  | 3677 |  | 3687 |  | 3697 |  | 3708 |  | 3718 |  | 3728 |
|  | 3667 |  | 3677 |  | 3687 |  | 3698 |  | 3708 |  | 3718 |  | 3728 |
|  | 3667 |  | 3677 |  | 3688 |  | 3698 |  | 3708 |  | 3718 |  | 3729 |
|  | 3667 |  | 3678 |  | 3688 |  | 3698 |  | 3708 |  | 3719 |  | 3729 |
|  | 3668 |  | 3678 |  | 3688 |  | 3698 |  | 3709 |  | 3719 |  | 3729 |
|  | 3668 |  | 3678 |  | 3688 |  | 3699 |  | 3709 |  | 3719 |  | 3729 |
|  | 3668 |  | 3678 |  | 3689 |  | 3699 |  | 3709 |  | 3719 |  | 3730 |
|  | 3668 |  | 3679 |  | 3689 |  | 3699 |  | 3709 |  | 3720 |  | 3730 |
|  | 3669 |  | 3679 |  | 3689 |  | 3699 |  | 3710 |  | 3720 |  | 3730 |
|  | 3669 |  | 3679 |  | 3689 |  | 3700 |  | 3710 |  | 3720 |  | 3730 |
|  | 3669 |  | 3679 |  | 3690 |  | 3700 |  | 3710 |  | 3720 |  | 3731 |
|  | 3669 |  | 3680 |  | 3690 |  | 3700 |  | 3710 |  | 3721 |  | 3731 |
|  | 3670 |  | 3680 |  | 3690 |  | 3700 |  | 3711 |  | 3721 |  | 3731 |
|  | 3670 |  | 3680 |  | 3690 |  | 3701 |  | 3711 |  | 3721 |  | 3731 |

SD4 4 RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| Trt. | Bl nb |  | Bl. | Trt |  |  | Bl nb |  | $\frac{\mathrm{Bl} .}{\mathrm{nb}} .$ | Trt | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3732 | PPD | 3742 | PPD | 3752 | PPD | 3762 | PPD | 3773 | PPD | 3783 | PPD | 3793 |
|  | 3732 |  | 3742 |  | 3752 |  | 3763 |  | 3773 |  | 3783 |  | 3793 |
|  | 3732 |  | 3742 |  | 3753 |  | 3763 |  | 3773 |  | 3783 |  | 3794 |
|  | 3732 |  | 3743 |  | 3753 |  | 3763 |  | 3773 |  | 3784 |  | 3794 |
|  | 3733 |  | 3743 |  | 3753 |  | 3763 |  | 3774 |  | 3784 |  | 3794 |
|  | 3733 |  | 3743 |  | 3753 |  | 3764 |  | 3774 |  | 3784 |  | 3794 |
|  | 3733 |  | 3743 |  | 3754 |  | 3764 |  | 3774 |  | 3784 |  | 3795 |
|  | 3733 |  | 3744 |  | 3754 |  | 3764 |  | 3774 |  | 3785 |  | 3795 |
|  | 3734 |  | 3744 |  | 3754 |  | 3764 |  | 3775 |  | 3785 |  | 3795 |
|  | 3734 |  | 3744 |  | 3754 |  | 3765 |  | 3775 |  | 3785 |  | 3795 |
|  | 3734 |  | 3744 |  | 3755 |  | 3765 |  | 3775 |  | 3785 |  | 3796 |
|  | 3734 |  | 3745 |  | 3755 |  | 3765 |  | 3775 |  | 3786 |  | 3796 |
|  | 3735 |  | 3745 |  | 3755 |  | 3765 |  | 3776 |  | 3786 |  | 3796 |
|  | 3735 |  | 3745 |  | 3755 |  | 3766 |  | 3776 |  | 3786 |  | 3796 |
|  | 3735 |  | 3745 |  | 3756 |  | 3766 |  | 3776 |  | 3786 |  | 3797 |
|  | 3735 |  | 3746 |  | 3756 |  | 3766 |  | 3776 |  | 3787 |  | 3797 |
|  | 3736 |  | 3746 |  | 3756 |  | 3766 |  | 3777 |  | 3787 |  | 3797 |
|  | 3736 |  | 3746 |  | 3756 |  | 3767 |  | 3777 |  | 3787 |  | 3797 |
|  | 3736 |  | 3746 |  | 3757 |  | 3767 |  | 3777 |  | 3787 |  | 3798 |
|  | 3736 |  | 3747 |  | 3757 |  | 3767 |  | 3777 |  | 3788 |  | 3798 |
|  | 3737 |  | 3747 |  | 3757 |  | 3767 |  | 3778 |  | 3788 |  | 3798 |
|  | 3737 |  | 3747 |  | 3757 |  | 3768 |  | 3778 |  | 3788 |  | 3798 |
|  | 3737 |  | 3747 |  | 3758 |  | 3768 |  | 3778 |  | 3788 |  | 3799 |
|  | 3737 |  | 3748 |  | 3758 |  | 3768 |  | 3778 |  | 3789 |  | 3799 |
|  | 3738 |  | 3748 |  | 3758 |  | 3768 |  | 3779 |  | 3789 |  | 3799 |
|  | 3738 |  | 3748 |  | 3758 |  | 3769 |  | 3779 |  | 3789 |  | 3799 |
|  | 3738 |  | 3748 |  | 3759 |  | 3769 |  | 3779 |  | 3789 |  | 3800 |
|  | 3738 |  | 3749 |  | 3759 |  | 3769 |  | 3779 |  | 3790 |  | 3800 |
|  | 3739 |  | 3749 |  | 3759 |  | 3769 |  | 3780 |  | 3790 |  | 3800 |
|  | 3739 |  | 3749 |  | 3759 |  | 3770 |  | 3780 |  | 3790 |  | 3800 |
|  | 3739 |  | 3749 |  | 3760 |  | 3770 |  | 3780 |  | 3790 |  | 3801 |
|  | 3739 |  | 3750 |  | 3760 |  | 3770 |  | 3780 |  | 3791 |  | 3801 |
|  | 3740 |  | 3750 |  | 3760 |  | 3770 |  | 3781 |  | 3791 |  | 3801 |
|  | 3740 |  | 3750 |  | 3760 |  | 3771 |  | 3781 |  | 3791 |  | 3801 |
|  | 3740 |  | 3750 |  | 3761 |  | 3771 |  | 3781 |  | 3791 |  | 3802 |
|  | 3740 |  | 3751 |  | 3761 |  | 3771 |  | 3781 |  | 3792 |  | 3802 |
|  | 3741 |  | 3751 |  | 3761 |  | 3771 |  | 3782 |  | 3792 |  | 3802 |
|  | 3741 |  | 3751 |  | 3761 |  | 3772 |  | 3782 |  | 3792 |  | 3802 |
|  | 3741 |  | 3751 |  | 3762 |  | 3772 |  | 3782 |  | 3792 |  | 3803 |
|  | 3741 |  | 3752 |  | 3762 |  | 3772 |  | 3782 |  | 3793 |  | 3803 |
|  | 3742 |  | 3752 |  | 3762 |  | 3772 |  | 3783 |  | 3793 |  | 3803 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3803 | PPD | 3814 | PPD | 3824 | PPD | 3834 | PPD | 3844 | PPD | 3855 | PPD | 3865 |
|  | 3804 |  | 3814 |  | 3824 |  | 3834 |  | 3845 |  | 3855 |  | 3865 |
|  | 3804 |  | 3814 |  | 3824 |  | 3835 |  | 3845 |  | 3855 |  | 3865 |
|  | 3804 |  | 3814 |  | 3825 |  | 3835 |  | 3845 |  | 3855 |  | 3866 |
|  | 3804 |  | 3815 |  | 3825 |  | 3835 |  | 3845 |  | 3856 |  | 3866 |
|  | 3805 |  | 3815 |  | 3825 |  | 3835 |  | 3846 |  | 3856 |  | 3866 |
|  | 3805 |  | 3815 |  | 3825 |  | 3836 |  | 3846 |  | 3856 |  | 3866 |
|  | 3805 |  | 3815 |  | 3826 |  | 3836 |  | 3846 |  | 3856 |  | 3867 |
|  | 3805 |  | 3816 |  | 3826 |  | 3836 |  | 3846 |  | 3857 |  | 3867 |
|  | 3806 |  | 3816 |  | 3826 |  | 3836 |  | 3847 |  | 3857 |  | 3867 |
|  | 3806 |  | 3816 |  | 3826 |  | 3837 |  | 3847 |  | 3857 |  | 3867 |
|  | 3806 |  | 3816 |  | 3827 |  | 3837 |  | 3847 |  | 3857 |  | 3868 |
|  | 3806 |  | 3817 |  | 3827 |  | 3837 |  | 3847 |  | 3858 |  | 3868 |
|  | 3807 |  | 3817 |  | 3827 |  | 3837 |  | 3848 |  | 3858 |  | 3868 |
|  | 3807 |  | 3817 |  | 3827 |  | 3838 |  | 3848 |  | 3858 |  | 3868 |
|  | 3807 |  | 3817 |  | 3828 |  | 3838 |  | 3848 |  | 3858 |  | 3869 |
|  | 3807 |  | 3818 |  | 3828 |  | 3838 |  | 3848 |  | 3859 |  | 3869 |
|  | 3808 |  | 3818 |  | 3828 |  | 3838 |  | 3849 |  | 3859 |  | 3869 |
|  | 3808 |  | 3818 |  | 3828 |  | 3839 |  | 3849 |  | 3859 |  | 3869 |
|  | 3808 |  | 3818 |  | 3829 |  | 3839 |  | 3849 |  | 3859 |  | 3870 |
|  | 3808 |  | 3819 |  | 3829 |  | 3839 |  | 3849 |  | 3860 |  | 3870 |
|  | 3809 |  | 3819 |  | 3829 |  | 3839 |  | 3850 |  | 3860 |  | 3870 |
|  | 3809 |  | 3819 |  | 3829 |  | 3840 |  | 3850 |  | 3860 |  | 3870 |
|  | 3809 |  | 3819 |  | 3830 |  | 3840 |  | 3850 |  | 3860 |  | 3871 |
|  | 3809 |  | 3820 |  | 3830 |  | 3840 |  | 3850 |  | 3861 |  | 3871 |
|  | 3810 |  | 3820 |  | 3830 |  | 3840 |  | 3851 |  | 3861 |  | 3871 |
|  | 3810 |  | 3820 |  | 3830 |  | 3841 |  | 3851 |  | 3861 |  | 3871 |
|  | 3810 |  | 3820 |  | 3831 |  | 3841 |  | 3851 |  | 3861 |  | 3872 |
|  | 3810 |  | 3821 |  | 3831 |  | 3841 |  | 3851 |  | 3862 |  | 3872 |
|  | 3811 |  | 3821 |  | 3831 |  | 3841 |  | 3852 |  | 3862 |  | 3872 |
|  | 3811 |  | 3821 |  | 3831 |  | 3842 |  | 3852 |  | 3862 |  | 3872 |
|  | 3811 |  | 3821 |  | 3832 |  | 3842 |  | 3852 |  | 3862 |  | 3873 |
|  | 3811 |  | 3822 |  | 3832 |  | 3842 |  | 3852 |  | 3863 |  | 3873 |
|  | 3812 |  | 3822 |  | 3832 |  | 3842 |  | 3853 |  | 3863 |  | 3873 |
|  | 3812 |  | 3822 |  | 3832 |  | 3843 |  | 3853 |  | 3863 |  | 3873 |
|  | 3812 |  | 3822 |  | 3833 |  | 3843 |  | 3853 |  | 3863 |  | 3874 |
|  | 3812 |  | 3823 |  | 3833 |  | 3843 |  | 3853 |  | 3864 |  | 3874 |
|  | 3813 |  | 3823 |  | 3833 |  | 3843 |  | 3854 |  | 3864 |  | 3874 |
|  | 3813 |  | 3823 |  | 3833 |  | 3844 |  | 3854 |  | 3864 |  | 3874 |
|  | 3813 |  | 3823 |  | 3834 |  | 3844 |  | 3854 |  | 3864 |  | 3875 |
|  | 3813 |  | 3824 |  | 3834 |  | 3844 |  | 3854 |  | 3865 |  | 3875 |

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  | Trt N | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3875 | PPD | 3885 | PPD | 3896 | PPD | 3906 | PPD | 3916 | PPD | 3926 | PPD | 3937 |
|  | 3875 |  | 3886 |  | 3896 |  | 3906 |  | 3916 |  | 3927 |  | 3937 |
|  | 3876 |  | 3886 |  | 3896 |  | 3906 |  | 3917 |  | 3927 |  | 3937 |
|  | 3876 |  | 3886 |  | 3896 |  | 3907 |  | 3917 |  | 3927 |  | 3937 |
|  | 3876 |  | 3886 |  | 3897 |  | 3907 |  | 3917 |  | 3927 |  | 3938 |
|  | 3876 |  | 3887 |  | 3897 |  | 3907 |  | 3917 |  | 3928 |  | 3938 |
|  | 3877 |  | 3887 |  | 3897 |  | 3907 |  | 3918 |  | 3928 |  | 3938 |
|  | 3877 |  | 3887 |  | 3897 |  | 3908 |  | 3918 |  | 3928 |  | 3938 |
|  | 3877 |  | 3887 |  | 3898 |  | 3908 |  | 3918 |  | 3928 |  | 3939 |
|  | 3877 |  | 3888 |  | 3898 |  | 3908 |  | 3918 |  | 3929 |  | 3939 |
|  | 3878 |  | 3888 |  | 3898 |  | 3908 |  | 3919 |  | 3929 |  | 3939 |
|  | 3878 |  | 3888 |  | 3898 |  | 3909 |  | 3919 |  | 3929 |  | 3939 |
|  | 3878 |  | 3888 |  | 3899 |  | 3909 |  | 3919 |  | 3929 |  | 3940 |
|  | 3878 |  | 3889 |  | 3899 |  | 3909 |  | 3919 |  | 3930 |  | 3940 |
|  | 3879 |  | 3889 |  | 3899 |  | 3909 |  | 3920 |  | 3930 |  | 3940 |
|  | 3879 |  | 3889 |  | 3899 |  | 3910 |  | 3920 |  | 3930 |  | 3940 |
|  | 3879 |  | 3889 |  | 3900 |  | 3910 |  | 3920 |  | 3930 |  | 3941 |
|  | 3879 |  | 3890 |  | 3900 |  | 3910 |  | 3920 |  | 3931 |  | 3941 |
|  | 3880 |  | 3890 |  | 3900 |  | 3910 |  | 3921 |  | 3931 |  | 3941 |
|  | 3880 |  | 3890 |  | 3900 |  | 3911 |  | 3921 |  | 3931 |  | 3941 |
|  | 3880 |  | 3890 |  | 3901 |  | 3911 |  | 3921 |  | 3931 |  | 3942 |
|  | 3880 |  | 3891 |  | 3901 |  | 3911 |  | 3921 |  | 3932 |  | 3942 |
|  | 3881 |  | 3891 |  | 3901 |  | 3911 |  | 3922 |  | 3932 |  | 3942 |
|  | 3881 |  | 3891 |  | 3901 |  | 3912 |  | 3922 |  | 3932 |  | 3942 |
|  | 3881 |  | 3891 |  | 3902 |  | 3912 |  | 3922 |  | 3932 |  | 3943 |
|  | 3881 |  | 3892 |  | 3902 |  | 3912 |  | 3922 |  | 3933 |  | 3943 |
|  | 3882 |  | 3892 |  | 3902 |  | 3912 |  | 3923 |  | 3933 |  | 3943 |
|  | 3882 |  | 3892 |  | 3902 |  | 3913 |  | 3923 |  | 3933 |  | 3943 |
|  | 3882 |  | 3892 |  | 3903 |  | 3913 |  | 3923 |  | 3933 |  | 3944 |
|  | 3882 |  | 3893 |  | 3903 |  | 3913 |  | 3923 |  | 3934 |  | 3944 |
|  | 3883 |  | 3893 |  | 3903 |  | 3913 |  | 3924 |  | 3934 |  | 3944 |
|  | 3883 |  | 3893 |  | 3903 |  | 3914 |  | 3924 |  | 3934 |  | 3944 |
|  | 3883 |  | 3893 |  | 3904 |  | 3914 |  | 3924 |  | 3934 |  | 3945 |
|  | 3883 |  | 3894 |  | 3904 |  | 3914 |  | 3924 |  | 3935 |  | 3945 |
|  | 3884 |  | 3894 |  | 3904 |  | 3914 |  | 3925 |  | 3935 |  | 3945 |
|  | 3884 |  | 3894 |  | 3904 |  | 3915 |  | 3925 |  | 3935 |  | 3945 |
|  | 3884 |  | 3894 |  | 3905 |  | 3915 |  | 3925 |  | 3935 |  | 3946 |
|  | 3884 |  | 3895 |  | 3905 |  | 3915 |  | 3925 |  | 3936 |  | 3946 |
|  | 3885 |  | 3895 |  | 3905 |  | 3915 |  | 3926 |  | 3936 |  | 3946 |
|  | 3885 |  | 3895 |  | 3905 |  | 3916 |  | 3926 |  | 3936 |  | 3946 |
|  | 3885 |  | 3895 |  | 3906 |  | 3916 |  | 3926 |  | 3936 |  | 3947 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | Trt |  |  |  |  | Bl nb |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3947 | PPD | 3957 | PPD | 3967 | PPD | 3978 | PPD | 3988 | PPD | 3998 | PPD | 4008 |
|  | 3947 |  | 3957 |  | 3968 |  | 3978 |  | 3988 |  | 3998 |  | 4009 |
|  | 3947 |  | 3958 |  | 3968 |  | 3978 |  | 3988 |  | 3999 |  | 4009 |
|  | 3948 |  | 3958 |  | 3968 |  | 3978 |  | 3989 |  | 3999 |  | 4009 |
|  | 3948 |  | 3958 |  | 3968 |  | 3979 |  | 3989 |  | 3999 |  | 4009 |
|  | 3948 |  | 3958 |  | 3969 |  | 3979 |  | 3989 |  | 3999 |  | 4010 |
|  | 3948 |  | 3959 |  | 3969 |  | 3979 |  | 3989 |  | 4000 |  | 4010 |
|  | 3949 |  | 3959 |  | 3969 |  | 3979 |  | 3990 |  | 4000 |  | 4010 |
|  | 3949 |  | 3959 |  | 3969 |  | 3980 |  | 3990 |  | 4000 |  | 4010 |
|  | 3949 |  | 3959 |  | 3970 |  | 3980 |  | 3990 |  | 4000 |  | 4011 |
|  | 3949 |  | 3960 |  | 3970 |  | 3980 |  | 3990 |  | 4001 |  | 4011 |
|  | 3950 |  | 3960 |  | 3970 |  | 3980 |  | 3991 |  | 4001 |  | 4011 |
|  | 3950 |  | 3960 |  | 3970 |  | 3981 |  | 3991 |  | 4001 |  | 4011 |
|  | 3950 |  | 3960 |  | 3971 |  | 3981 |  | 3991 |  | 4001 |  | 4012 |
|  | 3950 |  | 3961 |  | 3971 |  | 3981 |  | 3991 |  | 4002 |  | 4012 |
|  | 3951 |  | 3961 |  | 3971 |  | 3981 |  | 3992 |  | 4002 |  | 4012 |
|  | 3951 |  | 3961 |  | 3971 |  | 3982 |  | 3992 |  | 4002 |  | 4012 |
|  | 3951 |  | 3961 |  | 3972 |  | 3982 |  | 3992 |  | 4002 |  | 4013 |
|  | 3951 |  | 3962 |  | 3972 |  | 3982 |  | 3992 |  | 4003 |  | 4013 |
|  | 3952 |  | 3962 |  | 3972 |  | 3982 |  | 3993 |  | 4003 |  | 4013 |
|  | 3952 |  | 3962 |  | 3972 |  | 3983 |  | 3993 |  | 4003 |  | 4013 |
|  | 3952 |  | 3962 |  | 3973 |  | 3983 |  | 3993 |  | 4003 |  | 4014 |
|  | 3952 |  | 3963 |  | 3973 |  | 3983 |  | 3993 |  | 4004 |  | 4014 |
|  | 3953 |  | 3963 |  | 3973 |  | 3983 |  | 3994 |  | 4004 |  | 4014 |
|  | 3953 |  | 3963 |  | 3973 |  | 3984 |  | 3994 |  | 4004 |  | 4014 |
|  | 3953 |  | 3963 |  | 3974 |  | 3984 |  | 3994 |  | 4004 |  | 4015 |
|  | 3953 |  | 3964 |  | 3974 |  | 3984 |  | 3994 |  | 4005 |  | 4015 |
|  | 3954 |  | 3964 |  | 3974 |  | 3984 |  | 3995 |  | 4005 |  | 4015 |
|  | 3954 |  | 3964 |  | 3974 |  | 3985 |  | 3995 |  | 4005 |  | 4015 |
|  | 3954 |  | 3964 |  | 3975 |  | 3985 |  | 3995 |  | 4005 |  | 4016 |
|  | 3954 |  | 3965 |  | 3975 |  | 3985 |  | 3995 |  | 4006 |  | 4016 |
|  | 3955 |  | 3965 |  | 3975 |  | 3985 |  | 3996 |  | 4006 |  | 4016 |
|  | 3955 |  | 3965 |  | 3975 |  | 3986 |  | 3996 |  | 4006 |  | 4016 |
|  | 3955 |  | 3965 |  | 3976 |  | 3986 |  | 3996 |  | 4006 |  | 4017 |
|  | 3955 |  | 3966 |  | 3976 |  | 3986 |  | 3996 |  | 4007 |  | 4017 |
|  | 3956 |  | 3966 |  | 3976 |  | 3986 |  | 3997 |  | 4007 |  | 4017 |
|  | 3956 |  | 3966 |  | 3976 |  | 3987 |  | 3997 |  | 4007 |  | 4017 |
|  | 3956 |  | 3966 |  | 3977 |  | 3987 |  | 3997 |  | 4007 |  | 4018 |
|  | 3956 |  | 3967 |  | 3977 |  | 3987 |  | 3997 |  | 4008 |  | 4018 |
|  | 3957 |  | 3967 |  | 3977 |  | 3987 |  | 3998 |  | 4008 |  | 4018 |
|  | 3957 |  | 3967 |  | 3977 |  | 3988 |  | 3998 |  | 4008 |  | 4018 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. nb |  | Bl nb | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4019 | PPD | 4029 | PPD | 4039 | PPD | 4049 | PPD | 4060 | PPD | 4070 | PPD | 4080 |
|  | 4019 |  | 4029 |  | 4039 |  | 4050 |  | 4060 |  | 4070 |  | 4080 |
|  | 4019 |  | 4029 |  | 4040 |  | 4050 |  | 4060 |  | 4070 |  | 4081 |
|  | 4019 |  | 4030 |  | 4040 |  | 4050 |  | 4060 |  | 4071 |  | 4081 |
|  | 4020 |  | 4030 |  | 4040 |  | 4050 |  | 4061 |  | 4071 |  | 4081 |
|  | 4020 |  | 4030 |  | 4040 |  | 4051 |  | 4061 |  | 4071 |  | 4081 |
|  | 4020 |  | 4030 |  | 4041 |  | 4051 |  | 4061 |  | 4071 |  | 4082 |
|  | 4020 |  | 4031 |  | 4041 |  | 4051 |  | 4061 |  | 4072 |  | 4082 |
|  | 4021 |  | 4031 |  | 4041 |  | 4051 |  | 4062 |  | 4072 |  | 4082 |
|  | 4021 |  | 4031 |  | 4041 |  | 4052 |  | 4062 |  | 4072 |  | 4082 |
|  | 4021 |  | 4031 |  | 4042 |  | 4052 |  | 4062 |  | 4072 |  | 4083 |
|  | 4021 |  | 4032 |  | 4042 |  | 4052 |  | 4062 |  | 4073 |  | 4083 |
|  | 4022 |  | 4032 |  | 4042 |  | 4052 |  | 4063 |  | 4073 |  | 4083 |
|  | 4022 |  | 4032 |  | 4042 |  | 4053 |  | 4063 |  | 4073 |  | 4083 |
|  | 4022 |  | 4032 |  | 4043 |  | 4053 |  | 4063 |  | 4073 |  | 4084 |
|  | 4022 |  | 4033 |  | 4043 |  | 4053 |  | 4063 |  | 4074 |  | 4084 |
|  | 4023 |  | 4033 |  | 4043 |  | 4053 |  | 4064 |  | 4074 |  | 4084 |
|  | 4023 |  | 4033 |  | 4043 |  | 4054 |  | 4064 |  | 4074 |  | 4084 |
|  | 4023 |  | 4033 |  | 4044 |  | 4054 |  | 4064 |  | 4074 |  | 4085 |
|  | 4023 |  | 4034 |  | 4044 |  | 4054 |  | 4064 |  | 4075 |  | 4085 |
|  | 4024 |  | 4034 |  | 4044 |  | 4054 |  | 4065 |  | 4075 |  | 4085 |
|  | 4024 |  | 4034 |  | 4044 |  | 4055 |  | 4065 |  | 4075 |  | 4085 |
|  | 4024 |  | 4034 |  | 4045 |  | 4055 |  | 4065 |  | 4075 |  | 4086 |
|  | 4024 |  | 4035 |  | 4045 |  | 4055 |  | 4065 |  | 4076 |  | 4086 |
|  | 4025 |  | 4035 |  | 4045 |  | 4055 |  | 4066 |  | 4076 |  | 4086 |
|  | 4025 |  | 4035 |  | 4045 |  | 4056 |  | 4066 |  | 4076 |  | 4086 |
|  | 4025 |  | 4035 |  | 4046 |  | 4056 |  | 4066 |  | 4076 |  | 4087 |
|  | 4025 |  | 4036 |  | 4046 |  | 4056 |  | 4066 |  | 4077 |  | 4087 |
|  | 4026 |  | 4036 |  | 4046 |  | 4056 |  | 4067 |  | 4077 |  | 4087 |
|  | 4026 |  | 4036 |  | 4046 |  | 4057 |  | 4067 |  | 4077 |  | 4087 |
|  | 4026 |  | 4036 |  | 4047 |  | 4057 |  | 4067 |  | 4077 |  | 4088 |
|  | 4026 |  | 4037 |  | 4047 |  | 4057 |  | 4067 |  | 4078 |  | 4088 |
|  | 4027 |  | 4037 |  | 4047 |  | 4057 |  | 4068 |  | 4078 |  | 4088 |
|  | 4027 |  | 4037 |  | 4047 |  | 4058 |  | 4068 |  | 4078 |  | 4088 |
|  | 4027 |  | 4037 |  | 4048 |  | 4058 |  | 4068 |  | 4078 |  | 4089 |
|  | 4027 |  | 4038 |  | 4048 |  | 4058 |  | 4068 |  | 4079 |  | 4089 |
|  | 4028 |  | 4038 |  | 4048 |  | 4058 |  | 4069 |  | 4079 |  | 4089 |
|  | 4028 |  | 4038 |  | 4048 |  | 4059 |  | 4069 |  | 4079 |  | 4089 |
|  | 4028 |  | 4038 |  | 4049 |  | 4059 |  | 4069 |  | 4079 |  | 4090 |
|  | 4028 |  | 4039 |  | 4049 |  | 4059 |  | 4069 |  | 4080 |  | 4090 |
|  | 4029 |  | 4039 |  | 4049 |  | 4059 |  | 4070 |  | 4080 |  | 4090 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| Trt. | Bl nb |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4090 | PPD | 4101 | PPD | 4111 | PPD | 4121 | PPD | 4131 | PPD | 4142 | PPD | 4152 |
|  | 4091 |  | 4101 |  | 4111 |  | 4121 |  | 4132 |  | 4142 |  | 4152 |
|  | 4091 |  | 4101 |  | 4111 |  | 4122 |  | 4132 |  | 4142 |  | 4152 |
|  | 4091 |  | 4101 |  | 4112 |  | 4122 |  | 4132 |  | 4142 |  | 4153 |
|  | 4091 |  | 4102 |  | 4112 |  | 4122 |  | 4132 |  | 4143 |  | 4153 |
|  | 4092 |  | 4102 |  | 4112 |  | 4122 |  | 4133 |  | 4143 |  | 4153 |
|  | 4092 |  | 4102 |  | 4112 |  | 4123 |  | 4133 |  | 4143 |  | 4153 |
|  | 4092 |  | 4102 |  | 4113 |  | 4123 |  | 4133 |  | 4143 |  | 4154 |
|  | 4092 |  | 4103 |  | 4113 |  | 4123 |  | 4133 |  | 4144 |  | 4154 |
|  | 4093 |  | 4103 |  | 4113 |  | 4123 |  | 4134 |  | 4144 |  | 4154 |
|  | 4093 |  | 4103 |  | 4113 |  | 4124 |  | 4134 |  | 4144 |  | 4154 |
|  | 4093 |  | 4103 |  | 4114 |  | 4124 |  | 4134 |  | 4144 |  | 4155 |
|  | 4093 |  | 4104 |  | 4114 |  | 4124 |  | 4134 |  | 4145 |  | 4155 |
|  | 4094 |  | 4104 |  | 4114 |  | 4124 |  | 4135 |  | 4145 |  | 4155 |
|  | 4094 |  | 4104 |  | 4114 |  | 4125 |  | 4135 |  | 4145 |  | 4155 |
|  | 4094 |  | 4104 |  | 4115 |  | 4125 |  | 4135 |  | 4145 |  | 4156 |
|  | 4094 |  | 4105 |  | 4115 |  | 4125 |  | 4135 |  | 4146 |  | 4156 |
|  | 4095 |  | 4105 |  | 4115 |  | 4125 |  | 4136 |  | 4146 |  | 4156 |
|  | 4095 |  | 4105 |  | 4115 |  | 4126 |  | 4136 |  | 4146 |  | 4156 |
|  | 4095 |  | 4105 |  | 4116 |  | 4126 |  | 4136 |  | 4146 |  | 4157 |
|  | 4095 |  | 4106 |  | 4116 |  | 4126 |  | 4136 |  | 4147 |  | 4157 |
|  | 4096 |  | 4106 |  | 4116 |  | 4126 |  | 4137 |  | 4147 |  | 4157 |
|  | 4096 |  | 4106 |  | 4116 |  | 4127 |  | 4137 |  | 4147 |  | 4157 |
|  | 4096 |  | 4106 |  | 4117 |  | 4127 |  | 4137 |  | 4147 |  | 4158 |
|  | 4096 |  | 4107 |  | 4117 |  | 4127 |  | 4137 |  | 4148 |  | 4158 |
|  | 4097 |  | 4107 |  | 4117 |  | 4127 |  | 4138 |  | 4148 |  | 4158 |
|  | 4097 |  | 4107 |  | 4117 |  | 4128 |  | 4138 |  | 4148 |  | 4158 |
|  | 4097 |  | 4107 |  | 4118 |  | 4128 |  | 4138 |  | 4148 |  | 4159 |
|  | 4097 |  | 4108 |  | 4118 |  | 4128 |  | 4138 |  | 4149 |  | 4159 |
|  | 4098 |  | 4108 |  | 4118 |  | 4128 |  | 4139 |  | 4149 |  | 4159 |
|  | 4098 |  | 4108 |  | 4118 |  | 4129 |  | 4139 |  | 4149 |  | 4159 |
|  | 4098 |  | 4108 |  | 4119 |  | 4129 |  | 4139 |  | 4149 |  | 4160 |
|  | 4098 |  | 4109 |  | 4119 |  | 4129 |  | 4139 |  | 4150 |  | 4160 |
|  | 4099 |  | 4109 |  | 4119 |  | 4129 |  | 4140 |  | 4150 |  | 4160 |
|  | 4099 |  | 4109 |  | 4119 |  | 4130 |  | 4140 |  | 4150 |  | 4160 |
|  | 4099 |  | 4109 |  | 4120 |  | 4130 |  | 4140 |  | 4150 |  | 4161 |
|  | 4099 |  | 4110 |  | 4120 |  | 4130 |  | 4140 |  | 4151 |  | 4161 |
|  | 4100 |  | 4110 |  | 4120 |  | 4130 |  | 4141 |  | 4151 |  | 4161 |
|  | 4100 |  | 4110 |  | 4120 |  | 4131 |  | 4141 |  | 4151 |  | 4161 |
|  | 4100 |  | 4110 |  | 4121 |  | 4131 |  | 4141 |  | 4151 |  | 4162 |
|  | 4100 |  | 4111 |  | 4121 |  | 4131 |  | 4141 |  | 4152 |  | 4162 |

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl. |  | Bl nb |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4162 | PPD | 4172 | PPD | 4183 | PPD | 4193 | PPD | 4203 | PPD | 4213 | PPD | 4224 |
|  | 4162 |  | 4173 |  | 4183 |  | 4193 |  | 4203 |  | 4214 |  | 4224 |
|  | 4163 |  | 4173 |  | 4183 |  | 4193 |  | 4204 |  | 4214 |  | 4224 |
|  | 4163 |  | 4173 |  | 4183 |  | 4194 |  | 4204 |  | 4214 |  | 4224 |
|  | 4163 |  | 4173 |  | 4184 |  | 4194 |  | 4204 |  | 4214 |  | 4225 |
|  | 4163 |  | 4174 |  | 4184 |  | 4194 |  | 4204 |  | 4215 |  | 4225 |
|  | 4164 |  | 4174 |  | 4184 |  | 4194 |  | 4205 |  | 4215 |  | 4225 |
|  | 4164 |  | 4174 |  | 4184 |  | 4195 |  | 4205 |  | 4215 |  | 4225 |
|  | 4164 |  | 4174 |  | 4185 |  | 4195 |  | 4205 |  | 4215 |  | 4226 |
|  | 4164 |  | 4175 |  | 4185 |  | 4195 |  | 4205 |  | 4216 |  | 4226 |
|  | 4165 |  | 4175 |  | 4185 |  | 4195 |  | 4206 |  | 4216 |  | 4226 |
|  | 4165 |  | 4175 |  | 4185 |  | 4196 |  | 4206 |  | 4216 |  | 4226 |
|  | 4165 |  | 4175 |  | 4186 |  | 4196 |  | 4206 |  | 4216 |  | 4227 |
|  | 4165 |  | 4176 |  | 4186 |  | 4196 |  | 4206 |  | 4217 |  | 4227 |
|  | 4166 |  | 4176 |  | 4186 |  | 4196 |  | 4207 |  | 4217 |  | 4227 |
|  | 4166 |  | 4176 |  | 4186 |  | 4197 |  | 4207 |  | 4217 |  | 4227 |
|  | 4166 |  | 4176 |  | 4187 |  | 4197 |  | 4207 |  | 4217 |  | 4228 |
|  | 4166 |  | 4177 |  | 4187 |  | 4197 |  | 4207 |  | 4218 |  | 4228 |
|  | 4167 |  | 4177 |  | 4187 |  | 4197 |  | 4208 |  | 4218 |  | 4228 |
|  | 4167 |  | 4177 |  | 4187 |  | 4198 |  | 4208 |  | 4218 |  | 4228 |
|  | 4167 |  | 4177 |  | 4188 |  | 4198 |  | 4208 |  | 4218 |  | 4229 |
|  | 4167 |  | 4178 |  | 4188 |  | 4198 |  | 4208 |  | 4219 |  | 4229 |
|  | 4168 |  | 4178 |  | 4188 |  | 4198 |  | 4209 |  | 4219 |  | 4229 |
|  | 4168 |  | 4178 |  | 4188 |  | 4199 |  | 4209 |  | 4219 |  | 4229 |
|  | 4168 |  | 4178 |  | 4189 |  | 4199 |  | 4209 |  | 4219 |  | 4230 |
|  | 4168 |  | 4179 |  | 4189 |  | 4199 |  | 4209 |  | 4220 |  | 4230 |
|  | 4169 |  | 4179 |  | 4189 |  | 4199 |  | 4210 |  | 4220 |  | 4230 |
|  | 4169 |  | 4179 |  | 4189 |  | 4200 |  | 4210 |  | 4220 |  | 4230 |
|  | 4169 |  | 4179 |  | 4190 |  | 4200 |  | 4210 |  | 4220 |  | 4231 |
|  | 4169 |  | 4180 |  | 4190 |  | 4200 |  | 4210 |  | 4221 |  | 4231 |
|  | 4170 |  | 4180 |  | 4190 |  | 4200 |  | 4211 |  | 4221 |  | 4231 |
|  | 4170 |  | 4180 |  | 4190 |  | 4201 |  | 4211 |  | 4221 |  | 4231 |
|  | 4170 |  | 4180 |  | 4191 |  | 4201 |  | 4211 |  | 4221 |  | 4232 |
|  | 4170 |  | 4181 |  | 4191 |  | 4201 |  | 4211 |  | 4222 |  | 4232 |
|  | 4171 |  | 4181 |  | 4191 |  | 4201 |  | 4212 |  | 4222 |  | 4232 |
|  | 4171 |  | 4181 |  | 4191 |  | 4202 |  | 4212 |  | 4222 |  | 4232 |
|  | 4171 |  | 4181 |  | 4192 |  | 4202 |  | 4212 |  | 4222 |  | 4233 |
|  | 4171 |  | 4182 |  | 4192 |  | 4202 |  | 4212 |  | 4223 |  | 4233 |
|  | 4172 |  | 4182 |  | 4192 |  | 4202 |  | 4213 |  | 4223 |  | 4233 |
|  | 4172 |  | 4182 |  | 4192 |  | 4203 |  | 4213 |  | 4223 |  | 4233 |
|  | 4172 |  | 4182 |  | 4193 |  | 4203 |  | 4213 |  | 4223 |  | 4234 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| Trt. |  |  | $\mathrm{Bl} \mathrm{nb}^{\text {nb }}$ |  |  |  | $\mathrm{Bl} \text {. }$ |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4234 | PPD | 4244 | PPD | 4254 | PPD | 4265 | PPD | 4275 | PPD | 4285 | PPD | 4295 |
|  | 4234 |  | 4244 |  | 4255 |  | 4265 |  | 4275 |  | 4285 |  | 4296 |
|  | 4234 |  | 4245 |  | 4255 |  | 4265 |  | 4275 |  | 4286 |  | 4296 |
|  | 4235 |  | 4245 |  | 4255 |  | 4265 |  | 4276 |  | 4286 |  | 4296 |
|  | 4235 |  | 4245 |  | 4255 |  | 4266 |  | 4276 |  | 4286 |  | 4296 |
|  | 4235 |  | 4245 |  | 4256 |  | 4266 |  | 4276 |  | 4286 |  | 4297 |
|  | 4235 |  | 4246 |  | 4256 |  | 4266 |  | 4276 |  | 4287 |  | 4297 |
|  | 4236 |  | 4246 |  | 4256 |  | 4266 |  | 4277 |  | 4287 |  | 4297 |
|  | 4236 |  | 4246 |  | 4256 |  | 4267 |  | 4277 |  | 4287 |  | 4297 |
|  | 4236 |  | 4246 |  | 4257 |  | 4267 |  | 4277 |  | 4287 |  | 4298 |
|  | 4236 |  | 4247 |  | 4257 |  | 4267 |  | 4277 |  | 4288 |  | 4298 |
|  | 4237 |  | 4247 |  | 4257 |  | 4267 |  | 4278 |  | 4288 |  | 4298 |
|  | 4237 |  | 4247 |  | 4257 |  | 4268 |  | 4278 |  | 4288 |  | 4298 |
|  | 4237 |  | 4247 |  | 4258 |  | 4268 |  | 4278 |  | 4288 |  | 4299 |
|  | 4237 |  | 4248 |  | 4258 |  | 4268 |  | 4278 |  | 4289 |  | 4299 |
|  | 4238 |  | 4248 |  | 4258 |  | 4268 |  | 4279 |  | 4289 |  | 4299 |
|  | 4238 |  | 4248 |  | 4258 |  | 4269 |  | 4279 |  | 4289 |  | 4299 |
|  | 4238 |  | 4248 |  | 4259 |  | 4269 |  | 4279 |  | 4289 |  | 4300 |
|  | 4238 |  | 4249 |  | 4259 |  | 4269 |  | 4279 |  | 4290 |  | 4300 |
|  | 4239 |  | 4249 |  | 4259 |  | 4269 |  | 4280 |  | 4290 |  | 4300 |
|  | 4239 |  | 4249 |  | 4259 |  | 4270 |  | 4280 |  | 4290 |  | 4300 |
|  | 4239 |  | 4249 |  | 4260 |  | 4270 |  | 4280 |  | 4290 |  | 4301 |
|  | 4239 |  | 4250 |  | 4260 |  | 4270 |  | 4280 |  | 4291 |  | 4301 |
|  | 4240 |  | 4250 |  | 4260 |  | 4270 |  | 4281 |  | 4291 |  | 4301 |
|  | 4240 |  | 4250 |  | 4260 |  | 4271 |  | 4281 |  | 4291 |  | 4301 |
|  | 4240 |  | 4250 |  | 4261 |  | 4271 |  | 4281 |  | 4291 |  | 4302 |
|  | 4240 |  | 4251 |  | 4261 |  | 4271 |  | 4281 |  | 4292 |  | 4302 |
|  | 4241 |  | 4251 |  | 4261 |  | 4271 |  | 4282 |  | 4292 |  | 4302 |
|  | 4241 |  | 4251 |  | 4261 |  | 4272 |  | 4282 |  | 4292 |  | 4302 |
|  | 4241 |  | 4251 |  | 4262 |  | 4272 |  | 4282 |  | 4292 |  | 4303 |
|  | 4241 |  | 4252 |  | 4262 |  | 4272 |  | 4282 |  | 4293 |  | 4303 |
|  | 4242 |  | 4252 |  | 4262 |  | 4272 |  | 4283 |  | 4293 |  | 4303 |
|  | 4242 |  | 4252 |  | 4262 |  | 4273 |  | 4283 |  | 4293 |  | 4303 |
|  | 4242 |  | 4252 |  | 4263 |  | 4273 |  | 4283 |  | 4293 |  | 4304 |
|  | 4242 |  | 4253 |  | 4263 |  | 4273 |  | 4283 |  | 4294 |  | 4304 |
|  | 4243 |  | 4253 |  | 4263 |  | 4273 |  | 4284 |  | 4294 |  | 4304 |
|  | 4243 |  | 4253 |  | 4263 |  | 4274 |  | 4284 |  | 4294 |  | 4304 |
|  | 4243 |  | 4253 |  | 4264 |  | 4274 |  | 4284 |  | 4294 |  | 4305 |
|  | 4243 |  | 4254 |  | 4264 |  | 4274 |  | 4284 |  | 4295 |  | 4305 |
|  | 4244 |  | 4254 |  | 4264 |  | 4274 |  | 4285 |  | 4295 |  | 4305 |
|  | 4244 |  | 4254 |  | 4264 |  | 4275 |  | 4285 |  | 4295 |  | 4305 |

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl nb |  | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ | Trt | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. } \mathrm{Bl} . \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4306 | PPD | 4316 | PPD | 4326 | PPD | 4336 | PPD | 4347 | PPD | 4357 | PPD | 4367 |
|  | 4306 |  | 4316 |  | 4326 |  | 4337 |  | 4347 |  | 4357 |  | 4367 |
|  | 4306 |  | 4316 |  | 4327 |  | 4337 |  | 4347 |  | 4357 |  | 4368 |
|  | 4306 |  | 4317 |  | 4327 |  | 4337 |  | 4347 |  | 4358 |  | 4368 |
|  | 4307 |  | 4317 |  | 4327 |  | 4337 |  | 4348 |  | 4358 |  | 4368 |
|  | 4307 |  | 4317 |  | 4327 |  | 4338 |  | 4348 |  | 4358 |  | 4368 |
|  | 4307 |  | 4317 |  | 4328 |  | 4338 |  | 4348 |  | 4358 |  | 4369 |
|  | 4307 |  | 4318 |  | 4328 |  | 4338 |  | 4348 |  | 4359 |  | 4369 |
|  | 4308 |  | 4318 |  | 4328 |  | 4338 |  | 4349 |  | 4359 |  | 4369 |
|  | 4308 |  | 4318 |  | 4328 |  | 4339 |  | 4349 |  | 4359 |  | 4369 |
|  | 4308 |  | 4318 |  | 4329 |  | 4339 |  | 4349 |  | 4359 |  | 4370 |
|  | 4308 |  | 4319 |  | 4329 |  | 4339 |  | 4349 |  | 4360 |  | 4370 |
|  | 4309 |  | 4319 |  | 4329 |  | 4339 |  | 4350 |  | 4360 |  | 4370 |
|  | 4309 |  | 4319 |  | 4329 |  | 4340 |  | 4350 |  | 4360 |  | 4370 |
|  | 4309 |  | 4319 |  | 4330 |  | 4340 |  | 4350 |  | 4360 |  | 4371 |
|  | 4309 |  | 4320 |  | 4330 |  | 4340 |  | 4350 |  | 4361 |  | 4371 |
|  | 4310 |  | 4320 |  | 4330 |  | 4340 |  | 4351 |  | 4361 |  | 4371 |
|  | 4310 |  | 4320 |  | 4330 |  | 4341 |  | 4351 |  | 4361 |  | 4371 |
|  | 4310 |  | 4320 |  | 4331 |  | 4341 |  | 4351 |  | 4361 |  | 4372 |
|  | 4310 |  | 4321 |  | 4331 |  | 4341 |  | 4351 |  | 4362 |  | 4372 |
|  | 4311 |  | 4321 |  | 4331 |  | 4341 |  | 4352 |  | 4362 |  | 4372 |
|  | 4311 |  | 4321 |  | 4331 |  | 4342 |  | 4352 |  | 4362 |  | 4372 |
|  | 4311 |  | 4321 |  | 4332 |  | 4342 |  | 4352 |  | 4362 |  | 4373 |
|  | 4311 |  | 4322 |  | 4332 |  | 4342 |  | 4352 |  | 4363 |  | 4373 |
|  | 4312 |  | 4322 |  | 4332 |  | 4342 |  | 4353 |  | 4363 |  | 4373 |
|  | 4312 |  | 4322 |  | 4332 |  | 4343 |  | 4353 |  | 4363 |  | 4373 |
|  | 4312 |  | 4322 |  | 4333 |  | 4343 |  | 4353 |  | 4363 |  | 4374 |
|  | 4312 |  | 4323 |  | 4333 |  | 4343 |  | 4353 |  | 4364 |  | 4374 |
|  | 4313 |  | 4323 |  | 4333 |  | 4343 |  | 4354 |  | 4364 |  | 4374 |
|  | 4313 |  | 4323 |  | 4333 |  | 4344 |  | 4354 |  | 4364 |  | 4374 |
|  | 4313 |  | 4323 |  | 4334 |  | 4344 |  | 4354 |  | 4364 |  | 4375 |
|  | 4313 |  | 4324 |  | 4334 |  | 4344 |  | 4354 |  | 4365 |  | 4375 |
|  | 4314 |  | 4324 |  | 4334 |  | 4344 |  | 4355 |  | 4365 |  | 4375 |
|  | 4314 |  | 4324 |  | 4334 |  | 4345 |  | 4355 |  | 4365 |  | 4375 |
|  | 4314 |  | 4324 |  | 4335 |  | 4345 |  | 4355 |  | 4365 |  | 4376 |
|  | 4314 |  | 4325 |  | 4335 |  | 4345 |  | 4355 |  | 4366 |  | 4376 |
|  | 4315 |  | 4325 |  | 4335 |  | 4345 |  | 4356 |  | 4366 |  | 4376 |
|  | 4315 |  | 4325 |  | 4335 |  | 4346 |  | 4356 |  | 4366 |  | 4376 |
|  | 4315 |  | 4325 |  | 4336 |  | 4346 |  | 4356 |  | 4366 |  | 4377 |
|  | 4315 |  | 4326 |  | 4336 |  | 4346 |  | 4356 |  | 4367 |  | 4377 |
|  | 4316 |  | 4326 |  | 4336 |  | 4346 |  | 4357 |  | 4367 |  | 4377 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl. |  | Bl nb |  |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4377 | PPD | 4388 | PPD | 4398 | PPD | 4408 | PPD | 4418 | PPD | 4429 | PPD | 4439 |
|  | 4378 |  | 4388 |  | 4398 |  | 4408 |  | 4419 |  | 4429 |  | 4439 |
|  | 4378 |  | 4388 |  | 4398 |  | 4409 |  | 4419 |  | 4429 |  | 4439 |
|  | 4378 |  | 4388 |  | 4399 |  | 4409 |  | 4419 |  | 4429 |  | 4440 |
|  | 4378 |  | 4389 |  | 4399 |  | 4409 |  | 4419 |  | 4430 |  | 4440 |
|  | 4379 |  | 4389 |  | 4399 |  | 4409 |  | 4420 |  | 4430 |  | 4440 |
|  | 4379 |  | 4389 |  | 4399 |  | 4410 |  | 4420 |  | 4430 |  | 4440 |
|  | 4379 |  | 4389 |  | 4400 |  | 4410 |  | 4420 |  | 4430 |  | 4441 |
|  | 4379 |  | 4390 |  | 4400 |  | 4410 |  | 4420 |  | 4431 |  | 4441 |
|  | 4380 |  | 4390 |  | 4400 |  | 4410 |  | 4421 |  | 4431 |  | 4441 |
|  | 4380 |  | 4390 |  | 4400 |  | 4411 |  | 4421 |  | 4431 |  | 4441 |
|  | 4380 |  | 4390 |  | 4401 |  | 4411 |  | 4421 |  | 4431 |  | 4442 |
|  | 4380 |  | 4391 |  | 4401 |  | 4411 |  | 4421 |  | 4432 |  | 4442 |
|  | 4381 |  | 4391 |  | 4401 |  | 4411 |  | 4422 |  | 4432 |  | 4442 |
|  | 4381 |  | 4391 |  | 4401 |  | 4412 |  | 4422 |  | 4432 |  | 4442 |
|  | 4381 |  | 4391 |  | 4402 |  | 4412 |  | 4422 |  | 4432 |  | 4443 |
|  | 4381 |  | 4392 |  | 4402 |  | 4412 |  | 4422 |  | 4433 |  | 4443 |
|  | 4382 |  | 4392 |  | 4402 |  | 4412 |  | 4423 |  | 4433 |  | 4443 |
|  | 4382 |  | 4392 |  | 4402 |  | 4413 |  | 4423 |  | 4433 |  | 4443 |
|  | 4382 |  | 4392 |  | 4403 |  | 4413 |  | 4423 |  | 4433 |  | 4444 |
|  | 4382 |  | 4393 |  | 4403 |  | 4413 |  | 4423 |  | 4434 |  | 4444 |
|  | 4383 |  | 4393 |  | 4403 |  | 4413 |  | 4424 |  | 4434 |  | 4444 |
|  | 4383 |  | 4393 |  | 4403 |  | 4414 |  | 4424 |  | 4434 |  | 4444 |
|  | 4383 |  | 4393 |  | 4404 |  | 4414 |  | 4424 |  | 4434 |  | 4445 |
|  | 4383 |  | 4394 |  | 4404 |  | 4414 |  | 4424 |  | 4435 |  | 4445 |
|  | 4384 |  | 4394 |  | 4404 |  | 4414 |  | 4425 |  | 4435 |  | 4445 |
|  | 4384 |  | 4394 |  | 4404 |  | 4415 |  | 4425 |  | 4435 |  | 4445 |
|  | 4384 |  | 4394 |  | 4405 |  | 4415 |  | 4425 |  | 4435 |  | 4446 |
|  | 4384 |  | 4395 |  | 4405 |  | 4415 |  | 4425 |  | 4436 |  | 4446 |
|  | 4385 |  | 4395 |  | 4405 |  | 4415 |  | 4426 |  | 4436 |  | 4446 |
|  | 4385 |  | 4395 |  | 4405 |  | 4416 |  | 4426 |  | 4436 |  | 4446 |
|  | 4385 |  | 4395 |  | 4406 |  | 4416 |  | 4426 |  | 4436 |  | 4447 |
|  | 4385 |  | 4396 |  | 4406 |  | 4416 |  | 4426 |  | 4437 |  | 4447 |
|  | 4386 |  | 4396 |  | 4406 |  | 4416 |  | 4427 |  | 4437 |  | 4447 |
|  | 4386 |  | 4396 |  | 4406 |  | 4417 |  | 4427 |  | 4437 |  | 4447 |
|  | 4386 |  | 4396 |  | 4407 |  | 4417 |  | 4427 |  | 4437 |  | 4448 |
|  | 4386 |  | 4397 |  | 4407 |  | 4417 |  | 4427 |  | 4438 |  | 4448 |
|  | 4387 |  | 4397 |  | 4407 |  | 4417 |  | 4428 |  | 4438 |  | 4448 |
|  | 4387 |  | 4397 |  | 4407 |  | 4418 |  | 4428 |  | 4438 |  | 4448 |
|  | 4387 |  | 4397 |  | 4408 |  | 4418 |  | 4428 |  | 4438 |  | 4449 |
|  | 4387 |  | 4398 |  | 4408 |  | 4418 |  | 4428 |  | 4439 |  | 4449 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ |  | Trt | Bl nb |  |  |  | $\mathrm{Bl} \text {. }$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4449 | PPD | 4459 | PPD | 4470 | PPD | 4480 | PPD | 4490 | PPD | 4500 | PPD | 4511 |
|  | 4449 |  | 4460 |  | 4470 |  | 4480 |  | 4490 |  | 4501 |  | 4511 |
|  | 4450 |  | 4460 |  | 4470 |  | 4480 |  | 4491 |  | 4501 |  | 4511 |
|  | 4450 |  | 4460 |  | 4470 |  | 4481 |  | 4491 |  | 4501 |  | 4511 |
|  | 4450 |  | 4460 |  | 4471 |  | 4481 |  | 4491 |  | 4501 |  | 4512 |
|  | 4450 |  | 4461 |  | 4471 |  | 4481 |  | 4491 |  | 4502 |  | 4512 |
|  | 4451 |  | 4461 |  | 4471 |  | 4481 |  | 4492 |  | 4502 |  | 4512 |
|  | 4451 |  | 4461 |  | 4471 |  | 4482 |  | 4492 |  | 4502 |  | 4512 |
|  | 4451 |  | 4461 |  | 4472 |  | 4482 |  | 4492 |  | 4502 |  | 4513 |
|  | 4451 |  | 4462 |  | 4472 |  | 4482 |  | 4492 |  | 4503 |  | 4513 |
|  | 4452 |  | 4462 |  | 4472 |  | 4482 |  | 4493 |  | 4503 |  | 4513 |
|  | 4452 |  | 4462 |  | 4472 |  | 4483 |  | 4493 |  | 4503 |  | 4513 |
|  | 4452 |  | 4462 |  | 4473 |  | 4483 |  | 4493 |  | 4503 |  | 4514 |
|  | 4452 |  | 4463 |  | 4473 |  | 4483 |  | 4493 |  | 4504 |  | 4514 |
|  | 4453 |  | 4463 |  | 4473 |  | 4483 |  | 4494 |  | 4504 |  | 4514 |
|  | 4453 |  | 4463 |  | 4473 |  | 4484 |  | 4494 |  | 4504 |  | 4514 |
|  | 4453 |  | 4463 |  | 4474 |  | 4484 |  | 4494 |  | 4504 |  | 4515 |
|  | 4453 |  | 4464 |  | 4474 |  | 4484 |  | 4494 |  | 4505 |  | 4515 |
|  | 4454 |  | 4464 |  | 4474 |  | 4484 |  | 4495 |  | 4505 |  | 4515 |
|  | 4454 |  | 4464 |  | 4474 |  | 4485 |  | 4495 |  | 4505 |  | 4515 |
|  | 4454 |  | 4464 |  | 4475 |  | 4485 |  | 4495 |  | 4505 |  | 4516 |
|  | 4454 |  | 4465 |  | 4475 |  | 4485 |  | 4495 |  | 4506 |  | 4516 |
|  | 4455 |  | 4465 |  | 4475 |  | 4485 |  | 4496 |  | 4506 |  | 4516 |
|  | 4455 |  | 4465 |  | 4475 |  | 4486 |  | 4496 |  | 4506 |  | 4516 |
|  | 4455 |  | 4465 |  | 4476 |  | 4486 |  | 4496 |  | 4506 |  | 4517 |
|  | 4455 |  | 4466 |  | 4476 |  | 4486 |  | 4496 |  | 4507 |  | 4517 |
|  | 4456 |  | 4466 |  | 4476 |  | 4486 |  | 4497 |  | 4507 |  | 4517 |
|  | 4456 |  | 4466 |  | 4476 |  | 4487 |  | 4497 |  | 4507 |  | 4517 |
|  | 4456 |  | 4466 |  | 4477 |  | 4487 |  | 4497 |  | 4507 |  | 4518 |
|  | 4456 |  | 4467 |  | 4477 |  | 4487 |  | 4497 |  | 4508 |  | 4518 |
|  | 4457 |  | 4467 |  | 4477 |  | 4487 |  | 4498 |  | 4508 |  | 4518 |
|  | 4457 |  | 4467 |  | 4477 |  | 4488 |  | 4498 |  | 4508 |  | 4518 |
|  | 4457 |  | 4467 |  | 4478 |  | 4488 |  | 4498 |  | 4508 |  | 4519 |
|  | 4457 |  | 4468 |  | 4478 |  | 4488 |  | 4498 |  | 4509 |  | 4519 |
|  | 4458 |  | 4468 |  | 4478 |  | 4488 |  | 4499 |  | 4509 |  | 4519 |
|  | 4458 |  | 4468 |  | 4478 |  | 4489 |  | 4499 |  | 4509 |  | 4519 |
|  | 4458 |  | 4468 |  | 4479 |  | 4489 |  | 4499 |  | 4509 |  | 4520 |
|  | 4458 |  | 4469 |  | 4479 |  | 4489 |  | 4499 |  | 4510 |  | 4520 |
|  | 4459 |  | 4469 |  | 4479 |  | 4489 |  | 4500 |  | 4510 |  | 4520 |
|  | 4459 |  | 4469 |  | 4479 |  | 4490 |  | 4500 |  | 4510 |  | 4520 |
|  | 4459 |  | 4469 |  | 4480 |  | 4490 |  | 4500 |  | 4510 |  | 4521 |

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl nb |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4521 | PPD | 4531 | PPD | 4541 | PPD | 4552 | PPD | 4562 | PPD | 4572 | PPD | 4582 |
|  | 4521 |  | 4531 |  | 4542 |  | 4552 |  | 4562 |  | 4572 |  | 4583 |
|  | 4521 |  | 4532 |  | 4542 |  | 4552 |  | 4562 |  | 4573 |  | 4583 |
|  | 4522 |  | 4532 |  | 4542 |  | 4552 |  | 4563 |  | 4573 |  | 4583 |
|  | 4522 |  | 4532 |  | 4542 |  | 4553 |  | 4563 |  | 4573 |  | 4583 |
|  | 4522 |  | 4532 |  | 4543 |  | 4553 |  | 4563 |  | 4573 |  | 4584 |
|  | 4522 |  | 4533 |  | 4543 |  | 4553 |  | 4563 |  | 4574 |  | 4584 |
|  | 4523 |  | 4533 |  | 4543 |  | 4553 |  | 4564 |  | 4574 |  | 4584 |
|  | 4523 |  | 4533 |  | 4543 |  | 4554 |  | 4564 |  | 4574 |  | 4584 |
|  | 4523 |  | 4533 |  | 4544 |  | 4554 |  | 4564 |  | 4574 |  | 4585 |
|  | 4523 |  | 4534 |  | 4544 |  | 4554 |  | 4564 |  | 4575 |  | 4585 |
|  | 4524 |  | 4534 |  | 4544 |  | 4554 |  | 4565 |  | 4575 |  | 4585 |
|  | 4524 |  | 4534 |  | 4544 |  | 4555 |  | 4565 |  | 4575 |  | 4585 |
|  | 4524 |  | 4534 |  | 4545 |  | 4555 |  | 4565 |  | 4575 |  | 4586 |
|  | 4524 |  | 4535 |  | 4545 |  | 4555 |  | 4565 |  | 4576 |  | 4586 |
|  | 4525 |  | 4535 |  | 4545 |  | 4555 |  | 4566 |  | 4576 |  | 4586 |
|  | 4525 |  | 4535 |  | 4545 |  | 4556 |  | 4566 |  | 4576 |  | 4586 |
|  | 4525 |  | 4535 |  | 4546 |  | 4556 |  | 4566 |  | 4576 |  | 4587 |
|  | 4525 |  | 4536 |  | 4546 |  | 4556 |  | 4566 |  | 4577 |  | 4587 |
|  | 4526 |  | 4536 |  | 4546 |  | 4556 |  | 4567 |  | 4577 |  | 4587 |
|  | 4526 |  | 4536 |  | 4546 |  | 4557 |  | 4567 |  | 4577 |  | 4587 |
|  | 4526 |  | 4536 |  | 4547 |  | 4557 |  | 4567 |  | 4577 |  | 4588 |
|  | 4526 |  | 4537 |  | 4547 |  | 4557 |  | 4567 |  | 4578 |  | 4588 |
|  | 4527 |  | 4537 |  | 4547 |  | 4557 |  | 4568 |  | 4578 |  | 4588 |
|  | 4527 |  | 4537 |  | 4547 |  | 4558 |  | 4568 |  | 4578 |  | 4588 |
|  | 4527 |  | 4537 |  | 4548 |  | 4558 |  | 4568 |  | 4578 |  | 4589 |
|  | 4527 |  | 4538 |  | 4548 |  | 4558 |  | 4568 |  | 4579 |  | 4589 |
|  | 4528 |  | 4538 |  | 4548 |  | 4558 |  | 4569 |  | 4579 |  | 4589 |
|  | 4528 |  | 4538 |  | 4548 |  | 4559 |  | 4569 |  | 4579 |  | 4589 |
|  | 4528 |  | 4538 |  | 4549 |  | 4559 |  | 4569 |  | 4579 |  | 4590 |
|  | 4528 |  | 4539 |  | 4549 |  | 4559 |  | 4569 |  | 4580 |  | 4590 |
|  | 4529 |  | 4539 |  | 4549 |  | 4559 |  | 4570 |  | 4580 |  | 4590 |
|  | 4529 |  | 4539 |  | 4549 |  | 4560 |  | 4570 |  | 4580 |  | 4590 |
|  | 4529 |  | 4539 |  | 4550 |  | 4560 |  | 4570 |  | 4580 |  | 4591 |
|  | 4529 |  | 4540 |  | 4550 |  | 4560 |  | 4570 |  | 4581 |  | 4591 |
|  | 4530 |  | 4540 |  | 4550 |  | 4560 |  | 4571 |  | 4581 |  | 4591 |
|  | 4530 |  | 4540 |  | 4550 |  | 4561 |  | 4571 |  | 4581 |  | 4591 |
|  | 4530 |  | 4540 |  | 4551 |  | 4561 |  | 4571 |  | 4581 |  | 4592 |
|  | 4530 |  | 4541 |  | 4551 |  | 4561 |  | 4571 |  | 4582 |  | 4592 |
|  | 4531 |  | 4541 |  | 4551 |  | 4561 |  | 4572 |  | 4582 |  | 4592 |
|  | 4531 |  | 4541 |  | 4551 |  | 4562 |  | 4572 |  | 4582 |  | 4592 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl nb |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4593 | PPD | 4603 | PPD | 4613 | PPD | 4623 | PPD | 4634 | PPD | 4644 | PPD | 4654 |
|  | 4593 |  | 4603 |  | 4613 |  | 4624 |  | 4634 |  | 4644 |  | 4654 |
|  | 4593 |  | 4603 |  | 4614 |  | 4624 |  | 4634 |  | 4644 |  | 4655 |
|  | 4593 |  | 4604 |  | 4614 |  | 4624 |  | 4634 |  | 4645 |  | 4655 |
|  | 4594 |  | 4604 |  | 4614 |  | 4624 |  | 4635 |  | 4645 |  | 4655 |
|  | 4594 |  | 4604 |  | 4614 |  | 4625 |  | 4635 |  | 4645 |  | 4655 |
|  | 4594 |  | 4604 |  | 4615 |  | 4625 |  | 4635 |  | 4645 |  | 4656 |
|  | 4594 |  | 4605 |  | 4615 |  | 4625 |  | 4635 |  | 4646 |  | 4656 |
|  | 4595 |  | 4605 |  | 4615 |  | 4625 |  | 4636 |  | 4646 |  | 4656 |
|  | 4595 |  | 4605 |  | 4615 |  | 4626 |  | 4636 |  | 4646 |  | 4656 |
|  | 4595 |  | 4605 |  | 4616 |  | 4626 |  | 4636 |  | 4646 |  | 4657 |
|  | 4595 |  | 4606 |  | 4616 |  | 4626 |  | 4636 |  | 4647 |  | 4657 |
|  | 4596 |  | 4606 |  | 4616 |  | 4626 |  | 4637 |  | 4647 |  | 4657 |
|  | 4596 |  | 4606 |  | 4616 |  | 4627 |  | 4637 |  | 4647 |  | 4657 |
|  | 4596 |  | 4606 |  | 4617 |  | 4627 |  | 4637 |  | 4647 |  | 4658 |
|  | 4596 |  | 4607 |  | 4617 |  | 4627 |  | 4637 |  | 4648 |  | 4658 |
|  | 4597 |  | 4607 |  | 4617 |  | 4627 |  | 4638 |  | 4648 |  | 4658 |
|  | 4597 |  | 4607 |  | 4617 |  | 4628 |  | 4638 |  | 4648 |  | 4658 |
|  | 4597 |  | 4607 |  | 4618 |  | 4628 |  | 4638 |  | 4648 |  | 4659 |
|  | 4597 |  | 4608 |  | 4618 |  | 4628 |  | 4638 |  | 4649 |  | 4659 |
|  | 4598 |  | 4608 |  | 4618 |  | 4628 |  | 4639 |  | 4649 |  | 4659 |
|  | 4598 |  | 4608 |  | 4618 |  | 4629 |  | 4639 |  | 4649 |  | 4659 |
|  | 4598 |  | 4608 |  | 4619 |  | 4629 |  | 4639 |  | 4649 |  | 4660 |
|  | 4598 |  | 4609 |  | 4619 |  | 4629 |  | 4639 |  | 4650 |  | 4660 |
|  | 4599 |  | 4609 |  | 4619 |  | 4629 |  | 4640 |  | 4650 |  | 4660 |
|  | 4599 |  | 4609 |  | 4619 |  | 4630 |  | 4640 |  | 4650 |  | 4660 |
|  | 4599 |  | 4609 |  | 4620 |  | 4630 |  | 4640 |  | 4650 |  | 4661 |
|  | 4599 |  | 4610 |  | 4620 |  | 4630 |  | 4640 |  | 4651 |  | 4661 |
|  | 4600 |  | 4610 |  | 4620 |  | 4630 |  | 4641 |  | 4651 |  | 4661 |
|  | 4600 |  | 4610 |  | 4620 |  | 4631 |  | 4641 |  | 4651 |  | 4661 |
|  | 4600 |  | 4610 |  | 4621 |  | 4631 |  | 4641 |  | 4651 |  | 4662 |
|  | 4600 |  | 4611 |  | 4621 |  | 4631 |  | 4641 |  | 4652 |  | 4662 |
|  | 4601 |  | 4611 |  | 4621 |  | 4631 |  | 4642 |  | 4652 |  | 4662 |
|  | 4601 |  | 4611 |  | 4621 |  | 4632 |  | 4642 |  | 4652 |  | 4662 |
|  | 4601 |  | 4611 |  | 4622 |  | 4632 |  | 4642 |  | 4652 |  | 4663 |
|  | 4601 |  | 4612 |  | 4622 |  | 4632 |  | 4642 |  | 4653 |  | 4663 |
|  | 4602 |  | 4612 |  | 4622 |  | 4632 |  | 4643 |  | 4653 |  | 4663 |
|  | 4602 |  | 4612 |  | 4622 |  | 4633 |  | 4643 |  | 4653 |  | 4663 |
|  | 4602 |  | 4612 |  | 4623 |  | 4633 |  | 4643 |  | 4653 |  | 4664 |
|  | 4602 |  | 4613 |  | 4623 |  | 4633 |  | 4643 |  | 4654 |  | 4664 |
|  | 4603 |  | 4613 |  | 4623 |  | 4633 |  | 4644 |  | 4654 |  | 4664 |

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No n. } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4664 | PPD | 4675 | PPD | 4685 | PPD | 4695 | PPD | 4705 | PPD | 4716 | PPD | 4726 |
|  | 4665 |  | 4675 |  | 4685 |  | 4695 |  | 4706 |  | 4716 |  | 4726 |
|  | 4665 |  | 4675 |  | 4685 |  | 4696 |  | 4706 |  | 4716 |  | 4726 |
|  | 4665 |  | 4675 |  | 4686 |  | 4696 |  | 4706 |  | 4716 |  | 4727 |
|  | 4665 |  | 4676 |  | 4686 |  | 4696 |  | 4706 |  | 4717 |  | 4727 |
|  | 4666 |  | 4676 |  | 4686 |  | 4696 |  | 4707 |  | 4717 |  | 4727 |
|  | 4666 |  | 4676 |  | 4686 |  | 4697 |  | 4707 |  | 4717 |  | 4727 |
|  | 4666 |  | 4676 |  | 4687 |  | 4697 |  | 4707 |  | 4717 |  | 4728 |
|  | 4666 |  | 4677 |  | 4687 |  | 4697 |  | 4707 |  | 4718 |  | 4728 |
|  | 4667 |  | 4677 |  | 4687 |  | 4697 |  | 4708 |  | 4718 |  | 4728 |
|  | 4667 |  | 4677 |  | 4687 |  | 4698 |  | 4708 |  | 4718 |  | 4728 |
|  | 4667 |  | 4677 |  | 4688 |  | 4698 |  | 4708 |  | 4718 |  | 4729 |
|  | 4667 |  | 4678 |  | 4688 |  | 4698 |  | 4708 |  | 4719 |  | 4729 |
|  | 4668 |  | 4678 |  | 4688 |  | 4698 |  | 4709 |  | 4719 |  | 4729 |
|  | 4668 |  | 4678 |  | 4688 |  | 4699 |  | 4709 |  | 4719 |  | 4729 |
|  | 4668 |  | 4678 |  | 4689 |  | 4699 |  | 4709 |  | 4719 |  | 4730 |
|  | 4668 |  | 4679 |  | 4689 |  | 4699 |  | 4709 |  | 4720 |  | 4730 |
|  | 4669 |  | 4679 |  | 4689 |  | 4699 |  | 4710 |  | 4720 |  | 4730 |
|  | 4669 |  | 4679 |  | 4689 |  | 4700 |  | 4710 |  | 4720 |  | 4730 |
|  | 4669 |  | 4679 |  | 4690 |  | 4700 |  | 4710 |  | 4720 |  | 4731 |
|  | 4669 |  | 4680 |  | 4690 |  | 4700 |  | 4710 |  | 4721 |  | 4731 |
|  | 4670 |  | 4680 |  | 4690 |  | 4700 |  | 4711 |  | 4721 |  | 4731 |
|  | 4670 |  | 4680 |  | 4690 |  | 4701 |  | 4711 |  | 4721 |  | 4731 |
|  | 4670 |  | 4680 |  | 4691 |  | 4701 |  | 4711 |  | 4721 |  | 4732 |
|  | 4670 |  | 4681 |  | 4691 |  | 4701 |  | 4711 |  | 4722 |  | 4732 |
|  | 4671 |  | 4681 |  | 4691 |  | 4701 |  | 4712 |  | 4722 |  | 4732 |
|  | 4671 |  | 4681 |  | 4691 |  | 4702 |  | 4712 |  | 4722 |  | 4732 |
|  | 4671 |  | 4681 |  | 4692 |  | 4702 |  | 4712 |  | 4722 |  | 4733 |
|  | 4671 |  | 4682 |  | 4692 |  | 4702 |  | 4712 |  | 4723 |  | 4733 |
|  | 4672 |  | 4682 |  | 4692 |  | 4702 |  | 4713 |  | 4723 |  | 4733 |
|  | 4672 |  | 4682 |  | 4692 |  | 4703 |  | 4713 |  | 4723 |  | 4733 |
|  | 4672 |  | 4682 |  | 4693 |  | 4703 |  | 4713 |  | 4723 |  | 4734 |
|  | 4672 |  | 4683 |  | 4693 |  | 4703 |  | 4713 |  | 4724 |  | 4734 |
|  | 4673 |  | 4683 |  | 4693 |  | 4703 |  | 4714 |  | 4724 |  | 4734 |
|  | 4673 |  | 4683 |  | 4693 |  | 4704 |  | 4714 |  | 4724 |  | 4734 |
|  | 4673 |  | 4683 |  | 4694 |  | 4704 |  | 4714 |  | 4724 |  | 4735 |
|  | 4673 |  | 4684 |  | 4694 |  | 4704 |  | 4714 |  | 4725 |  | 4735 |
|  | 4674 |  | 4684 |  | 4694 |  | 4704 |  | 4715 |  | 4725 |  | 4735 |
|  | 4674 |  | 4684 |  | 4694 |  | 4705 |  | 4715 |  | 4725 |  | 4735 |
|  | 4674 |  | 4684 |  | 4695 |  | 4705 |  | 4715 |  | 4725 |  | 4736 |
|  | 4674 |  | 4685 |  | 4695 |  | 4705 |  | 4715 |  | 4726 |  | 4736 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl nb | Trt | Bl nb | Trt | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4736 | PPD | 4746 | PPD | 4757 | PPD | 4767 | PPD | 4777 | PPD | 4787 | PPD | 4798 |
|  | 4736 |  | 4747 |  | 4757 |  | 4767 |  | 4777 |  | 4788 |  | 4798 |
|  | 4737 |  | 4747 |  | 4757 |  | 4767 |  | 4778 |  | 4788 |  | 4798 |
|  | 4737 |  | 4747 |  | 4757 |  | 4768 |  | 4778 |  | 4788 |  | 4798 |
|  | 4737 |  | 4747 |  | 4758 |  | 4768 |  | 4778 |  | 4788 |  | 4799 |
|  | 4737 |  | 4748 |  | 4758 |  | 4768 |  | 4778 |  | 4789 |  | 4799 |
|  | 4738 |  | 4748 |  | 4758 |  | 4768 |  | 4779 |  | 4789 |  | 4799 |
|  | 4738 |  | 4748 |  | 4758 |  | 4769 |  | 4779 |  | 4789 |  | 4799 |
|  | 4738 |  | 4748 |  | 4759 |  | 4769 |  | 4779 |  | 4789 |  | 4800 |
|  | 4738 |  | 4749 |  | 4759 |  | 4769 |  | 4779 |  | 4790 |  | 4800 |
|  | 4739 |  | 4749 |  | 4759 |  | 4769 |  | 4780 |  | 4790 |  | 4800 |
|  | 4739 |  | 4749 |  | 4759 |  | 4770 |  | 4780 |  | 4790 |  | 4800 |
|  | 4739 |  | 4749 |  | 4760 |  | 4770 |  | 4780 |  | 4790 |  | 4801 |
|  | 4739 |  | 4750 |  | 4760 |  | 4770 |  | 4780 |  | 4791 |  | 4801 |
|  | 4740 |  | 4750 |  | 4760 |  | 4770 |  | 4781 |  | 4791 |  | 4801 |
|  | 4740 |  | 4750 |  | 4760 |  | 4771 |  | 4781 |  | 4791 |  | 4801 |
|  | 4740 |  | 4750 |  | 4761 |  | 4771 |  | 4781 |  | 4791 |  | 4802 |
|  | 4740 |  | 4751 |  | 4761 |  | 4771 |  | 4781 |  | 4792 |  | 4802 |
|  | 4741 |  | 4751 |  | 4761 |  | 4771 |  | 4782 |  | 4792 |  | 4802 |
|  | 4741 |  | 4751 |  | 4761 |  | 4772 |  | 4782 |  | 4792 |  | 4802 |
|  | 4741 |  | 4751 |  | 4762 |  | 4772 |  | 4782 |  | 4792 |  | 4803 |
|  | 4741 |  | 4752 |  | 4762 |  | 4772 |  | 4782 |  | 4793 |  | 4803 |
|  | 4742 |  | 4752 |  | 4762 |  | 4772 |  | 4783 |  | 4793 |  | 4803 |
|  | 4742 |  | 4752 |  | 4762 |  | 4773 |  | 4783 |  | 4793 |  | 4803 |
|  | 4742 |  | 4752 |  | 4763 |  | 4773 |  | 4783 |  | 4793 |  | 4804 |
|  | 4742 |  | 4753 |  | 4763 |  | 4773 |  | 4783 |  | 4794 |  | 4804 |
|  | 4743 |  | 4753 |  | 4763 |  | 4773 |  | 4784 |  | 4794 |  | 4804 |
|  | 4743 |  | 4753 |  | 4763 |  | 4774 |  | 4784 |  | 4794 |  | 4804 |
|  | 4743 |  | 4753 |  | 4764 |  | 4774 |  | 4784 |  | 4794 |  | 4805 |
|  | 4743 |  | 4754 |  | 4764 |  | 4774 |  | 4784 |  | 4795 |  | 4805 |
|  | 4744 |  | 4754 |  | 4764 |  | 4774 |  | 4785 |  | 4795 |  | 4805 |
|  | 4744 |  | 4754 |  | 4764 |  | 4775 |  | 4785 |  | 4795 |  | 4805 |
|  | 4744 |  | 4754 |  | 4765 |  | 4775 |  | 4785 |  | 4795 |  | 4806 |
|  | 4744 |  | 4755 |  | 4765 |  | 4775 |  | 4785 |  | 4796 |  | 4806 |
|  | 4745 |  | 4755 |  | 4765 |  | 4775 |  | 4786 |  | 4796 |  | 4806 |
|  | 4745 |  | 4755 |  | 4765 |  | 4776 |  | 4786 |  | 4796 |  | 4806 |
|  | 4745 |  | 4755 |  | 4766 |  | 4776 |  | 4786 |  | 4796 |  | 4807 |
|  | 4745 |  | 4756 |  | 4766 |  | 4776 |  | 4786 |  | 4797 |  | 4807 |
|  | 4746 |  | 4756 |  | 4766 |  | 4776 |  | 4787 |  | 4797 |  | 4807 |
|  | 4746 |  | 4756 |  | 4766 |  | 4777 |  | 4787 |  | 4797 |  | 4807 |
|  | 4746 |  | 4756 |  | 4767 |  | 4777 |  | 4787 |  | 4797 |  | 4808 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl. |  | Bl nb | Trt | Bl nb | Trt |  | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4808 | PPD | 4818 | PPD | 4828 | PPD | 4839 | PPD | 4849 | PPD | 4859 | PPD | 4869 |
|  | 4808 |  | 4818 |  | 4829 |  | 4839 |  | 4849 |  | 4859 |  | 4870 |
|  | 4808 |  | 4819 |  | 4829 |  | 4839 |  | 4849 |  | 4860 |  | 4870 |
|  | 4809 |  | 4819 |  | 4829 |  | 4839 |  | 4850 |  | 4860 |  | 4870 |
|  | 4809 |  | 4819 |  | 4829 |  | 4840 |  | 4850 |  | 4860 |  | 4870 |
|  | 4809 |  | 4819 |  | 4830 |  | 4840 |  | 4850 |  | 4860 |  | 4871 |
|  | 4809 |  | 4820 |  | 4830 |  | 4840 |  | 4850 |  | 4861 |  | 4871 |
|  | 4810 |  | 4820 |  | 4830 |  | 4840 |  | 4851 |  | 4861 |  | 4871 |
|  | 4810 |  | 4820 |  | 4830 |  | 4841 |  | 4851 |  | 4861 |  | 4871 |
|  | 4810 |  | 4820 |  | 4831 |  | 4841 |  | 4851 |  | 4861 |  | 4872 |
|  | 4810 |  | 4821 |  | 4831 |  | 4841 |  | 4851 |  | 4862 |  | 4872 |
|  | 4811 |  | 4821 |  | 4831 |  | 4841 |  | 4852 |  | 4862 |  | 4872 |
|  | 4811 |  | 4821 |  | 4831 |  | 4842 |  | 4852 |  | 4862 |  | 4872 |
|  | 4811 |  | 4821 |  | 4832 |  | 4842 |  | 4852 |  | 4862 |  | 4873 |
|  | 4811 |  | 4822 |  | 4832 |  | 4842 |  | 4852 |  | 4863 |  | 4873 |
|  | 4812 |  | 4822 |  | 4832 |  | 4842 |  | 4853 |  | 4863 |  | 4873 |
|  | 4812 |  | 4822 |  | 4832 |  | 4843 |  | 4853 |  | 4863 |  | 4873 |
|  | 4812 |  | 4822 |  | 4833 |  | 4843 |  | 4853 |  | 4863 |  | 4874 |
|  | 4812 |  | 4823 |  | 4833 |  | 4843 |  | 4853 |  | 4864 |  | 4874 |
|  | 4813 |  | 4823 |  | 4833 |  | 4843 |  | 4854 |  | 4864 |  | 4874 |
|  | 4813 |  | 4823 |  | 4833 |  | 4844 |  | 4854 |  | 4864 |  | 4874 |
|  | 4813 |  | 4823 |  | 4834 |  | 4844 |  | 4854 |  | 4864 |  | 4875 |
|  | 4813 |  | 4824 |  | 4834 |  | 4844 |  | 4854 |  | 4865 |  | 4875 |
|  | 4814 |  | 4824 |  | 4834 |  | 4844 |  | 4855 |  | 4865 |  | 4875 |
|  | 4814 |  | 4824 |  | 4834 |  | 4845 |  | 4855 |  | 4865 |  | 4875 |
|  | 4814 |  | 4824 |  | 4835 |  | 4845 |  | 4855 |  | 4865 |  | 4876 |
|  | 4814 |  | 4825 |  | 4835 |  | 4845 |  | 4855 |  | 4866 |  | 4876 |
|  | 4815 |  | 4825 |  | 4835 |  | 4845 |  | 4856 |  | 4866 |  | 4876 |
|  | 4815 |  | 4825 |  | 4835 |  | 4846 |  | 4856 |  | 4866 |  | 4876 |
|  | 4815 |  | 4825 |  | 4836 |  | 4846 |  | 4856 |  | 4866 |  | 4877 |
|  | 4815 |  | 4826 |  | 4836 |  | 4846 |  | 4856 |  | 4867 |  | 4877 |
|  | 4816 |  | 4826 |  | 4836 |  | 4846 |  | 4857 |  | 4867 |  | 4877 |
|  | 4816 |  | 4826 |  | 4836 |  | 4847 |  | 4857 |  | 4867 |  | 4877 |
|  | 4816 |  | 4826 |  | 4837 |  | 4847 |  | 4857 |  | 4867 |  | 4878 |
|  | 4816 |  | 4827 |  | 4837 |  | 4847 |  | 4857 |  | 4868 |  | 4878 |
|  | 4817 |  | 4827 |  | 4837 |  | 4847 |  | 4858 |  | 4868 |  | 4878 |
|  | 4817 |  | 4827 |  | 4837 |  | 4848 |  | 4858 |  | 4868 |  | 4878 |
|  | 4817 |  | 4827 |  | 4838 |  | 4848 |  | 4858 |  | 4868 |  | 4879 |
|  | 4817 |  | 4828 |  | 4838 |  | 4848 |  | 4858 |  | 4869 |  | 4879 |
|  | 4818 |  | 4828 |  | 4838 |  | 4848 |  | 4859 |  | 4869 |  | 4879 |
|  | 4818 |  | 4828 |  | 4838 |  | 4849 |  | 4859 |  | 4869 |  | 4879 |

Treatment number associated to material : HZ/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl nb |  | Bl nb | Trt | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4880 | PPD | 4890 | PPD | 4900 | PPD | 4910 | PPD | 4921 | PPD | 4931 | PPD | 4941 |
|  | 4880 |  | 4890 |  | 4900 |  | 4911 |  | 4921 |  | 4931 |  | 4941 |
|  | 4880 |  | 4890 |  | 4901 |  | 4911 |  | 4921 |  | 4931 |  | 4942 |
|  | 4880 |  | 4891 |  | 4901 |  | 4911 |  | 4921 |  | 4932 |  | 4942 |
|  | 4881 |  | 4891 |  | 4901 |  | 4911 |  | 4922 |  | 4932 |  | 4942 |
|  | 4881 |  | 4891 |  | 4901 |  | 4912 |  | 4922 |  | 4932 |  | 4942 |
|  | 4881 |  | 4891 |  | 4902 |  | 4912 |  | 4922 |  | 4932 |  | 4943 |
|  | 4881 |  | 4892 |  | 4902 |  | 4912 |  | 4922 |  | 4933 |  | 4943 |
|  | 4882 |  | 4892 |  | 4902 |  | 4912 |  | 4923 |  | 4933 |  | 4943 |
|  | 4882 |  | 4892 |  | 4902 |  | 4913 |  | 4923 |  | 4933 |  | 4943 |
|  | 4882 |  | 4892 |  | 4903 |  | 4913 |  | 4923 |  | 4933 |  | 4944 |
|  | 4882 |  | 4893 |  | 4903 |  | 4913 |  | 4923 |  | 4934 |  | 4944 |
|  | 4883 |  | 4893 |  | 4903 |  | 4913 |  | 4924 |  | 4934 |  | 4944 |
|  | 4883 |  | 4893 |  | 4903 |  | 4914 |  | 4924 |  | 4934 |  | 4944 |
|  | 4883 |  | 4893 |  | 4904 |  | 4914 |  | 4924 |  | 4934 |  | 4945 |
|  | 4883 |  | 4894 |  | 4904 |  | 4914 |  | 4924 |  | 4935 |  | 4945 |
|  | 4884 |  | 4894 |  | 4904 |  | 4914 |  | 4925 |  | 4935 |  | 4945 |
|  | 4884 |  | 4894 |  | 4904 |  | 4915 |  | 4925 |  | 4935 |  | 4945 |
|  | 4884 |  | 4894 |  | 4905 |  | 4915 |  | 4925 |  | 4935 |  | 4946 |
|  | 4884 |  | 4895 |  | 4905 |  | 4915 |  | 4925 |  | 4936 |  | 4946 |
|  | 4885 |  | 4895 |  | 4905 |  | 4915 |  | 4926 |  | 4936 |  | 4946 |
|  | 4885 |  | 4895 |  | 4905 |  | 4916 |  | 4926 |  | 4936 |  | 4946 |
|  | 4885 |  | 4895 |  | 4906 |  | 4916 |  | 4926 |  | 4936 |  | 4947 |
|  | 4885 |  | 4896 |  | 4906 |  | 4916 |  | 4926 |  | 4937 |  | 4947 |
|  | 4886 |  | 4896 |  | 4906 |  | 4916 |  | 4927 |  | 4937 |  | 4947 |
|  | 4886 |  | 4896 |  | 4906 |  | 4917 |  | 4927 |  | 4937 |  | 4947 |
|  | 4886 |  | 4896 |  | 4907 |  | 4917 |  | 4927 |  | 4937 |  | 4948 |
|  | 4886 |  | 4897 |  | 4907 |  | 4917 |  | 4927 |  | 4938 |  | 4948 |
|  | 4887 |  | 4897 |  | 4907 |  | 4917 |  | 4928 |  | 4938 |  | 4948 |
|  | 4887 |  | 4897 |  | 4907 |  | 4918 |  | 4928 |  | 4938 |  | 4948 |
|  | 4887 |  | 4897 |  | 4908 |  | 4918 |  | 4928 |  | 4938 |  | 4949 |
|  | 4887 |  | 4898 |  | 4908 |  | 4918 |  | 4928 |  | 4939 |  | 4949 |
|  | 4888 |  | 4898 |  | 4908 |  | 4918 |  | 4929 |  | 4939 |  | 4949 |
|  | 4888 |  | 4898 |  | 4908 |  | 4919 |  | 4929 |  | 4939 |  | 4949 |
|  | 4888 |  | 4898 |  | 4909 |  | 4919 |  | 4929 |  | 4939 |  | 4950 |
|  | 4888 |  | 4899 |  | 4909 |  | 4919 |  | 4929 |  | 4940 |  | 4950 |
|  | 4889 |  | 4899 |  | 4909 |  | 4919 |  | 4930 |  | 4940 |  | 4950 |
|  | 4889 |  | 4899 |  | 4909 |  | 4920 |  | 4930 |  | 4940 |  | 4950 |
|  | 4889 |  | 4899 |  | 4910 |  | 4920 |  | 4930 |  | 4940 |  | 4951 |
|  | 4889 |  | 4900 |  | 4910 |  | 4920 |  | 4930 |  | 4941 |  | 4951 |
|  | 4890 |  | 4900 |  | 4910 |  | 4920 |  | 4931 |  | 4941 |  | 4951 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl nb |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4951 | PPD | 4962 | PPD | 4972 | PPD | 4982 | PPD | 4992 | PPD | 5003 | PPD | 5013 |
|  | 4952 |  | 4962 |  | 4972 |  | 4982 |  | 4993 |  | 5003 |  | 5013 |
|  | 4952 |  | 4962 |  | 4972 |  | 4983 |  | 4993 |  | 5003 |  | 5013 |
|  | 4952 |  | 4962 |  | 4973 |  | 4983 |  | 4993 |  | 5003 |  | 5014 |
|  | 4952 |  | 4963 |  | 4973 |  | 4983 |  | 4993 |  | 5004 |  | 5014 |
|  | 4953 |  | 4963 |  | 4973 |  | 4983 |  | 4994 |  | 5004 |  | 5014 |
|  | 4953 |  | 4963 |  | 4973 |  | 4984 |  | 4994 |  | 5004 |  | 5014 |
|  | 4953 |  | 4963 |  | 4974 |  | 4984 |  | 4994 |  | 5004 |  | 5015 |
|  | 4953 |  | 4964 |  | 4974 |  | 4984 |  | 4994 |  | 5005 |  | 5015 |
|  | 4954 |  | 4964 |  | 4974 |  | 4984 |  | 4995 |  | 5005 |  | 5015 |
|  | 4954 |  | 4964 |  | 4974 |  | 4985 |  | 4995 |  | 5005 |  | 5015 |
|  | 4954 |  | 4964 |  | 4975 |  | 4985 |  | 4995 |  | 5005 |  | 5016 |
|  | 4954 |  | 4965 |  | 4975 |  | 4985 |  | 4995 |  | 5006 |  | 5016 |
|  | 4955 |  | 4965 |  | 4975 |  | 4985 |  | 4996 |  | 5006 |  | 5016 |
|  | 4955 |  | 4965 |  | 4975 |  | 4986 |  | 4996 |  | 5006 |  | 5016 |
|  | 4955 |  | 4965 |  | 4976 |  | 4986 |  | 4996 |  | 5006 |  | 5017 |
|  | 4955 |  | 4966 |  | 4976 |  | 4986 |  | 4996 |  | 5007 |  | 5017 |
|  | 4956 |  | 4966 |  | 4976 |  | 4986 |  | 4997 |  | 5007 |  | 5017 |
|  | 4956 |  | 4966 |  | 4976 |  | 4987 |  | 4997 |  | 5007 |  | 5017 |
|  | 4956 |  | 4966 |  | 4977 |  | 4987 |  | 4997 |  | 5007 |  | 5018 |
|  | 4956 |  | 4967 |  | 4977 |  | 4987 |  | 4997 |  | 5008 |  | 5018 |
|  | 4957 |  | 4967 |  | 4977 |  | 4987 |  | 4998 |  | 5008 |  | 5018 |
|  | 4957 |  | 4967 |  | 4977 |  | 4988 |  | 4998 |  | 5008 |  | 5018 |
|  | 4957 |  | 4967 |  | 4978 |  | 4988 |  | 4998 |  | 5008 |  | 5019 |
|  | 4957 |  | 4968 |  | 4978 |  | 4988 |  | 4998 |  | 5009 |  | 5019 |
|  | 4958 |  | 4968 |  | 4978 |  | 4988 |  | 4999 |  | 5009 |  | 5019 |
|  | 4958 |  | 4968 |  | 4978 |  | 4989 |  | 4999 |  | 5009 |  | 5019 |
|  | 4958 |  | 4968 |  | 4979 |  | 4989 |  | 4999 |  | 5009 |  | 5020 |
|  | 4958 |  | 4969 |  | 4979 |  | 4989 |  | 4999 |  | 5010 |  | 5020 |
|  | 4959 |  | 4969 |  | 4979 |  | 4989 |  | 5000 |  | 5010 |  | 5020 |
|  | 4959 |  | 4969 |  | 4979 |  | 4990 |  | 5000 |  | 5010 |  | 5020 |
|  | 4959 |  | 4969 |  | 4980 |  | 4990 |  | 5000 |  | 5010 |  | 5021 |
|  | 4959 |  | 4970 |  | 4980 |  | 4990 |  | 5000 |  | 5011 |  | 5021 |
|  | 4960 |  | 4970 |  | 4980 |  | 4990 |  | 5001 |  | 5011 |  | 5021 |
|  | 4960 |  | 4970 |  | 4980 |  | 4991 |  | 5001 |  | 5011 |  | 5021 |
|  | 4960 |  | 4970 |  | 4981 |  | 4991 |  | 5001 |  | 5011 |  | 5022 |
|  | 4960 |  | 4971 |  | 4981 |  | 4991 |  | 5001 |  | 5012 |  | 5022 |
|  | 4961 |  | 4971 |  | 4981 |  | 4991 |  | 5002 |  | 5012 |  | 5022 |
|  | 4961 |  | 4971 |  | 4981 |  | 4992 |  | 5002 |  | 5012 |  | 5022 |
|  | 4961 |  | 4971 |  | 4982 |  | 4992 |  | 5002 |  | 5012 |  | 5023 |
|  | 4961 |  | 4972 |  | 4982 |  | 4992 |  | 5002 |  | 5013 |  | 5023 |

SD4 4 RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| Trt. |  | Trt | Bl. |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | Trt |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5023 | PPD | 5033 | PPD | 5044 | PPD | 5054 | PPD | 5064 | PPD | 5074 | PPD | 5085 |
|  | 5023 |  | 5034 |  | 5044 |  | 5054 |  | 5064 |  | 5075 |  | 5085 |
|  | 5024 |  | 5034 |  | 5044 |  | 5054 |  | 5065 |  | 5075 |  | 5085 |
|  | 5024 |  | 5034 |  | 5044 |  | 5055 |  | 5065 |  | 5075 |  | 5085 |
|  | 5024 |  | 5034 |  | 5045 |  | 5055 |  | 5065 |  | 5075 |  | 5086 |
|  | 5024 |  | 5035 |  | 5045 |  | 5055 |  | 5065 |  | 5076 |  | 5086 |
|  | 5025 |  | 5035 |  | 5045 |  | 5055 |  | 5066 |  | 5076 |  | 5086 |
|  | 5025 |  | 5035 |  | 5045 |  | 5056 |  | 5066 |  | 5076 |  | 5086 |
|  | 5025 |  | 5035 |  | 5046 |  | 5056 |  | 5066 |  | 5076 |  | 5087 |
|  | 5025 |  | 5036 |  | 5046 |  | 5056 |  | 5066 |  | 5077 |  | 5087 |
|  | 5026 |  | 5036 |  | 5046 |  | 5056 |  | 5067 |  | 5077 |  | 5087 |
|  | 5026 |  | 5036 |  | 5046 |  | 5057 |  | 5067 |  | 5077 |  | 5087 |
|  | 5026 |  | 5036 |  | 5047 |  | 5057 |  | 5067 |  | 5077 |  | 5088 |
|  | 5026 |  | 5037 |  | 5047 |  | 5057 |  | 5067 |  | 5078 |  | 5088 |
|  | 5027 |  | 5037 |  | 5047 |  | 5057 |  | 5068 |  | 5078 |  | 5088 |
|  | 5027 |  | 5037 |  | 5047 |  | 5058 |  | 5068 |  | 5078 |  | 5088 |
|  | 5027 |  | 5037 |  | 5048 |  | 5058 |  | 5068 |  | 5078 |  | 5089 |
|  | 5027 |  | 5038 |  | 5048 |  | 5058 |  | 5068 |  | 5079 |  | 5089 |
|  | 5028 |  | 5038 |  | 5048 |  | 5058 |  | 5069 |  | 5079 |  | 5089 |
|  | 5028 |  | 5038 |  | 5048 |  | 5059 |  | 5069 |  | 5079 |  | 5089 |
|  | 5028 |  | 5038 |  | 5049 |  | 5059 |  | 5069 |  | 5079 |  | 5090 |
|  | 5028 |  | 5039 |  | 5049 |  | 5059 |  | 5069 |  | 5080 |  | 5090 |
|  | 5029 |  | 5039 |  | 5049 |  | 5059 |  | 5070 |  | 5080 |  | 5090 |
|  | 5029 |  | 5039 |  | 5049 |  | 5060 |  | 5070 |  | 5080 |  | 5090 |
|  | 5029 |  | 5039 |  | 5050 |  | 5060 |  | 5070 |  | 5080 |  | 5091 |
|  | 5029 |  | 5040 |  | 5050 |  | 5060 |  | 5070 |  | 5081 |  | 5091 |
|  | 5030 |  | 5040 |  | 5050 |  | 5060 |  | 5071 |  | 5081 |  | 5091 |
|  | 5030 |  | 5040 |  | 5050 |  | 5061 |  | 5071 |  | 5081 |  | 5091 |
|  | 5030 |  | 5040 |  | 5051 |  | 5061 |  | 5071 |  | 5081 |  | 5092 |
|  | 5030 |  | 5041 |  | 5051 |  | 5061 |  | 5071 |  | 5082 |  | 5092 |
|  | 5031 |  | 5041 |  | 5051 |  | 5061 |  | 5072 |  | 5082 |  | 5092 |
|  | 5031 |  | 5041 |  | 5051 |  | 5062 |  | 5072 |  | 5082 |  | 5092 |
|  | 5031 |  | 5041 |  | 5052 |  | 5062 |  | 5072 |  | 5082 |  | 5093 |
|  | 5031 |  | 5042 |  | 5052 |  | 5062 |  | 5072 |  | 5083 |  | 5093 |
|  | 5032 |  | 5042 |  | 5052 |  | 5062 |  | 5073 |  | 5083 |  | 5093 |
|  | 5032 |  | 5042 |  | 5052 |  | 5063 |  | 5073 |  | 5083 |  | 5093 |
|  | 5032 |  | 5042 |  | 5053 |  | 5063 |  | 5073 |  | 5083 |  | 5094 |
|  | 5032 |  | 5043 |  | 5053 |  | 5063 |  | 5073 |  | 5084 |  | 5094 |
|  | 5033 |  | 5043 |  | 5053 |  | 5063 |  | 5074 |  | 5084 |  | 5094 |
|  | 5033 |  | 5043 |  | 5053 |  | 5064 |  | 5074 |  | 5084 |  | 5094 |
|  | 5033 |  | 5043 |  | 5054 |  | 5064 |  | 5074 |  | 5084 |  | 5095 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5095 | PPD | 5105 | PPD | 5115 | PPD | 5126 | PPD | 5136 | PPD | 5146 | PPD | 5156 |
|  | 5095 |  | 5105 |  | 5116 |  | 5126 |  | 5136 |  | 5146 |  | 5157 |
|  | 5095 |  | 5106 |  | 5116 |  | 5126 |  | 5136 |  | 5147 |  | 5157 |
|  | 5096 |  | 5106 |  | 5116 |  | 5126 |  | 5137 |  | 5147 |  | 5157 |
|  | 5096 |  | 5106 |  | 5116 |  | 5127 |  | 5137 |  | 5147 |  | 5157 |
|  | 5096 |  | 5106 |  | 5117 |  | 5127 |  | 5137 |  | 5147 |  | 5158 |
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Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |
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Treatment number associated to material : Hz/su-PreChemo

| Trt. |  | Trt |  |  |  |  | $\mathrm{Bl} \text {. }$ | Trt | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
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SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. } \\ & \text { No nl. } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
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Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl . |  | Bl . |  |  | Trt |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
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|  | 5390 |  | 5400 |  | 5410 |  | 5420 |  | 5431 |  | 5441 |  | 5451 |
|  | 5390 |  | 5400 |  | 5410 |  | 5421 |  | 5431 |  | 5441 |  | 5451 |
|  | 5390 |  | 5400 |  | 5411 |  | 5421 |  | 5431 |  | 5441 |  | 5452 |
|  | 5390 |  | 5401 |  | 5411 |  | 5421 |  | 5431 |  | 5442 |  | 5452 |
|  | 5391 |  | 5401 |  | 5411 |  | 5421 |  | 5432 |  | 5442 |  | 5452 |
|  | 5391 |  | 5401 |  | 5411 |  | 5422 |  | 5432 |  | 5442 |  | 5452 |
|  | 5391 |  | 5401 |  | 5412 |  | 5422 |  | 5432 |  | 5442 |  | 5453 |
|  | 5391 |  | 5402 |  | 5412 |  | 5422 |  | 5432 |  | 5443 |  | 5453 |
|  | 5392 |  | 5402 |  | 5412 |  | 5422 |  | 5433 |  | 5443 |  | 5453 |
|  | 5392 |  | 5402 |  | 5412 |  | 5423 |  | 5433 |  | 5443 |  | 5453 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl nb |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5454 | PPD | 5464 | PPD | 5474 | PPD | 5484 | PPD | 5495 | PPD | 5505 | PPD | 5515 |
|  | 5454 |  | 5464 |  | 5474 |  | 5485 |  | 5495 |  | 5505 |  | 5515 |
|  | 5454 |  | 5464 |  | 5475 |  | 5485 |  | 5495 |  | 5505 |  | 5516 |
|  | 5454 |  | 5465 |  | 5475 |  | 5485 |  | 5495 |  | 5506 |  | 5516 |
|  | 5455 |  | 5465 |  | 5475 |  | 5485 |  | 5496 |  | 5506 |  | 5516 |
|  | 5455 |  | 5465 |  | 5475 |  | 5486 |  | 5496 |  | 5506 |  | 5516 |
|  | 5455 |  | 5465 |  | 5476 |  | 5486 |  | 5496 |  | 5506 |  | 5517 |
|  | 5455 |  | 5466 |  | 5476 |  | 5486 |  | 5496 |  | 5507 |  | 5517 |
|  | 5456 |  | 5466 |  | 5476 |  | 5486 |  | 5497 |  | 5507 |  | 5517 |
|  | 5456 |  | 5466 |  | 5476 |  | 5487 |  | 5497 |  | 5507 |  | 5517 |
|  | 5456 |  | 5466 |  | 5477 |  | 5487 |  | 5497 |  | 5507 |  | 5518 |
|  | 5456 |  | 5467 |  | 5477 |  | 5487 |  | 5497 |  | 5508 |  | 5518 |
|  | 5457 |  | 5467 |  | 5477 |  | 5487 |  | 5498 |  | 5508 |  | 5518 |
|  | 5457 |  | 5467 |  | 5477 |  | 5488 |  | 5498 |  | 5508 |  | 5518 |
|  | 5457 |  | 5467 |  | 5478 |  | 5488 |  | 5498 |  | 5508 |  | 5519 |
|  | 5457 |  | 5468 |  | 5478 |  | 5488 |  | 5498 |  | 5509 |  | 5519 |
|  | 5458 |  | 5468 |  | 5478 |  | 5488 |  | 5499 |  | 5509 |  | 5519 |
|  | 5458 |  | 5468 |  | 5478 |  | 5489 |  | 5499 |  | 5509 |  | 5519 |
|  | 5458 |  | 5468 |  | 5479 |  | 5489 |  | 5499 |  | 5509 |  | 5520 |
|  | 5458 |  | 5469 |  | 5479 |  | 5489 |  | 5499 |  | 5510 |  | 5520 |
|  | 5459 |  | 5469 |  | 5479 |  | 5489 |  | 5500 |  | 5510 |  | 5520 |
|  | 5459 |  | 5469 |  | 5479 |  | 5490 |  | 5500 |  | 5510 |  | 5520 |
|  | 5459 |  | 5469 |  | 5480 |  | 5490 |  | 5500 |  | 5510 |  | 5521 |
|  | 5459 |  | 5470 |  | 5480 |  | 5490 |  | 5500 |  | 5511 |  | 5521 |
|  | 5460 |  | 5470 |  | 5480 |  | 5490 |  | 5501 |  | 5511 |  | 5521 |
|  | 5460 |  | 5470 |  | 5480 |  | 5491 |  | 5501 |  | 5511 |  | 5521 |
|  | 5460 |  | 5470 |  | 5481 |  | 5491 |  | 5501 |  | 5511 |  | 5522 |
|  | 5460 |  | 5471 |  | 5481 |  | 5491 |  | 5501 |  | 5512 |  | 5522 |
|  | 5461 |  | 5471 |  | 5481 |  | 5491 |  | 5502 |  | 5512 |  | 5522 |
|  | 5461 |  | 5471 |  | 5481 |  | 5492 |  | 5502 |  | 5512 |  | 5522 |
|  | 5461 |  | 5471 |  | 5482 |  | 5492 |  | 5502 |  | 5512 |  | 5523 |
|  | 5461 |  | 5472 |  | 5482 |  | 5492 |  | 5502 |  | 5513 |  | 5523 |
|  | 5462 |  | 5472 |  | 5482 |  | 5492 |  | 5503 |  | 5513 |  | 5523 |
|  | 5462 |  | 5472 |  | 5482 |  | 5493 |  | 5503 |  | 5513 |  | 5523 |
|  | 5462 |  | 5472 |  | 5483 |  | 5493 |  | 5503 |  | 5513 |  | 5524 |
|  | 5462 |  | 5473 |  | 5483 |  | 5493 |  | 5503 |  | 5514 |  | 5524 |
|  | 5463 |  | 5473 |  | 5483 |  | 5493 |  | 5504 |  | 5514 |  | 5524 |
|  | 5463 |  | 5473 |  | 5483 |  | 5494 |  | 5504 |  | 5514 |  | 5524 |
|  | 5463 |  | 5473 |  | 5484 |  | 5494 |  | 5504 |  | 5514 |  | 5525 |
|  | 5463 |  | 5474 |  | 5484 |  | 5494 |  | 5504 |  | 5515 |  | 5525 |
|  | 5464 |  | 5474 |  | 5484 |  | 5494 |  | 5505 |  | 5515 |  | 5525 |

Treatment number associated to material : Hz/su-PreChemo

| $\begin{array}{r} \text { Trt. } \\ \text { N } \end{array}$ | $\mathrm{Bl} \mathrm{nb}^{\text {n }}$ | Trt |  | Trt | $\mathrm{Bl} \text {. }$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | Trt | $\mathrm{Bl} \text {. }$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5525 | PPD | 5536 | PPD | 5546 | PPD |  | PPD |  | PPD |  | PPD |  |
|  | 5526 | PPD | 5536 |  | 5546 |  | 5556 |  | 5567 |  | 5577 |  | 5587 |
|  | 5526 |  | 5536 |  | 5546 |  | 5557 |  | 5567 |  | 5577 |  | 5587 |
|  | 5526 |  | 5536 |  | 5547 |  | 5557 |  | 5567 |  | 5577 |  | 5588 |
|  | 5526 |  | 5537 |  | 5547 |  | 5557 |  | 5567 |  | 5578 |  | 5588 |
|  | 5527 |  | 5537 |  | 5547 |  | 5557 |  | 5568 |  | 5578 |  | 5588 |
|  | 5527 |  | 5537 |  | 5547 |  | 5558 |  | 5568 |  | 5578 |  | 5588 |
|  | 5527 |  | 5537 |  | 5548 |  | 5558 |  | 5568 |  | 5578 |  | 5589 |
|  | 5527 |  | 5538 |  | 5548 |  | 5558 |  | 5568 |  | 5579 |  | 5589 |
|  | 5528 |  | 5538 |  | 5548 |  | 5558 |  | 5569 |  | 5579 |  | 5589 |
|  | 5528 |  | 5538 |  | 5548 |  | 5559 |  | 5569 |  | 5579 |  | 5589 |
|  | 5528 |  | 5538 |  | 5549 |  | 5559 |  | 5569 |  | 5579 |  | 5590 |
|  | 5528 |  | 5539 |  | 5549 |  | 5559 |  | 5569 |  | 5580 |  | 5590 |
|  | 5529 |  | 5539 |  | 5549 |  | 5559 |  | 5570 |  | 5580 |  | 5590 |
|  | 5529 |  | 5539 |  | 5549 |  | 5560 |  | 5570 |  | 5580 |  | 5590 |
|  | 5529 |  | 5539 |  | 5550 |  | 5560 |  | 5570 |  | 5580 |  | 5591 |
|  | 5529 |  | 5540 |  | 5550 |  | 5560 |  | 5570 |  | 5581 |  | 5591 |
|  | 5530 |  | 5540 |  | 5550 |  | 5560 |  | 5571 |  | 5581 |  | 5591 |
|  | 5530 |  | 5540 |  | 5550 |  | 5561 |  | 5571 |  | 5581 |  | 5591 |
|  | 5530 |  | 5540 |  | 5551 |  | 5561 |  | 5571 |  | 5581 |  | 5592 |
|  | 5530 |  | 5541 |  | 5551 |  | 5561 |  | 5571 |  | 5582 |  | 5592 |
|  | 5531 |  | 5541 |  | 5551 |  | 5561 |  | 5572 |  | 5582 |  | 5592 |
|  | 5531 |  | 5541 |  | 5551 |  | 5562 |  | 5572 |  | 5582 |  | 5592 |
|  | 5531 |  | 5541 |  | 5552 |  | 5562 |  | 5572 |  | 5582 |  | 5593 |
|  | 5531 |  | 5542 |  | 5552 |  | 5562 |  | 5572 |  | 5583 |  | 5593 |
|  | 5532 |  | 5542 |  | 5552 |  | 5562 |  | 5573 |  | 5583 |  | 5593 |
|  | 5532 |  | 5542 |  | 5552 |  | 5563 |  | 5573 |  | 5583 |  | 5593 |
|  | 5532 |  | 5542 |  | 5553 |  | 5563 |  | 5573 |  | 5583 |  | 5594 |
|  | 5532 |  | 5543 |  | 5553 |  | 5563 |  | 5573 |  | 5584 |  | 5594 |
|  | 5533 |  | 5543 |  | 5553 |  | 5563 |  | 5574 |  | 5584 |  | 5594 |
|  | 5533 |  | 5543 |  | 5553 |  | 5564 |  | 5574 |  | 5584 |  | 5594 |
|  | 5533 |  | 5543 |  | 5554 |  | 5564 |  | 5574 |  | 5584 |  | 5595 |
|  | 5533 |  | 5544 |  | 5554 |  | 5564 |  | 5574 |  | 5585 |  | 5595 |
|  | 5534 |  | 5544 |  | 5554 |  | 5564 |  | 5575 |  | 5585 |  | 5595 |
|  | 5534 |  | 5544 |  | 5554 |  | 5565 |  | 5575 |  | 5585 |  | 5595 |
|  | 5534 |  | 5544 |  | 5555 |  | 5565 |  | 5575 |  | 5585 |  | 5596 |
|  | 5534 |  | 5545 |  | 5555 |  | 5565 |  | 5575 |  | 5586 |  | 5596 |
|  | 5535 |  | 5545 |  | 5555 |  | 5565 |  | 5576 |  | 5586 |  | 5596 |
|  | 5535 |  | 5545 |  | 5555 |  | 5566 |  | 5576 |  | 5586 |  | 5596 |
|  | 5535 |  | 5545 |  | 5556 |  | 5566 |  | 5576 |  | 5586 |  | 5597 |
|  | 5535 |  | 5546 |  | 5556 |  | 5566 |  | 5576 |  | 5587 |  | 5597 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  |  |  |  |  |  |  | $\mathrm{Bl} \text {. }$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD |  |  |  |  |  | PPD |  | PPD |  | PPD | 5648 | PPD | 5659 |
|  |  |  |  |  |  |  |  |  |  | 5649 |  | 5659 |
|  |  |  |  |  |  |  |  |  |  | 5649 |  | 5659 |
|  |  |  |  |  |  |  |  |  |  | 5649 |  | 5659 |
|  |  |  |  |  |  |  |  |  |  | 5649 |  | 5660 |
|  |  |  |  |  |  |  |  |  |  | 5650 |  | 5660 |
|  |  |  |  |  |  |  |  |  |  | 5650 |  | 5660 |
|  |  |  |  |  |  |  |  |  |  | 5650 |  | 5660 |
|  |  |  |  |  |  |  |  |  |  | 5650 |  | 5661 |
|  |  |  |  |  |  |  |  |  |  | 5651 |  | 5661 |
|  |  |  |  |  |  |  |  |  |  | 5651 |  | 5661 |
|  |  |  |  |  |  |  |  |  |  | 5651 |  | 5661 |
|  |  |  |  |  |  |  |  |  |  | 5651 |  | 5662 |
|  |  |  |  |  |  |  |  |  |  | 5652 |  | 5662 |
|  |  |  |  |  |  |  |  |  |  | 5652 |  | 5662 |
|  |  |  |  |  |  |  |  |  |  | 5652 |  | 5662 |
|  |  |  |  |  |  |  |  |  |  | 5652 |  | 5663 |
|  |  |  |  |  |  |  |  |  |  | 5653 |  | 5663 |
|  |  |  |  |  |  |  |  |  |  | 5653 |  | 5663 |
|  |  |  |  |  |  |  |  |  |  | 5653 |  | 5663 |
|  |  |  |  |  |  |  |  |  |  | 5653 |  | 5664 |
|  |  |  |  |  |  |  |  |  |  | 5654 |  | 5664 |
|  |  |  |  |  |  |  |  |  |  | 5654 |  | 5664 |
|  |  |  |  |  |  |  |  |  |  | 5654 |  | 5664 |
|  |  |  |  |  |  |  |  |  |  | 5654 |  | 5665 |
|  |  |  |  |  |  |  |  |  |  | 5655 |  | 5665 |
|  |  |  |  |  |  |  |  |  |  | 5655 |  | 5665 |
|  |  |  |  |  |  |  |  |  |  | 5655 |  | 5665 |
|  |  |  |  |  |  |  |  |  |  | 5655 |  | 5666 |
|  |  |  |  |  |  |  |  |  |  | 5656 |  | 5666 |
|  |  |  |  |  |  |  |  |  |  | 5656 |  | 5666 |
|  |  |  |  |  |  |  |  |  |  | 5656 |  | 5666 |
|  |  |  |  |  |  |  |  |  |  | 5656 |  | 5667 |
|  |  |  |  |  |  |  |  |  |  | 5657 |  | 5667 |
|  |  |  |  |  |  |  |  |  |  | 5657 |  | 5667 |
|  |  |  |  |  |  |  |  |  |  | 5657 |  | 5667 |
|  |  |  |  |  |  |  |  |  |  | 5657 |  | 5668 |
|  |  |  |  |  |  |  |  |  |  | 5658 |  | 5668 |
|  |  |  |  |  |  |  |  |  |  | 5658 |  | 5668 |
|  |  |  |  |  |  |  |  |  |  | 5658 |  | 5668 |
|  |  |  |  |  |  |  |  |  |  | 5658 |  | 5669 |

SD4 4 RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. | Trt |  | Trt |  | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5669 | PPD | 5679 | PPD | 5689 | PPD | 5700 | PPD | 5710 | PPD | 5720 | PPD | 5730 |
|  | 5669 |  | 5679 |  | 5690 |  | 5700 |  | 5710 |  | 5720 |  | 5731 |
|  | 5669 |  | 5680 |  | 5690 |  | 5700 |  | 5710 |  | 5721 |  | 5731 |
|  | 5670 |  | 5680 |  | 5690 |  | 5700 |  | 5711 |  | 5721 |  | 5731 |
|  | 5670 |  | 5680 |  | 5690 |  | 5701 |  | 5711 |  | 5721 |  | 5731 |
|  | 5670 |  | 5680 |  | 5691 |  | 5701 |  | 5711 |  | 5721 |  | 5732 |
|  | 5670 |  | 5681 |  | 5691 |  | 5701 |  | 5711 |  | 5722 |  | 5732 |
|  | 5671 |  | 5681 |  | 5691 |  | 5701 |  | 5712 |  | 5722 |  | 5732 |
|  | 5671 |  | 5681 |  | 5691 |  | 5702 |  | 5712 |  | 5722 |  | 5732 |
|  | 5671 |  | 5681 |  | 5692 |  | 5702 |  | 5712 |  | 5722 |  | 5733 |
|  | 5671 |  | 5682 |  | 5692 |  | 5702 |  | 5712 |  | 5723 |  | 5733 |
|  | 5672 |  | 5682 |  | 5692 |  | 5702 |  | 5713 |  | 5723 |  | 5733 |
|  | 5672 |  | 5682 |  | 5692 |  | 5703 |  | 5713 |  | 5723 |  | 5733 |
|  | 5672 |  | 5682 |  | 5693 |  | 5703 |  | 5713 |  | 5723 |  | 5734 |
|  | 5672 |  | 5683 |  | 5693 |  | 5703 |  | 5713 |  | 5724 |  | 5734 |
|  | 5673 |  | 5683 |  | 5693 |  | 5703 |  | 5714 |  | 5724 |  | 5734 |
|  | 5673 |  | 5683 |  | 5693 |  | 5704 |  | 5714 |  | 5724 |  | 5734 |
|  | 5673 |  | 5683 |  | 5694 |  | 5704 |  | 5714 |  | 5724 |  | 5735 |
|  | 5673 |  | 5684 |  | 5694 |  | 5704 |  | 5714 |  | 5725 |  | 5735 |
|  | 5674 |  | 5684 |  | 5694 |  | 5704 |  | 5715 |  | 5725 |  | 5735 |
|  | 5674 |  | 5684 |  | 5694 |  | 5705 |  | 5715 |  | 5725 |  | 5735 |
|  | 5674 |  | 5684 |  | 5695 |  | 5705 |  | 5715 |  | 5725 |  | 5736 |
|  | 5674 |  | 5685 |  | 5695 |  | 5705 |  | 5715 |  | 5726 |  | 5736 |
|  | 5675 |  | 5685 |  | 5695 |  | 5705 |  | 5716 |  | 5726 |  | 5736 |
|  | 5675 |  | 5685 |  | 5695 |  | 5706 |  | 5716 |  | 5726 |  | 5736 |
|  | 5675 |  | 5685 |  | 5696 |  | 5706 |  | 5716 |  | 5726 |  | 5737 |
|  | 5675 |  | 5686 |  | 5696 |  | 5706 |  | 5716 |  | 5727 |  | 5737 |
|  | 5676 |  | 5686 |  | 5696 |  | 5706 |  | 5717 |  | 5727 |  | 5737 |
|  | 5676 |  | 5686 |  | 5696 |  | 5707 |  | 5717 |  | 5727 |  | 5737 |
|  | 5676 |  | 5686 |  | 5697 |  | 5707 |  | 5717 |  | 5727 |  | 5738 |
|  | 5676 |  | 5687 |  | 5697 |  | 5707 |  | 5717 |  | 5728 |  | 5738 |
|  | 5677 |  | 5687 |  | 5697 |  | 5707 |  | 5718 |  | 5728 |  | 5738 |
|  | 5677 |  | 5687 |  | 5697 |  | 5708 |  | 5718 |  | 5728 |  | 5738 |
|  | 5677 |  | 5687 |  | 5698 |  | 5708 |  | 5718 |  | 5728 |  | 5739 |
|  | 5677 |  | 5688 |  | 5698 |  | 5708 |  | 5718 |  | 5729 |  | 5739 |
|  | 5678 |  | 5688 |  | 5698 |  | 5708 |  | 5719 |  | 5729 |  | 5739 |
|  | 5678 |  | 5688 |  | 5698 |  | 5709 |  | 5719 |  | 5729 |  | 5739 |
|  | 5678 |  | 5688 |  | 5699 |  | 5709 |  | 5719 |  | 5729 |  | 5740 |
|  | 5678 |  | 5689 |  | 5699 |  | 5709 |  | 5719 |  | 5730 |  | 5740 |
|  | 5679 |  | 5689 |  | 5699 |  | 5709 |  | 5720 |  | 5730 |  | 5740 |
|  | 5679 |  | 5689 |  | 5699 |  | 5710 |  | 5720 |  | 5730 |  | 5740 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| Trt. |  |  | Bl nb |  | Bl nb |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | Trt | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5741 | PPD | 5751 | PPD | 5761 | PPD | 5771 | PPD | 5782 | PPD | 5792 | PPD | 5802 |
|  | 5741 |  | 5751 |  | 5761 |  | 5772 |  | 5782 |  | 5792 |  | 5802 |
|  | 5741 |  | 5751 |  | 5762 |  | 5772 |  | 5782 |  | 5792 |  | 5803 |
|  | 5741 |  | 5752 |  | 5762 |  | 5772 |  | 5782 |  | 5793 |  | 5803 |
|  | 5742 |  | 5752 |  | 5762 |  | 5772 |  | 5783 |  | 5793 |  | 5803 |
|  | 5742 |  | 5752 |  | 5762 |  | 5773 |  | 5783 |  | 5793 |  | 5803 |
|  | 5742 |  | 5752 |  | 5763 |  | 5773 |  | 5783 |  | 5793 |  | 5804 |
|  | 5742 |  | 5753 |  | 5763 |  | 5773 |  | 5783 |  | 5794 |  | 5804 |
|  | 5743 |  | 5753 |  | 5763 |  | 5773 |  | 5784 |  | 5794 |  | 5804 |
|  | 5743 |  | 5753 |  | 5763 |  | 5774 |  | 5784 |  | 5794 |  | 5804 |
|  | 5743 |  | 5753 |  | 5764 |  | 5774 |  | 5784 |  | 5794 |  | 5805 |
|  | 5743 |  | 5754 |  | 5764 |  | 5774 |  | 5784 |  | 5795 |  | 5805 |
|  | 5744 |  | 5754 |  | 5764 |  | 5774 |  | 5785 |  | 5795 |  | 5805 |
|  | 5744 |  | 5754 |  | 5764 |  | 5775 |  | 5785 |  | 5795 |  | 5805 |
|  | 5744 |  | 5754 |  | 5765 |  | 5775 |  | 5785 |  | 5795 |  | 5806 |
|  | 5744 |  | 5755 |  | 5765 |  | 5775 |  | 5785 |  | 5796 |  | 5806 |
|  | 5745 |  | 5755 |  | 5765 |  | 5775 |  | 5786 |  | 5796 |  | 5806 |
|  | 5745 |  | 5755 |  | 5765 |  | 5776 |  | 5786 |  | 5796 |  | 5806 |
|  | 5745 |  | 5755 |  | 5766 |  | 5776 |  | 5786 |  | 5796 |  | 5807 |
|  | 5745 |  | 5756 |  | 5766 |  | 5776 |  | 5786 |  | 5797 |  | 5807 |
|  | 5746 |  | 5756 |  | 5766 |  | 5776 |  | 5787 |  | 5797 |  | 5807 |
|  | 5746 |  | 5756 |  | 5766 |  | 5777 |  | 5787 |  | 5797 |  | 5807 |
|  | 5746 |  | 5756 |  | 5767 |  | 5777 |  | 5787 |  | 5797 |  | 5808 |
|  | 5746 |  | 5757 |  | 5767 |  | 5777 |  | 5787 |  | 5798 |  | 5808 |
|  | 5747 |  | 5757 |  | 5767 |  | 5777 |  | 5788 |  | 5798 |  | 5808 |
|  | 5747 |  | 5757 |  | 5767 |  | 5778 |  | 5788 |  | 5798 |  | 5808 |
|  | 5747 |  | 5757 |  | 5768 |  | 5778 |  | 5788 |  | 5798 |  | 5809 |
|  | 5747 |  | 5758 |  | 5768 |  | 5778 |  | 5788 |  | 5799 |  | 5809 |
|  | 5748 |  | 5758 |  | 5768 |  | 5778 |  | 5789 |  | 5799 |  | 5809 |
|  | 5748 |  | 5758 |  | 5768 |  | 5779 |  | 5789 |  | 5799 |  | 5809 |
|  | 5748 |  | 5758 |  | 5769 |  | 5779 |  | 5789 |  | 5799 |  | 5810 |
|  | 5748 |  | 5759 |  | 5769 |  | 5779 |  | 5789 |  | 5800 |  | 5810 |
|  | 5749 |  | 5759 |  | 5769 |  | 5779 |  | 5790 |  | 5800 |  | 5810 |
|  | 5749 |  | 5759 |  | 5769 |  | 5780 |  | 5790 |  | 5800 |  | 5810 |
|  | 5749 |  | 5759 |  | 5770 |  | 5780 |  | 5790 |  | 5800 |  | 5811 |
|  | 5749 |  | 5760 |  | 5770 |  | 5780 |  | 5790 |  | 5801 |  | 5811 |
|  | 5750 |  | 5760 |  | 5770 |  | 5780 |  | 5791 |  | 5801 |  | 5811 |
|  | 5750 |  | 5760 |  | 5770 |  | 5781 |  | 5791 |  | 5801 |  | 5811 |
|  | 5750 |  | 5760 |  | 5771 |  | 5781 |  | 5791 |  | 5801 |  | 5812 |
|  | 5750 |  | 5761 |  | 5771 |  | 5781 |  | 5791 |  | 5802 |  | 5812 |
|  | 5751 |  | 5761 |  | 5771 |  | 5781 |  | 5792 |  | 5802 |  | 5812 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5812 | PPD | 5823 | PPD | 5833 | PPD | 5843 | PPD | 5853 | PPD | 5864 | PPD | 5874 |
|  | 5813 |  | 5823 |  | 5833 |  | 5843 |  | 5854 |  | 5864 |  | 5874 |
|  | 5813 |  | 5823 |  | 5833 |  | 5844 |  | 5854 |  | 5864 |  | 5874 |
|  | 5813 |  | 5823 |  | 5834 |  | 5844 |  | 5854 |  | 5864 |  | 5875 |
|  | 5813 |  | 5824 |  | 5834 |  | 5844 |  | 5854 |  | 5865 |  | 5875 |
|  | 5814 |  | 5824 |  | 5834 |  | 5844 |  | 5855 |  | 5865 |  | 5875 |
|  | 5814 |  | 5824 |  | 5834 |  | 5845 |  | 5855 |  | 5865 |  | 5875 |
|  | 5814 |  | 5824 |  | 5835 |  | 5845 |  | 5855 |  | 5865 |  | 5876 |
|  | 5814 |  | 5825 |  | 5835 |  | 5845 |  | 5855 |  | 5866 |  | 5876 |
|  | 5815 |  | 5825 |  | 5835 |  | 5845 |  | 5856 |  | 5866 |  | 5876 |
|  | 5815 |  | 5825 |  | 5835 |  | 5846 |  | 5856 |  | 5866 |  | 5876 |
|  | 5815 |  | 5825 |  | 5836 |  | 5846 |  | 5856 |  | 5866 |  | 5877 |
|  | 5815 |  | 5826 |  | 5836 |  | 5846 |  | 5856 |  | 5867 |  | 5877 |
|  | 5816 |  | 5826 |  | 5836 |  | 5846 |  | 5857 |  | 5867 |  | 5877 |
|  | 5816 |  | 5826 |  | 5836 |  | 5847 |  | 5857 |  | 5867 |  | 5877 |
|  | 5816 |  | 5826 |  | 5837 |  | 5847 |  | 5857 |  | 5867 |  | 5878 |
|  | 5816 |  | 5827 |  | 5837 |  | 5847 |  | 5857 |  | 5868 |  | 5878 |
|  | 5817 |  | 5827 |  | 5837 |  | 5847 |  | 5858 |  | 5868 |  | 5878 |
|  | 5817 |  | 5827 |  | 5837 |  | 5848 |  | 5858 |  | 5868 |  | 5878 |
|  | 5817 |  | 5827 |  | 5838 |  | 5848 |  | 5858 |  | 5868 |  | 5879 |
|  | 5817 |  | 5828 |  | 5838 |  | 5848 |  | 5858 |  | 5869 |  | 5879 |
|  | 5818 |  | 5828 |  | 5838 |  | 5848 |  | 5859 |  | 5869 |  | 5879 |
|  | 5818 |  | 5828 |  | 5838 |  | 5849 |  | 5859 |  | 5869 |  | 5879 |
|  | 5818 |  | 5828 |  | 5839 |  | 5849 |  | 5859 |  | 5869 |  | 5880 |
|  | 5818 |  | 5829 |  | 5839 |  | 5849 |  | 5859 |  | 5870 |  | 5880 |
|  | 5819 |  | 5829 |  | 5839 |  | 5849 |  | 5860 |  | 5870 |  | 5880 |
|  | 5819 |  | 5829 |  | 5839 |  | 5850 |  | 5860 |  | 5870 |  | 5880 |
|  | 5819 |  | 5829 |  | 5840 |  | 5850 |  | 5860 |  | 5870 |  | 5881 |
|  | 5819 |  | 5830 |  | 5840 |  | 5850 |  | 5860 |  | 5871 |  | 5881 |
|  | 5820 |  | 5830 |  | 5840 |  | 5850 |  | 5861 |  | 5871 |  | 5881 |
|  | 5820 |  | 5830 |  | 5840 |  | 5851 |  | 5861 |  | 5871 |  | 5881 |
|  | 5820 |  | 5830 |  | 5841 |  | 5851 |  | 5861 |  | 5871 |  | 5882 |
|  | 5820 |  | 5831 |  | 5841 |  | 5851 |  | 5861 |  | 5872 |  | 5882 |
|  | 5821 |  | 5831 |  | 5841 |  | 5851 |  | 5862 |  | 5872 |  | 5882 |
|  | 5821 |  | 5831 |  | 5841 |  | 5852 |  | 5862 |  | 5872 |  | 5882 |
|  | 5821 |  | 5831 |  | 5842 |  | 5852 |  | 5862 |  | 5872 |  | 5883 |
|  | 5821 |  | 5832 |  | 5842 |  | 5852 |  | 5862 |  | 5873 |  | 5883 |
|  | 5822 |  | 5832 |  | 5842 |  | 5852 |  | 5863 |  | 5873 |  | 5883 |
|  | 5822 |  | 5832 |  | 5842 |  | 5853 |  | 5863 |  | 5873 |  | 5883 |
|  | 5822 |  | 5832 |  | 5843 |  | 5853 |  | 5863 |  | 5873 |  | 5884 |
|  | 5822 |  | 5833 |  | 5843 |  | 5853 |  | 5863 |  | 5874 |  | 5884 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl nb |  | Bl nb |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD |  |  |  |  |  | PPD |  | PPD |  | PPD | 5935 | PPD | 5946 |
|  |  |  |  |  |  |  |  |  |  | 5936 | 5946 |  |
|  |  |  |  |  |  |  |  |  |  | 5936 | 5946 |  |
|  |  |  |  |  |  |  |  |  |  | 5936 | 5946 |  |
|  |  |  |  |  |  |  |  |  |  | 5936 | 5947 |  |
|  |  |  |  |  |  |  |  |  |  | 5937 | 5947 |  |
|  |  |  |  |  |  |  |  |  |  | 5937 | 5947 |  |
|  |  |  |  |  |  |  |  |  |  | 5937 | 5947 |  |
|  |  |  |  |  |  |  |  |  |  | 5937 | 5948 |  |
|  |  |  |  |  |  |  |  |  |  | 5938 | 5948 |  |
|  |  |  |  |  |  |  |  |  |  | 5938 | 5948 |  |
|  |  |  |  |  |  |  |  |  |  | 5938 | 5948 |  |
|  |  |  |  |  |  |  |  |  |  | 5938 | 5949 |  |
|  |  |  |  |  |  |  |  |  |  | 5939 | 5949 |  |
|  |  |  |  |  |  |  |  |  |  | 5939 | 5949 |  |
|  |  |  |  |  |  |  |  |  |  | 5939 | 5949 |  |
|  |  |  |  |  |  |  |  |  |  | 5939 | 5950 |  |
|  |  |  |  |  |  |  |  |  |  | 5940 | 5950 |  |
|  |  |  |  |  |  |  |  |  |  | 5940 | 5950 |  |
|  |  |  |  |  |  |  |  |  |  | 5940 | 5950 |  |
|  |  |  |  |  |  |  |  |  |  | 5940 | 5951 |  |
|  |  |  |  |  |  |  |  |  |  | 5941 | 5951 |  |
|  |  |  |  |  |  |  |  |  |  | 5941 | 5951 |  |
|  |  |  |  |  |  |  |  |  |  | 5941 | 5951 |  |
|  |  |  |  |  |  |  |  |  |  | 5941 | 5952 |  |
|  |  |  |  |  |  |  |  |  |  | 5942 | 5952 |  |
|  |  |  |  |  |  |  |  |  |  | 5942 | 5952 |  |
|  |  |  |  |  |  |  |  |  |  | 5942 | 5952 |  |
|  |  |  |  |  |  |  |  |  |  | 5942 | 5953 |  |
|  |  |  |  |  |  |  |  |  |  | 5943 | 5953 |  |
|  |  |  |  |  |  |  |  |  |  | 5943 | 5953 |  |
|  |  |  |  |  |  |  |  |  |  | 5943 | 5953 |  |
|  |  |  |  |  |  |  |  |  |  | 5943 | 5954 |  |
|  |  |  |  |  |  |  |  |  |  | 5944 | 5954 |  |
|  |  |  |  |  |  |  |  |  |  | 5944 | 5954 |  |
|  |  |  |  |  |  |  |  |  |  | 5944 | 5954 |  |
|  |  |  |  |  |  |  |  |  |  | 5944 | 5955 |  |
|  |  |  |  |  |  |  |  |  |  | 5945 | 5955 |  |
|  |  |  |  |  |  |  |  |  |  | 5945 | 5955 |  |
|  |  |  |  |  |  |  |  |  |  | 5945 | 5955 |  |
|  |  |  |  |  |  |  |  |  |  | 5945 | 5956 |  |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-PreChemo


SD4 $\backslash$ RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \operatorname{Trt} \\ \mathrm{N} \end{array}$ |  | Trt. Bl. <br> No nb |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1 | PPD | 11 | PPD | 21 | PPD | 31 | PPD | 42 | PPD | 52 | PPD | 62 |
|  | 1 |  | 11 |  | 21 |  | 32 |  | 42 |  | 52 |  | 62 |
|  | 1 |  | 11 |  | 22 |  | 32 |  | 42 |  | 52 |  | 63 |
|  | 1 |  | 12 |  | 22 |  | 32 |  | 42 |  | 53 |  | 63 |
|  | 2 |  | 12 |  | 22 |  | 32 |  | 43 |  | 53 |  | 63 |
|  | 2 |  | 12 |  | 22 |  | 33 |  | 43 |  | 53 |  | 63 |
|  | 2 |  | 12 |  | 23 |  | 33 |  | 43 |  | 53 |  | 64 |
|  | 2 |  | 13 |  | 23 |  | 33 |  | 43 |  | 54 |  | 64 |
|  | 3 |  | 13 |  | 23 |  | 33 |  | 44 |  | 54 |  | 64 |
|  | 3 |  | 13 |  | 23 |  | 34 |  | 44 |  | 54 |  | 64 |
|  | 3 |  | 13 |  | 24 |  | 34 |  | 44 |  | 54 |  | 65 |
|  | 3 |  | 14 |  | 24 |  | 34 |  | 44 |  | 55 |  | 65 |
|  | 4 |  | 14 |  | 24 |  | 34 |  | 45 |  | 55 |  | 65 |
|  | 4 |  | 14 |  | 24 |  | 35 |  | 45 |  | 55 |  | 65 |
|  | 4 |  | 14 |  | 25 |  | 35 |  | 45 |  | 55 |  | 66 |
|  | 4 |  | 15 |  | 25 |  | 35 |  | 45 |  | 56 |  | 66 |
|  | 5 |  | 15 |  | 25 |  | 35 |  | 46 |  | 56 |  | 66 |
|  | 5 |  | 15 |  | 25 |  | 36 |  | 46 |  | 56 |  | 66 |
|  | 5 |  | 15 |  | 26 |  | 36 |  | 46 |  | 56 |  | 67 |
|  | 5 |  | 16 |  | 26 |  | 36 |  | 46 |  | 57 |  | 67 |
|  | 6 |  | 16 |  | 26 |  | 36 |  | 47 |  | 57 |  | 67 |
|  | 6 |  | 16 |  | 26 |  | 37 |  | 47 |  | 57 |  | 67 |
|  | 6 |  | 16 |  | 27 |  | 37 |  | 47 |  | 57 |  | 68 |
|  | 6 |  | 17 |  | 27 |  | 37 |  | 47 |  | 58 |  | 68 |
|  | 7 |  | 17 |  | 27 |  | 37 |  | 48 |  | 58 |  | 68 |
|  | 7 |  | 17 |  | 27 |  | 38 |  | 48 |  | 58 |  | 68 |
|  | 7 |  | 17 |  | 28 |  | 38 |  | 48 |  | 58 |  | 69 |
|  | 7 |  | 18 |  | 28 |  | 38 |  | 48 |  | 59 |  | 69 |
|  | 8 |  | 18 |  | 28 |  | 38 |  | 49 |  | 59 |  | 69 |
|  | 8 |  | 18 |  | 28 |  | 39 |  | 49 |  | 59 |  | 69 |
|  | 8 |  | 18 |  | 29 |  | 39 |  | 49 |  | 59 |  | 70 |
|  | 8 |  | 19 |  | 29 |  | 39 |  | 49 |  | 60 |  | 70 |
|  | 9 |  | 19 |  | 29 |  | 39 |  | 50 |  | 60 |  | 70 |
|  | 9 |  | 19 |  | 29 |  | 40 |  | 50 |  | 60 |  | 70 |
|  | 9 |  | 19 |  | 30 |  | 40 |  | 50 |  | 60 |  | 71 |
|  | 9 |  | 20 |  | 30 |  | 40 |  | 50 |  | 61 |  | 71 |
|  | 10 |  | 20 |  | 30 |  | 40 |  | 51 |  | 61 |  | 71 |
|  | 10 |  | 20 |  | 30 |  | 41 |  | 51 |  | 61 |  | 71 |
|  | 10 |  | 20 |  | 31 |  | 41 |  | 51 |  | 61 |  | 72 |
|  | 10 |  | 21 |  | 31 |  | 41 |  | 51 |  | 62 |  | 72 |
|  | 11 |  | 21 |  | 31 |  | 41 |  | 52 |  | 62 |  | 72 |

SD4\RDE\ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \operatorname{Trt} \\ \mathrm{N} \end{array}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | Trt. Bl. |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 72 | PPD | 83 | PPD | 93 | PPD | 103 | PPD | 113 | PPD | 124 | PPD | 134 |
|  | 73 |  | 83 |  | 93 |  | 103 |  | 114 |  | 124 |  | 134 |
|  | 73 |  | 83 |  | 93 |  | 104 |  | 114 |  | 124 |  | 134 |
|  | 73 |  | 83 |  | 94 |  | 104 |  | 114 |  | 124 |  | 135 |
|  | 73 |  | 84 |  | 94 |  | 104 |  | 114 |  | 125 |  | 135 |
|  | 74 |  | 84 |  | 94 |  | 104 |  | 115 |  | 125 |  | 135 |
|  | 74 |  | 84 |  | 94 |  | 105 |  | 115 |  | 125 |  | 135 |
|  | 74 |  | 84 |  | 95 |  | 105 |  | 115 |  | 125 |  | 136 |
|  | 74 |  | 85 |  | 95 |  | 105 |  | 115 |  | 126 |  | 136 |
|  | 75 |  | 85 |  | 95 |  | 105 |  | 116 |  | 126 |  | 136 |
|  | 75 |  | 85 |  | 95 |  | 106 |  | 116 |  | 126 |  | 136 |
|  | 75 |  | 85 |  | 96 |  | 106 |  | 116 |  | 126 |  | 137 |
|  | 75 |  | 86 |  | 96 |  | 106 |  | 116 |  | 127 |  | 137 |
|  | 76 |  | 86 |  | 96 |  | 106 |  | 117 |  | 127 |  | 137 |
|  | 76 |  | 86 |  | 96 |  | 107 |  | 117 |  | 127 |  | 137 |
|  | 76 |  | 86 |  | 97 |  | 107 |  | 117 |  | 127 |  | 138 |
|  | 76 |  | 87 |  | 97 |  | 107 |  | 117 |  | 128 |  | 138 |
|  | 77 |  | 87 |  | 97 |  | 107 |  | 118 |  | 128 |  | 138 |
|  | 77 |  | 87 |  | 97 |  | 108 |  | 118 |  | 128 |  | 138 |
|  | 77 |  | 87 |  | 98 |  | 108 |  | 118 |  | 128 |  | 139 |
|  | 77 |  | 88 |  | 98 |  | 108 |  | 118 |  | 129 |  | 139 |
|  | 78 |  | 88 |  | 98 |  | 108 |  | 119 |  | 129 |  | 139 |
|  | 78 |  | 88 |  | 98 |  | 109 |  | 119 |  | 129 |  | 139 |
|  | 78 |  | 88 |  | 99 |  | 109 |  | 119 |  | 129 |  | 140 |
|  | 78 |  | 89 |  | 99 |  | 109 |  | 119 |  | 130 |  | 140 |
|  | 79 |  | 89 |  | 99 |  | 109 |  | 120 |  | 130 |  | 140 |
|  | 79 |  | 89 |  | 99 |  | 110 |  | 120 |  | 130 |  | 140 |
|  | 79 |  | 89 |  | 100 |  | 110 |  | 120 |  | 130 |  | 141 |
|  | 79 |  | 90 |  | 100 |  | 110 |  | 120 |  | 131 |  | 141 |
|  | 80 |  | 90 |  | 100 |  | 110 |  | 121 |  | 131 |  | 141 |
|  | 80 |  | 90 |  | 100 |  | 111 |  | 121 |  | 131 |  | 141 |
|  | 80 |  | 90 |  | 101 |  | 111 |  | 121 |  | 131 |  | 142 |
|  | 80 |  | 91 |  | 101 |  | 111 |  | 121 |  | 132 |  | 142 |
|  | 81 |  | 91 |  | 101 |  | 111 |  | 122 |  | 132 |  | 142 |
|  | 81 |  | 91 |  | 101 |  | 112 |  | 122 |  | 132 |  | 142 |
|  | 81 |  | 91 |  | 102 |  | 112 |  | 122 |  | 132 |  | 143 |
|  | 81 |  | 92 |  | 102 |  | 112 |  | 122 |  | 133 |  | 143 |
|  | 82 |  | 92 |  | 102 |  | 112 |  | 123 |  | 133 |  | 143 |
|  | 82 |  | 92 |  | 102 |  | 113 |  | 123 |  | 133 |  | 143 |
|  | 82 |  | 92 |  | 103 |  | 113 |  | 123 |  | 133 |  | 144 |
|  | 82 |  | 93 |  | 103 |  | 113 |  | 123 |  | 134 |  | 144 |

SD4\RDE\ENABLE
ZOSTER-028 (A.10FEB2017)

Randomisation list

Treatment number associated to material : Placeb-PreChemo

| Trt. No |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Tret. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 144 | PPD | 154 | PPD | 165 | PPD | 175 | PPD | 185 | PPD | 195 | PPD | 206 |
|  | 144 |  | 155 |  | 165 |  | 175 |  | 185 |  | 196 |  | 206 |
|  | 145 |  | 155 |  | 165 |  | 175 |  | 186 |  | 196 |  | 206 |
|  | 145 |  | 155 |  | 165 |  | 176 |  | 186 |  | 196 |  | 206 |
|  | 145 |  | 155 |  | 166 |  | 176 |  | 186 |  | 196 |  | 207 |
|  | 145 |  | 156 |  | 166 |  | 176 |  | 186 |  | 197 |  | 207 |
|  | 146 |  | 156 |  | 166 |  | 176 |  | 187 |  | 197 |  | 207 |
|  | 146 |  | 156 |  | 166 |  | 177 |  | 187 |  | 197 |  | 207 |
|  | 146 |  | 156 |  | 167 |  | 177 |  | 187 |  | 197 |  | 208 |
|  | 146 |  | 157 |  | 167 |  | 177 |  | 187 |  | 198 |  | 208 |
|  | 147 |  | 157 |  | 167 |  | 177 |  | 188 |  | 198 |  | 208 |
|  | 147 |  | 157 |  | 167 |  | 178 |  | 188 |  | 198 |  | 208 |
|  | 147 |  | 157 |  | 168 |  | 178 |  | 188 |  | 198 |  | 209 |
|  | 147 |  | 158 |  | 168 |  | 178 |  | 188 |  | 199 |  | 209 |
|  | 148 |  | 158 |  | 168 |  | 178 |  | 189 |  | 199 |  | 209 |
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SD4\RDE\ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | Trt. Bl.No nb |  | Trt. Bl.No nb |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
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SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Tret. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. } \mathrm{Bl} . \\ & \text { No nb } \end{aligned}$ |  |
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SD4\RDE\ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \operatorname{Trt} \\ \mathrm{N} \end{array}$ |  | Trt. Bl.No nb |  | Trt. Bl. No nb |  | Trt. Bl. |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | Trt. Bl. |  |
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| PPD | 359 | PPD | 370 | PPD | 380 | PPD | 390 | PPD | 400 | PPD | 411 | PPD | 421 |
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|  | 365 |  | 375 |  | 386 |  | 396 |  | 406 |  | 416 |  | 427 |
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SD4\RDE\ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \operatorname{Trt} \\ \mathrm{N} \end{array}$ | Bl . | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Tret. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
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| PPD | 431 | PPD | 441 | PPD | 452 | PPD | 462 | PPD | 472 | PPD | 482 | PPD | 493 |
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SD4 $\backslash$ RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Randomisation list

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{aligned} & \text { Tret. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{gathered} \text { Trt. } \\ \text { No nb. } \end{gathered}$ |  |
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|  | 508 |  | 518 |  | 528 |  | 539 |  | 549 |  | 559 |  | 569 |
|  | 508 |  | 518 |  | 529 |  | 539 |  | 549 |  | 559 |  | 570 |
|  | 508 |  | 519 |  | 529 |  | 539 |  | 549 |  | 560 |  | 570 |
|  | 509 |  | 519 |  | 529 |  | 539 |  | 550 |  | 560 |  | 570 |
|  | 509 |  | 519 |  | 529 |  | 540 |  | 550 |  | 560 |  | 570 |
|  | 509 |  | 519 |  | 530 |  | 540 |  | 550 |  | 560 |  | 571 |
|  | 509 |  | 520 |  | 530 |  | 540 |  | 550 |  | 561 |  | 571 |
|  | 510 |  | 520 |  | 530 |  | 540 |  | 551 |  | 561 |  | 571 |
|  | 510 |  | 520 |  | 530 |  | 541 |  | 551 |  | 561 |  | 571 |
|  | 510 |  | 520 |  | 531 |  | 541 |  | 551 |  | 561 |  | 572 |
|  | 510 |  | 521 |  | 531 |  | 541 |  | 551 |  | 562 |  | 572 |
|  | 511 |  | 521 |  | 531 |  | 541 |  | 552 |  | 562 |  | 572 |
|  | 511 |  | 521 |  | 531 |  | 542 |  | 552 |  | 562 |  | 572 |
|  | 511 |  | 521 |  | 532 |  | 542 |  | 552 |  | 562 |  | 573 |
|  | 511 |  | 522 |  | 532 |  | 542 |  | 552 |  | 563 |  | 573 |
|  | 512 |  | 522 |  | 532 |  | 542 |  | 553 |  | 563 |  | 573 |
|  | 512 |  | 522 |  | 532 |  | 543 |  | 553 |  | 563 |  | 573 |
|  | 512 |  | 522 |  | 533 |  | 543 |  | 553 |  | 563 |  | 574 |
|  | 512 |  | 523 |  | 533 |  | 543 |  | 553 |  | 564 |  | 574 |
|  | 513 |  | 523 |  | 533 |  | 543 |  | 554 |  | 564 |  | 574 |
|  | 513 |  | 523 |  | 533 |  | 544 |  | 554 |  | 564 |  | 574 |

SD4\RDE\ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \text { Trt } \\ \mathrm{N} \end{array}$ | Bl nb | $\begin{aligned} & \text { Tret. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. } \\ & \text { No nl. } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. } \mathrm{Bl} . \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Tret. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 575 | PPD | 585 | PPD | 595 | PPD | 605 | PPD | 616 | PPD | 626 | PPD | 636 |
|  | 575 |  | 585 |  | 595 |  | 606 |  | 616 |  | 626 |  | 636 |
|  | 575 |  | 585 |  | 596 |  | 606 |  | 616 |  | 626 |  | 637 |
|  | 575 |  | 586 |  | 596 |  | 606 |  | 616 |  | 627 |  | 637 |
|  | 576 |  | 586 |  | 596 |  | 606 |  | 617 |  | 627 |  | 637 |
|  | 576 |  | 586 |  | 596 |  | 607 |  | 617 |  | 627 |  | 637 |
|  | 576 |  | 586 |  | 597 |  | 607 |  | 617 |  | 627 |  | 638 |
|  | 576 |  | 587 |  | 597 |  | 607 |  | 617 |  | 628 |  | 638 |
|  | 577 |  | 587 |  | 597 |  | 607 |  | 618 |  | 628 |  | 638 |
|  | 577 |  | 587 |  | 597 |  | 608 |  | 618 |  | 628 |  | 638 |
|  | 577 |  | 587 |  | 598 |  | 608 |  | 618 |  | 628 |  | 639 |
|  | 577 |  | 588 |  | 598 |  | 608 |  | 618 |  | 629 |  | 639 |
|  | 578 |  | 588 |  | 598 |  | 608 |  | 619 |  | 629 |  | 639 |
|  | 578 |  | 588 |  | 598 |  | 609 |  | 619 |  | 629 |  | 639 |
|  | 578 |  | 588 |  | 599 |  | 609 |  | 619 |  | 629 |  | 640 |
|  | 578 |  | 589 |  | 599 |  | 609 |  | 619 |  | 630 |  | 640 |
|  | 579 |  | 589 |  | 599 |  | 609 |  | 620 |  | 630 |  | 640 |
|  | 579 |  | 589 |  | 599 |  | 610 |  | 620 |  | 630 |  | 640 |
|  | 579 |  | 589 |  | 600 |  | 610 |  | 620 |  | 630 |  | 641 |
|  | 579 |  | 590 |  | 600 |  | 610 |  | 620 |  | 631 |  | 641 |
|  | 580 |  | 590 |  | 600 |  | 610 |  | 621 |  | 631 |  | 641 |
|  | 580 |  | 590 |  | 600 |  | 611 |  | 621 |  | 631 |  | 641 |
|  | 580 |  | 590 |  | 601 |  | 611 |  | 621 |  | 631 |  | 642 |
|  | 580 |  | 591 |  | 601 |  | 611 |  | 621 |  | 632 |  | 642 |
|  | 581 |  | 591 |  | 601 |  | 611 |  | 622 |  | 632 |  | 642 |
|  | 581 |  | 591 |  | 601 |  | 612 |  | 622 |  | 632 |  | 642 |
|  | 581 |  | 591 |  | 602 |  | 612 |  | 622 |  | 632 |  | 643 |
|  | 581 |  | 592 |  | 602 |  | 612 |  | 622 |  | 633 |  | 643 |
|  | 582 |  | 592 |  | 602 |  | 612 |  | 623 |  | 633 |  | 643 |
|  | 582 |  | 592 |  | 602 |  | 613 |  | 623 |  | 633 |  | 643 |
|  | 582 |  | 592 |  | 603 |  | 613 |  | 623 |  | 633 |  | 644 |
|  | 582 |  | 593 |  | 603 |  | 613 |  | 623 |  | 634 |  | 644 |
|  | 583 |  | 593 |  | 603 |  | 613 |  | 624 |  | 634 |  | 644 |
|  | 583 |  | 593 |  | 603 |  | 614 |  | 624 |  | 634 |  | 644 |
|  | 583 |  | 593 |  | 604 |  | 614 |  | 624 |  | 634 |  | 645 |
|  | 583 |  | 594 |  | 604 |  | 614 |  | 624 |  | 635 |  | 645 |
|  | 584 |  | 594 |  | 604 |  | 614 |  | 625 |  | 635 |  | 645 |
|  | 584 |  | 594 |  | 604 |  | 615 |  | 625 |  | 635 |  | 645 |
|  | 584 |  | 594 |  | 605 |  | 615 |  | 625 |  | 635 |  | 646 |
|  | 584 |  | 595 |  | 605 |  | 615 |  | 625 |  | 636 |  | 646 |
|  | 585 |  | 595 |  | 605 |  | 615 |  | 626 |  | 636 |  | 646 |

SD4 $\backslash$ RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Randomisation list

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \text { Trt. } \\ \text { N } \end{array}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | Trt. Bl.No nb |  | Trt. Bl. |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | Trt. Bl. <br> No nb |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 646 | PPD | 657 | PPD | 667 | PPD | 677 | PPD | 687 | PPD | 698 | PPD | 708 |
|  | 647 |  | 657 |  | 667 |  | 677 |  | 688 |  | 698 |  | 708 |
|  | 647 |  | 657 |  | 667 |  | 678 |  | 688 |  | 698 |  | 708 |
|  | 647 |  | 657 |  | 668 |  | 678 |  | 688 |  | 698 |  | 709 |
|  | 647 |  | 658 |  | 668 |  | 678 |  | 688 |  | 699 |  | 709 |
|  | 648 |  | 658 |  | 668 |  | 678 |  | 689 |  | 699 |  | 709 |
|  | 648 |  | 658 |  | 668 |  | 679 |  | 689 |  | 699 |  | 709 |
|  | 648 |  | 658 |  | 669 |  | 679 |  | 689 |  | 699 |  | 710 |
|  | 648 |  | 659 |  | 669 |  | 679 |  | 689 |  | 700 |  | 710 |
|  | 649 |  | 659 |  | 669 |  | 679 |  | 690 |  | 700 |  | 710 |
|  | 649 |  | 659 |  | 669 |  | 680 |  | 690 |  | 700 |  | 710 |
|  | 649 |  | 659 |  | 670 |  | 680 |  | 690 |  | 700 |  | 711 |
|  | 649 |  | 660 |  | 670 |  | 680 |  | 690 |  | 701 |  | 711 |
|  | 650 |  | 660 |  | 670 |  | 680 |  | 691 |  | 701 |  | 711 |
|  | 650 |  | 660 |  | 670 |  | 681 |  | 691 |  | 701 |  | 711 |
|  | 650 |  | 660 |  | 671 |  | 681 |  | 691 |  | 701 |  | 712 |
|  | 650 |  | 661 |  | 671 |  | 681 |  | 691 |  | 702 |  | 712 |
|  | 651 |  | 661 |  | 671 |  | 681 |  | 692 |  | 702 |  | 712 |
|  | 651 |  | 661 |  | 671 |  | 682 |  | 692 |  | 702 |  | 712 |
|  | 651 |  | 661 |  | 672 |  | 682 |  | 692 |  | 702 |  | 713 |
|  | 651 |  | 662 |  | 672 |  | 682 |  | 692 |  | 703 |  | 713 |
|  | 652 |  | 662 |  | 672 |  | 682 |  | 693 |  | 703 |  | 713 |
|  | 652 |  | 662 |  | 672 |  | 683 |  | 693 |  | 703 |  | 713 |
|  | 652 |  | 662 |  | 673 |  | 683 |  | 693 |  | 703 |  | 714 |
|  | 652 |  | 663 |  | 673 |  | 683 |  | 693 |  | 704 |  | 714 |
|  | 653 |  | 663 |  | 673 |  | 683 |  | 694 |  | 704 |  | 714 |
|  | 653 |  | 663 |  | 673 |  | 684 |  | 694 |  | 704 |  | 714 |
|  | 653 |  | 663 |  | 674 |  | 684 |  | 694 |  | 704 |  | 715 |
|  | 653 |  | 664 |  | 674 |  | 684 |  | 694 |  | 705 |  | 715 |
|  | 654 |  | 664 |  | 674 |  | 684 |  | 695 |  | 705 |  | 715 |
|  | 654 |  | 664 |  | 674 |  | 685 |  | 695 |  | 705 |  | 715 |
|  | 654 |  | 664 |  | 675 |  | 685 |  | 695 |  | 705 |  | 716 |
|  | 654 |  | 665 |  | 675 |  | 685 |  | 695 |  | 706 |  | 716 |
|  | 655 |  | 665 |  | 675 |  | 685 |  | 696 |  | 706 |  | 716 |
|  | 655 |  | 665 |  | 675 |  | 686 |  | 696 |  | 706 |  | 716 |
|  | 655 |  | 665 |  | 676 |  | 686 |  | 696 |  | 706 |  | 717 |
|  | 655 |  | 666 |  | 676 |  | 686 |  | 696 |  | 707 |  | 717 |
|  | 656 |  | 666 |  | 676 |  | 686 |  | 697 |  | 707 |  | 717 |
|  | 656 |  | 666 |  | 676 |  | 687 |  | 697 |  | 707 |  | 717 |
|  | 656 |  | 666 |  | 677 |  | 687 |  | 697 |  | 707 |  | 718 |
|  | 656 |  | 667 |  | 677 |  | 687 |  | 697 |  | 708 |  | 718 |

SD4 $\backslash$ RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Randomisation list

Treatment number associated to material : Placeb-PreChemo

| Trt. |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Tret. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 718 | PPD | 728 | PPD | 739 | PPD | 749 | PPD | 759 | PPD | 769 | PPD | 780 |
|  | 718 |  | 729 |  | 739 |  | 749 |  | 759 |  | 770 |  | 780 |
|  | 719 |  | 729 |  | 739 |  | 749 |  | 760 |  | 770 |  | 780 |
|  | 719 |  | 729 |  | 739 |  | 750 |  | 760 |  | 770 |  | 780 |
|  | 719 |  | 729 |  | 740 |  | 750 |  | 760 |  | 770 |  | 781 |
|  | 719 |  | 730 |  | 740 |  | 750 |  | 760 |  | 771 |  | 781 |
|  | 720 |  | 730 |  | 740 |  | 750 |  | 761 |  | 771 |  | 781 |
|  | 720 |  | 730 |  | 740 |  | 751 |  | 761 |  | 771 |  | 781 |
|  | 720 |  | 730 |  | 741 |  | 751 |  | 761 |  | 771 |  | 782 |
|  | 720 |  | 731 |  | 741 |  | 751 |  | 761 |  | 772 |  | 782 |
|  | 721 |  | 731 |  | 741 |  | 751 |  | 762 |  | 772 |  | 782 |
|  | 721 |  | 731 |  | 741 |  | 752 |  | 762 |  | 772 |  | 782 |
|  | 721 |  | 731 |  | 742 |  | 752 |  | 762 |  | 772 |  | 783 |
|  | 721 |  | 732 |  | 742 |  | 752 |  | 762 |  | 773 |  | 783 |
|  | 722 |  | 732 |  | 742 |  | 752 |  | 763 |  | 773 |  | 783 |
|  | 722 |  | 732 |  | 742 |  | 753 |  | 763 |  | 773 |  | 783 |
|  | 722 |  | 732 |  | 743 |  | 753 |  | 763 |  | 773 |  | 784 |
|  | 722 |  | 733 |  | 743 |  | 753 |  | 763 |  | 774 |  | 784 |
|  | 723 |  | 733 |  | 743 |  | 753 |  | 764 |  | 774 |  | 784 |
|  | 723 |  | 733 |  | 743 |  | 754 |  | 764 |  | 774 |  | 784 |
|  | 723 |  | 733 |  | 744 |  | 754 |  | 764 |  | 774 |  | 785 |
|  | 723 |  | 734 |  | 744 |  | 754 |  | 764 |  | 775 |  | 785 |
|  | 724 |  | 734 |  | 744 |  | 754 |  | 765 |  | 775 |  | 785 |
|  | 724 |  | 734 |  | 744 |  | 755 |  | 765 |  | 775 |  | 785 |
|  | 724 |  | 734 |  | 745 |  | 755 |  | 765 |  | 775 |  | 786 |
|  | 724 |  | 735 |  | 745 |  | 755 |  | 765 |  | 776 |  | 786 |
|  | 725 |  | 735 |  | 745 |  | 755 |  | 766 |  | 776 |  | 786 |
|  | 725 |  | 735 |  | 745 |  | 756 |  | 766 |  | 776 |  | 786 |
|  | 725 |  | 735 |  | 746 |  | 756 |  | 766 |  | 776 |  | 787 |
|  | 725 |  | 736 |  | 746 |  | 756 |  | 766 |  | 777 |  | 787 |
|  | 726 |  | 736 |  | 746 |  | 756 |  | 767 |  | 777 |  | 787 |
|  | 726 |  | 736 |  | 746 |  | 757 |  | 767 |  | 777 |  | 787 |
|  | 726 |  | 736 |  | 747 |  | 757 |  | 767 |  | 777 |  | 788 |
|  | 726 |  | 737 |  | 747 |  | 757 |  | 767 |  | 778 |  | 788 |
|  | 727 |  | 737 |  | 747 |  | 757 |  | 768 |  | 778 |  | 788 |
|  | 727 |  | 737 |  | 747 |  | 758 |  | 768 |  | 778 |  | 788 |
|  | 727 |  | 737 |  | 748 |  | 758 |  | 768 |  | 778 |  | 789 |
|  | 727 |  | 738 |  | 748 |  | 758 |  | 768 |  | 779 |  | 789 |
|  | 728 |  | 738 |  | 748 |  | 758 |  | 769 |  | 779 |  | 789 |
|  | 728 |  | 738 |  | 748 |  | 759 |  | 769 |  | 779 |  | 789 |
|  | 728 |  | 738 |  | 749 |  | 759 |  | 769 |  | 779 |  | 790 |

SD4 $\backslash$ RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \operatorname{Trt} \\ \mathrm{N} \end{array}$ | Bl. nb | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. } \mathrm{Bl} . \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 790 | PPD | 800 | PPD | 810 | PPD | 821 | PPD | 831 | PPD | 841 | PPD | 851 |
|  | 790 |  | 800 |  | 811 |  | 821 |  | 831 |  | 841 |  | 852 |
|  | 790 |  | 801 |  | 811 |  | 821 |  | 831 |  | 842 |  | 852 |
|  | 791 |  | 801 |  | 811 |  | 821 |  | 832 |  | 842 |  | 852 |
|  | 791 |  | 801 |  | 811 |  | 822 |  | 832 |  | 842 |  | 852 |
|  | 791 |  | 801 |  | 812 |  | 822 |  | 832 |  | 842 |  | 853 |
|  | 791 |  | 802 |  | 812 |  | 822 |  | 832 |  | 843 |  | 853 |
|  | 792 |  | 802 |  | 812 |  | 822 |  | 833 |  | 843 |  | 853 |
|  | 792 |  | 802 |  | 812 |  | 823 |  | 833 |  | 843 |  | 853 |
|  | 792 |  | 802 |  | 813 |  | 823 |  | 833 |  | 843 |  | 854 |
|  | 792 |  | 803 |  | 813 |  | 823 |  | 833 |  | 844 |  | 854 |
|  | 793 |  | 803 |  | 813 |  | 823 |  | 834 |  | 844 |  | 854 |
|  | 793 |  | 803 |  | 813 |  | 824 |  | 834 |  | 844 |  | 854 |
|  | 793 |  | 803 |  | 814 |  | 824 |  | 834 |  | 844 |  | 855 |
|  | 793 |  | 804 |  | 814 |  | 824 |  | 834 |  | 845 |  | 855 |
|  | 794 |  | 804 |  | 814 |  | 824 |  | 835 |  | 845 |  | 855 |
|  | 794 |  | 804 |  | 814 |  | 825 |  | 835 |  | 845 |  | 855 |
|  | 794 |  | 804 |  | 815 |  | 825 |  | 835 |  | 845 |  | 856 |
|  | 794 |  | 805 |  | 815 |  | 825 |  | 835 |  | 846 |  | 856 |
|  | 795 |  | 805 |  | 815 |  | 825 |  | 836 |  | 846 |  | 856 |
|  | 795 |  | 805 |  | 815 |  | 826 |  | 836 |  | 846 |  | 856 |
|  | 795 |  | 805 |  | 816 |  | 826 |  | 836 |  | 846 |  | 857 |
|  | 795 |  | 806 |  | 816 |  | 826 |  | 836 |  | 847 |  | 857 |
|  | 796 |  | 806 |  | 816 |  | 826 |  | 837 |  | 847 |  | 857 |
|  | 796 |  | 806 |  | 816 |  | 827 |  | 837 |  | 847 |  | 857 |
|  | 796 |  | 806 |  | 817 |  | 827 |  | 837 |  | 847 |  | 858 |
|  | 796 |  | 807 |  | 817 |  | 827 |  | 837 |  | 848 |  | 858 |
|  | 797 |  | 807 |  | 817 |  | 827 |  | 838 |  | 848 |  | 858 |
|  | 797 |  | 807 |  | 817 |  | 828 |  | 838 |  | 848 |  | 858 |
|  | 797 |  | 807 |  | 818 |  | 828 |  | 838 |  | 848 |  | 859 |
|  | 797 |  | 808 |  | 818 |  | 828 |  | 838 |  | 849 |  | 859 |
|  | 798 |  | 808 |  | 818 |  | 828 |  | 839 |  | 849 |  | 859 |
|  | 798 |  | 808 |  | 818 |  | 829 |  | 839 |  | 849 |  | 859 |
|  | 798 |  | 808 |  | 819 |  | 829 |  | 839 |  | 849 |  | 860 |
|  | 798 |  | 809 |  | 819 |  | 829 |  | 839 |  | 850 |  | 860 |
|  | 799 |  | 809 |  | 819 |  | 829 |  | 840 |  | 850 |  | 860 |
|  | 799 |  | 809 |  | 819 |  | 830 |  | 840 |  | 850 |  | 860 |
|  | 799 |  | 809 |  | 820 |  | 830 |  | 840 |  | 850 |  | 861 |
|  | 799 |  | 810 |  | 820 |  | 830 |  | 840 |  | 851 |  | 861 |
|  | 800 |  | 810 |  | 820 |  | 830 |  | 841 |  | 851 |  | 861 |
|  | 800 |  | 810 |  | 820 |  | 831 |  | 841 |  | 851 |  | 861 |

SD4 $\backslash$ RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Randomisation list

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Tret. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 862 | PPD | 872 | PPD | 882 | PPD | 892 | PPD | 903 | PPD | 913 | PPD | 923 |
|  | 862 |  | 872 |  | 882 |  | 893 |  | 903 |  | 913 |  | 923 |
|  | 862 |  | 872 |  | 883 |  | 893 |  | 903 |  | 913 |  | 924 |
|  | 862 |  | 873 |  | 883 |  | 893 |  | 903 |  | 914 |  | 924 |
|  | 863 |  | 873 |  | 883 |  | 893 |  | 904 |  | 914 |  | 924 |
|  | 863 |  | 873 |  | 883 |  | 894 |  | 904 |  | 914 |  | 924 |
|  | 863 |  | 873 |  | 884 |  | 894 |  | 904 |  | 914 |  | 925 |
|  | 863 |  | 874 |  | 884 |  | 894 |  | 904 |  | 915 |  | 925 |
|  | 864 |  | 874 |  | 884 |  | 894 |  | 905 |  | 915 |  | 925 |
|  | 864 |  | 874 |  | 884 |  | 895 |  | 905 |  | 915 |  | 925 |
|  | 864 |  | 874 |  | 885 |  | 895 |  | 905 |  | 915 |  | 926 |
|  | 864 |  | 875 |  | 885 |  | 895 |  | 905 |  | 916 |  | 926 |
|  | 865 |  | 875 |  | 885 |  | 895 |  | 906 |  | 916 |  | 926 |
|  | 865 |  | 875 |  | 885 |  | 896 |  | 906 |  | 916 |  | 926 |
|  | 865 |  | 875 |  | 886 |  | 896 |  | 906 |  | 916 |  | 927 |
|  | 865 |  | 876 |  | 886 |  | 896 |  | 906 |  | 917 |  | 927 |
|  | 866 |  | 876 |  | 886 |  | 896 |  | 907 |  | 917 |  | 927 |
|  | 866 |  | 876 |  | 886 |  | 897 |  | 907 |  | 917 |  | 927 |
|  | 866 |  | 876 |  | 887 |  | 897 |  | 907 |  | 917 |  | 928 |
|  | 866 |  | 877 |  | 887 |  | 897 |  | 907 |  | 918 |  | 928 |
|  | 867 |  | 877 |  | 887 |  | 897 |  | 908 |  | 918 |  | 928 |
|  | 867 |  | 877 |  | 887 |  | 898 |  | 908 |  | 918 |  | 928 |
|  | 867 |  | 877 |  | 888 |  | 898 |  | 908 |  | 918 |  | 929 |
|  | 867 |  | 878 |  | 888 |  | 898 |  | 908 |  | 919 |  | 929 |
|  | 868 |  | 878 |  | 888 |  | 898 |  | 909 |  | 919 |  | 929 |
|  | 868 |  | 878 |  | 888 |  | 899 |  | 909 |  | 919 |  | 929 |
|  | 868 |  | 878 |  | 889 |  | 899 |  | 909 |  | 919 |  | 930 |
|  | 868 |  | 879 |  | 889 |  | 899 |  | 909 |  | 920 |  | 930 |
|  | 869 |  | 879 |  | 889 |  | 899 |  | 910 |  | 920 |  | 930 |
|  | 869 |  | 879 |  | 889 |  | 900 |  | 910 |  | 920 |  | 930 |
|  | 869 |  | 879 |  | 890 |  | 900 |  | 910 |  | 920 |  | 931 |
|  | 869 |  | 880 |  | 890 |  | 900 |  | 910 |  | 921 |  | 931 |
|  | 870 |  | 880 |  | 890 |  | 900 |  | 911 |  | 921 |  | 931 |
|  | 870 |  | 880 |  | 890 |  | 901 |  | 911 |  | 921 |  | 931 |
|  | 870 |  | 880 |  | 891 |  | 901 |  | 911 |  | 921 |  | 932 |
|  | 870 |  | 881 |  | 891 |  | 901 |  | 911 |  | 922 |  | 932 |
|  | 871 |  | 881 |  | 891 |  | 901 |  | 912 |  | 922 |  | 932 |
|  | 871 |  | 881 |  | 891 |  | 902 |  | 912 |  | 922 |  | 932 |
|  | 871 |  | 881 |  | 892 |  | 902 |  | 912 |  | 922 |  | 933 |
|  | 871 |  | 882 |  | 892 |  | 902 |  | 912 |  | 923 |  | 933 |
|  | 872 |  | 882 |  | 892 |  | 902 |  | 913 |  | 923 |  | 933 |

SD4 $\backslash$ RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | Trt. Bl.No nb |  | Trt. Bl.No nb |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | Trt. Bl. |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 933 | PPD | 944 | PPD | 954 | PPD | 964 | PPD | 974 | PPD | 985 | PPD | 995 |
|  | 934 |  | 944 |  | 954 |  | 964 |  | 975 |  | 985 |  | 995 |
|  | 934 |  | 944 |  | 954 |  | 965 |  | 975 |  | 985 |  | 995 |
|  | 934 |  | 944 |  | 955 |  | 965 |  | 975 |  | 985 |  | 996 |
|  | 934 |  | 945 |  | 955 |  | 965 |  | 975 |  | 986 |  | 996 |
|  | 935 |  | 945 |  | 955 |  | 965 |  | 976 |  | 986 |  | 996 |
|  | 935 |  | 945 |  | 955 |  | 966 |  | 976 |  | 986 |  | 996 |
|  | 935 |  | 945 |  | 956 |  | 966 |  | 976 |  | 986 |  | 997 |
|  | 935 |  | 946 |  | 956 |  | 966 |  | 976 |  | 987 |  | 997 |
|  | 936 |  | 946 |  | 956 |  | 966 |  | 977 |  | 987 |  | 997 |
|  | 936 |  | 946 |  | 956 |  | 967 |  | 977 |  | 987 |  | 997 |
|  | 936 |  | 946 |  | 957 |  | 967 |  | 977 |  | 987 |  | 998 |
|  | 936 |  | 947 |  | 957 |  | 967 |  | 977 |  | 988 |  | 998 |
|  | 937 |  | 947 |  | 957 |  | 967 |  | 978 |  | 988 |  | 998 |
|  | 937 |  | 947 |  | 957 |  | 968 |  | 978 |  | 988 |  | 998 |
|  | 937 |  | 947 |  | 958 |  | 968 |  | 978 |  | 988 |  | 999 |
|  | 937 |  | 948 |  | 958 |  | 968 |  | 978 |  | 989 |  | 999 |
|  | 938 |  | 948 |  | 958 |  | 968 |  | 979 |  | 989 |  | 999 |
|  | 938 |  | 948 |  | 958 |  | 969 |  | 979 |  | 989 |  | 999 |
|  | 938 |  | 948 |  | 959 |  | 969 |  | 979 |  | 989 |  | 1000 |
|  | 938 |  | 949 |  | 959 |  | 969 |  | 979 |  | 990 |  | 1000 |
|  | 939 |  | 949 |  | 959 |  | 969 |  | 980 |  | 990 |  | 1000 |
|  | 939 |  | 949 |  | 959 |  | 970 |  | 980 |  | 990 |  | 1000 |
|  | 939 |  | 949 |  | 960 |  | 970 |  | 980 |  | 990 |  | 1001 |
|  | 939 |  | 950 |  | 960 |  | 970 |  | 980 |  | 991 |  | 1001 |
|  | 940 |  | 950 |  | 960 |  | 970 |  | 981 |  | 991 |  | 1001 |
|  | 940 |  | 950 |  | 960 |  | 971 |  | 981 |  | 991 |  | 1001 |
|  | 940 |  | 950 |  | 961 |  | 971 |  | 981 |  | 991 |  | 1002 |
|  | 940 |  | 951 |  | 961 |  | 971 |  | 981 |  | 992 |  | 1002 |
|  | 941 |  | 951 |  | 961 |  | 971 |  | 982 |  | 992 |  | 1002 |
|  | 941 |  | 951 |  | 961 |  | 972 |  | 982 |  | 992 |  | 1002 |
|  | 941 |  | 951 |  | 962 |  | 972 |  | 982 |  | 992 |  | 1003 |
|  | 941 |  | 952 |  | 962 |  | 972 |  | 982 |  | 993 |  | 1003 |
|  | 942 |  | 952 |  | 962 |  | 972 |  | 983 |  | 993 |  | 1003 |
|  | 942 |  | 952 |  | 962 |  | 973 |  | 983 |  | 993 |  | 1003 |
|  | 942 |  | 952 |  | 963 |  | 973 |  | 983 |  | 993 |  | 1004 |
|  | 942 |  | 953 |  | 963 |  | 973 |  | 983 |  | 994 |  | 1004 |
|  | 943 |  | 953 |  | 963 |  | 973 |  | 984 |  | 994 |  | 1004 |
|  | 943 |  | 953 |  | 963 |  | 974 |  | 984 |  | 994 |  | 1004 |
|  | 943 |  | 953 |  | 964 |  | 974 |  | 984 |  | 994 |  | 1005 |
|  | 943 |  | 954 |  | 964 |  | 974 |  | 984 |  | 995 |  | 1005 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. |  |  |  |  | Bl nb |  | Bl nb |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1005 | PPD | 1015 | PPD | 1026 | PPD | 1036 | PPD | 1046 | PPD | 1056 | PPD | 1067 |
|  | 1005 |  | 1016 |  | 1026 |  | 1036 |  | 1046 |  | 1057 |  | 1067 |
|  | 1006 |  | 1016 |  | 1026 |  | 1036 |  | 1047 |  | 1057 |  | 1067 |
|  | 1006 |  | 1016 |  | 1026 |  | 1037 |  | 1047 |  | 1057 |  | 1067 |
|  | 1006 |  | 1016 |  | 1027 |  | 1037 |  | 1047 |  | 1057 |  | 1068 |
|  | 1006 |  | 1017 |  | 1027 |  | 1037 |  | 1047 |  | 1058 |  | 1068 |
|  | 1007 |  | 1017 |  | 1027 |  | 1037 |  | 1048 |  | 1058 |  | 1068 |
|  | 1007 |  | 1017 |  | 1027 |  | 1038 |  | 1048 |  | 1058 |  | 1068 |
|  | 1007 |  | 1017 |  | 1028 |  | 1038 |  | 1048 |  | 1058 |  | 1069 |
|  | 1007 |  | 1018 |  | 1028 |  | 1038 |  | 1048 |  | 1059 |  | 1069 |
|  | 1008 |  | 1018 |  | 1028 |  | 1038 |  | 1049 |  | 1059 |  | 1069 |
|  | 1008 |  | 1018 |  | 1028 |  | 1039 |  | 1049 |  | 1059 |  | 1069 |
|  | 1008 |  | 1018 |  | 1029 |  | 1039 |  | 1049 |  | 1059 |  | 1070 |
|  | 1008 |  | 1019 |  | 1029 |  | 1039 |  | 1049 |  | 1060 |  | 1070 |
|  | 1009 |  | 1019 |  | 1029 |  | 1039 |  | 1050 |  | 1060 |  | 1070 |
|  | 1009 |  | 1019 |  | 1029 |  | 1040 |  | 1050 |  | 1060 |  | 1070 |
|  | 1009 |  | 1019 |  | 1030 |  | 1040 |  | 1050 |  | 1060 |  | 1071 |
|  | 1009 |  | 1020 |  | 1030 |  | 1040 |  | 1050 |  | 1061 |  | 1071 |
|  | 1010 |  | 1020 |  | 1030 |  | 1040 |  | 1051 |  | 1061 |  | 1071 |
|  | 1010 |  | 1020 |  | 1030 |  | 1041 |  | 1051 |  | 1061 |  | 1071 |
|  | 1010 |  | 1020 |  | 1031 |  | 1041 |  | 1051 |  | 1061 |  | 1072 |
|  | 1010 |  | 1021 |  | 1031 |  | 1041 |  | 1051 |  | 1062 |  | 1072 |
|  | 1011 |  | 1021 |  | 1031 |  | 1041 |  | 1052 |  | 1062 |  | 1072 |
|  | 1011 |  | 1021 |  | 1031 |  | 1042 |  | 1052 |  | 1062 |  | 1072 |
|  | 1011 |  | 1021 |  | 1032 |  | 1042 |  | 1052 |  | 1062 |  | 1073 |
|  | 1011 |  | 1022 |  | 1032 |  | 1042 |  | 1052 |  | 1063 |  | 1073 |
|  | 1012 |  | 1022 |  | 1032 |  | 1042 |  | 1053 |  | 1063 |  | 1073 |
|  | 1012 |  | 1022 |  | 1032 |  | 1043 |  | 1053 |  | 1063 |  | 1073 |
|  | 1012 |  | 1022 |  | 1033 |  | 1043 |  | 1053 |  | 1063 |  | 1074 |
|  | 1012 |  | 1023 |  | 1033 |  | 1043 |  | 1053 |  | 1064 |  | 1074 |
|  | 1013 |  | 1023 |  | 1033 |  | 1043 |  | 1054 |  | 1064 |  | 1074 |
|  | 1013 |  | 1023 |  | 1033 |  | 1044 |  | 1054 |  | 1064 |  | 1074 |
|  | 1013 |  | 1023 |  | 1034 |  | 1044 |  | 1054 |  | 1064 |  | 1075 |
|  | 1013 |  | 1024 |  | 1034 |  | 1044 |  | 1054 |  | 1065 |  | 1075 |
|  | 1014 |  | 1024 |  | 1034 |  | 1044 |  | 1055 |  | 1065 |  | 1075 |
|  | 1014 |  | 1024 |  | 1034 |  | 1045 |  | 1055 |  | 1065 |  | 1075 |
|  | 1014 |  | 1024 |  | 1035 |  | 1045 |  | 1055 |  | 1065 |  | 1076 |
|  | 1014 |  | 1025 |  | 1035 |  | 1045 |  | 1055 |  | 1066 |  | 1076 |
|  | 1015 |  | 1025 |  | 1035 |  | 1045 |  | 1056 |  | 1066 |  | 1076 |
|  | 1015 |  | 1025 |  | 1035 |  | 1046 |  | 1056 |  | 1066 |  | 1076 |
|  | 1015 |  | 1025 |  | 1036 |  | 1046 |  | 1056 |  | 1066 |  | 1077 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \text { Trt } \\ \mathrm{N} \end{array}$ | Bl nb | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | Trt. Bl. <br> No nb |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1077 | PPD | 1087 | PPD | 1097 | PPD | 1108 | PPD | 1118 | PPD | 1128 | PPD | 1138 |
|  | 1077 |  | 1087 |  | 1098 |  | 1108 |  | 1118 |  | 1128 |  | 1139 |
|  | 1077 |  | 1088 |  | 1098 |  | 1108 |  | 1118 |  | 1129 |  | 1139 |
|  | 1078 |  | 1088 |  | 1098 |  | 1108 |  | 1119 |  | 1129 |  | 1139 |
|  | 1078 |  | 1088 |  | 1098 |  | 1109 |  | 1119 |  | 1129 |  | 1139 |
|  | 1078 |  | 1088 |  | 1099 |  | 1109 |  | 1119 |  | 1129 |  | 1140 |
|  | 1078 |  | 1089 |  | 1099 |  | 1109 |  | 1119 |  | 1130 |  | 1140 |
|  | 1079 |  | 1089 |  | 1099 |  | 1109 |  | 1120 |  | 1130 |  | 1140 |
|  | 1079 |  | 1089 |  | 1099 |  | 1110 |  | 1120 |  | 1130 |  | 1140 |
|  | 1079 |  | 1089 |  | 1100 |  | 1110 |  | 1120 |  | 1130 |  | 1141 |
|  | 1079 |  | 1090 |  | 1100 |  | 1110 |  | 1120 |  | 1131 |  | 1141 |
|  | 1080 |  | 1090 |  | 1100 |  | 1110 |  | 1121 |  | 1131 |  | 1141 |
|  | 1080 |  | 1090 |  | 1100 |  | 1111 |  | 1121 |  | 1131 |  | 1141 |
|  | 1080 |  | 1090 |  | 1101 |  | 1111 |  | 1121 |  | 1131 |  | 1142 |
|  | 1080 |  | 1091 |  | 1101 |  | 1111 |  | 1121 |  | 1132 |  | 1142 |
|  | 1081 |  | 1091 |  | 1101 |  | 1111 |  | 1122 |  | 1132 |  | 1142 |
|  | 1081 |  | 1091 |  | 1101 |  | 1112 |  | 1122 |  | 1132 |  | 1142 |
|  | 1081 |  | 1091 |  | 1102 |  | 1112 |  | 1122 |  | 1132 |  | 1143 |
|  | 1081 |  | 1092 |  | 1102 |  | 1112 |  | 1122 |  | 1133 |  | 1143 |
|  | 1082 |  | 1092 |  | 1102 |  | 1112 |  | 1123 |  | 1133 |  | 1143 |
|  | 1082 |  | 1092 |  | 1102 |  | 1113 |  | 1123 |  | 1133 |  | 1143 |
|  | 1082 |  | 1092 |  | 1103 |  | 1113 |  | 1123 |  | 1133 |  | 1144 |
|  | 1082 |  | 1093 |  | 1103 |  | 1113 |  | 1123 |  | 1134 |  | 1144 |
|  | 1083 |  | 1093 |  | 1103 |  | 1113 |  | 1124 |  | 1134 |  | 1144 |
|  | 1083 |  | 1093 |  | 1103 |  | 1114 |  | 1124 |  | 1134 |  | 1144 |
|  | 1083 |  | 1093 |  | 1104 |  | 1114 |  | 1124 |  | 1134 |  | 1145 |
|  | 1083 |  | 1094 |  | 1104 |  | 1114 |  | 1124 |  | 1135 |  | 1145 |
|  | 1084 |  | 1094 |  | 1104 |  | 1114 |  | 1125 |  | 1135 |  | 1145 |
|  | 1084 |  | 1094 |  | 1104 |  | 1115 |  | 1125 |  | 1135 |  | 1145 |
|  | 1084 |  | 1094 |  | 1105 |  | 1115 |  | 1125 |  | 1135 |  | 1146 |
|  | 1084 |  | 1095 |  | 1105 |  | 1115 |  | 1125 |  | 1136 |  | 1146 |
|  | 1085 |  | 1095 |  | 1105 |  | 1115 |  | 1126 |  | 1136 |  | 1146 |
|  | 1085 |  | 1095 |  | 1105 |  | 1116 |  | 1126 |  | 1136 |  | 1146 |
|  | 1085 |  | 1095 |  | 1106 |  | 1116 |  | 1126 |  | 1136 |  | 1147 |
|  | 1085 |  | 1096 |  | 1106 |  | 1116 |  | 1126 |  | 1137 |  | 1147 |
|  | 1086 |  | 1096 |  | 1106 |  | 1116 |  | 1127 |  | 1137 |  | 1147 |
|  | 1086 |  | 1096 |  | 1106 |  | 1117 |  | 1127 |  | 1137 |  | 1147 |
|  | 1086 |  | 1096 |  | 1107 |  | 1117 |  | 1127 |  | 1137 |  | 1148 |
|  | 1086 |  | 1097 |  | 1107 |  | 1117 |  | 1127 |  | 1138 |  | 1148 |
|  | 1087 |  | 1097 |  | 1107 |  | 1117 |  | 1128 |  | 1138 |  | 1148 |
|  | 1087 |  | 1097 |  | 1107 |  | 1118 |  | 1128 |  | 1138 |  | 1148 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{gathered} \operatorname{Trt} \\ \mathrm{N} \end{gathered}$ | Bl nb | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Tre. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{gathered} \text { Trt. Bl. } \\ \text { No nb } \end{gathered}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1149 | PPD | 1159 | PPD | 1169 | PPD | 1179 | PPD | 1190 | PPD | 1200 | PPD | 1210 |
|  | 1149 |  | 1159 |  | 1169 |  | 1180 |  | 1190 |  | 1200 |  | 1210 |
|  | 1149 |  | 1159 |  | 1170 |  | 1180 |  | 1190 |  | 1200 |  | 1211 |
|  | 1149 |  | 1160 |  | 1170 |  | 1180 |  | 1190 |  | 1201 |  | 1211 |
|  | 1150 |  | 1160 |  | 1170 |  | 1180 |  | 1191 |  | 1201 |  | 1211 |
|  | 1150 |  | 1160 |  | 1170 |  | 1181 |  | 1191 |  | 1201 |  | 1211 |
|  | 1150 |  | 1160 |  | 1171 |  | 1181 |  | 1191 |  | 1201 |  | 1212 |
|  | 1150 |  | 1161 |  | 1171 |  | 1181 |  | 1191 |  | 1202 |  | 1212 |
|  | 1151 |  | 1161 |  | 1171 |  | 1181 |  | 1192 |  | 1202 |  | 1212 |
|  | 1151 |  | 1161 |  | 1171 |  | 1182 |  | 1192 |  | 1202 |  | 1212 |
|  | 1151 |  | 1161 |  | 1172 |  | 1182 |  | 1192 |  | 1202 |  | 1213 |
|  | 1151 |  | 1162 |  | 1172 |  | 1182 |  | 1192 |  | 1203 |  | 1213 |
|  | 1152 |  | 1162 |  | 1172 |  | 1182 |  | 1193 |  | 1203 |  | 1213 |
|  | 1152 |  | 1162 |  | 1172 |  | 1183 |  | 1193 |  | 1203 |  | 1213 |
|  | 1152 |  | 1162 |  | 1173 |  | 1183 |  | 1193 |  | 1203 |  | 1214 |
|  | 1152 |  | 1163 |  | 1173 |  | 1183 |  | 1193 |  | 1204 |  | 1214 |
|  | 1153 |  | 1163 |  | 1173 |  | 1183 |  | 1194 |  | 1204 |  | 1214 |
|  | 1153 |  | 1163 |  | 1173 |  | 1184 |  | 1194 |  | 1204 |  | 1214 |
|  | 1153 |  | 1163 |  | 1174 |  | 1184 |  | 1194 |  | 1204 |  | 1215 |
|  | 1153 |  | 1164 |  | 1174 |  | 1184 |  | 1194 |  | 1205 |  | 1215 |
|  | 1154 |  | 1164 |  | 1174 |  | 1184 |  | 1195 |  | 1205 |  | 1215 |
|  | 1154 |  | 1164 |  | 1174 |  | 1185 |  | 1195 |  | 1205 |  | 1215 |
|  | 1154 |  | 1164 |  | 1175 |  | 1185 |  | 1195 |  | 1205 |  | 1216 |
|  | 1154 |  | 1165 |  | 1175 |  | 1185 |  | 1195 |  | 1206 |  | 1216 |
|  | 1155 |  | 1165 |  | 1175 |  | 1185 |  | 1196 |  | 1206 |  | 1216 |
|  | 1155 |  | 1165 |  | 1175 |  | 1186 |  | 1196 |  | 1206 |  | 1216 |
|  | 1155 |  | 1165 |  | 1176 |  | 1186 |  | 1196 |  | 1206 |  | 1217 |
|  | 1155 |  | 1166 |  | 1176 |  | 1186 |  | 1196 |  | 1207 |  | 1217 |
|  | 1156 |  | 1166 |  | 1176 |  | 1186 |  | 1197 |  | 1207 |  | 1217 |
|  | 1156 |  | 1166 |  | 1176 |  | 1187 |  | 1197 |  | 1207 |  | 1217 |
|  | 1156 |  | 1166 |  | 1177 |  | 1187 |  | 1197 |  | 1207 |  | 1218 |
|  | 1156 |  | 1167 |  | 1177 |  | 1187 |  | 1197 |  | 1208 |  | 1218 |
|  | 1157 |  | 1167 |  | 1177 |  | 1187 |  | 1198 |  | 1208 |  | 1218 |
|  | 1157 |  | 1167 |  | 1177 |  | 1188 |  | 1198 |  | 1208 |  | 1218 |
|  | 1157 |  | 1167 |  | 1178 |  | 1188 |  | 1198 |  | 1208 |  | 1219 |
|  | 1157 |  | 1168 |  | 1178 |  | 1188 |  | 1198 |  | 1209 |  | 1219 |
|  | 1158 |  | 1168 |  | 1178 |  | 1188 |  | 1199 |  | 1209 |  | 1219 |
|  | 1158 |  | 1168 |  | 1178 |  | 1189 |  | 1199 |  | 1209 |  | 1219 |
|  | 1158 |  | 1168 |  | 1179 |  | 1189 |  | 1199 |  | 1209 |  | 1220 |
|  | 1158 |  | 1169 |  | 1179 |  | 1189 |  | 1199 |  | 1210 |  | 1220 |
|  | 1159 |  | 1169 |  | 1179 |  | 1189 |  | 1200 |  | 1210 |  | 1220 |

SD4 \RDE $\backslash$ ENABLE
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Treatment number associated to material : Placeb-PreChemo

| Tre. |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | Trt. Bl. |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1220 | PPD | 1231 | PPD | 1241 | PPD | 1251 | PPD | 1261 | PPD | 1272 | PPD | 1282 |
|  | 1221 |  | 1231 |  | 1241 |  | 1251 |  | 1262 |  | 1272 |  | 1282 |
|  | 1221 |  | 1231 |  | 1241 |  | 1252 |  | 1262 |  | 1272 |  | 1282 |
|  | 1221 |  | 1231 |  | 1242 |  | 1252 |  | 1262 |  | 1272 |  | 1283 |
|  | 1221 |  | 1232 |  | 1242 |  | 1252 |  | 1262 |  | 1273 |  | 1283 |
|  | 1222 |  | 1232 |  | 1242 |  | 1252 |  | 1263 |  | 1273 |  | 1283 |
|  | 1222 |  | 1232 |  | 1242 |  | 1253 |  | 1263 |  | 1273 |  | 1283 |
|  | 1222 |  | 1232 |  | 1243 |  | 1253 |  | 1263 |  | 1273 |  | 1284 |
|  | 1222 |  | 1233 |  | 1243 |  | 1253 |  | 1263 |  | 1274 |  | 1284 |
|  | 1223 |  | 1233 |  | 1243 |  | 1253 |  | 1264 |  | 1274 |  | 1284 |
|  | 1223 |  | 1233 |  | 1243 |  | 1254 |  | 1264 |  | 1274 |  | 1284 |
|  | 1223 |  | 1233 |  | 1244 |  | 1254 |  | 1264 |  | 1274 |  | 1285 |
|  | 1223 |  | 1234 |  | 1244 |  | 1254 |  | 1264 |  | 1275 |  | 1285 |
|  | 1224 |  | 1234 |  | 1244 |  | 1254 |  | 1265 |  | 1275 |  | 1285 |
|  | 1224 |  | 1234 |  | 1244 |  | 1255 |  | 1265 |  | 1275 |  | 1285 |
|  | 1224 |  | 1234 |  | 1245 |  | 1255 |  | 1265 |  | 1275 |  | 1286 |
|  | 1224 |  | 1235 |  | 1245 |  | 1255 |  | 1265 |  | 1276 |  | 1286 |
|  | 1225 |  | 1235 |  | 1245 |  | 1255 |  | 1266 |  | 1276 |  | 1286 |
|  | 1225 |  | 1235 |  | 1245 |  | 1256 |  | 1266 |  | 1276 |  | 1286 |
|  | 1225 |  | 1235 |  | 1246 |  | 1256 |  | 1266 |  | 1276 |  | 1287 |
|  | 1225 |  | 1236 |  | 1246 |  | 1256 |  | 1266 |  | 1277 |  | 1287 |
|  | 1226 |  | 1236 |  | 1246 |  | 1256 |  | 1267 |  | 1277 |  | 1287 |
|  | 1226 |  | 1236 |  | 1246 |  | 1257 |  | 1267 |  | 1277 |  | 1287 |
|  | 1226 |  | 1236 |  | 1247 |  | 1257 |  | 1267 |  | 1277 |  | 1288 |
|  | 1226 |  | 1237 |  | 1247 |  | 1257 |  | 1267 |  | 1278 |  | 1288 |
|  | 1227 |  | 1237 |  | 1247 |  | 1257 |  | 1268 |  | 1278 |  | 1288 |
|  | 1227 |  | 1237 |  | 1247 |  | 1258 |  | 1268 |  | 1278 |  | 1288 |
|  | 1227 |  | 1237 |  | 1248 |  | 1258 |  | 1268 |  | 1278 |  | 1289 |
|  | 1227 |  | 1238 |  | 1248 |  | 1258 |  | 1268 |  | 1279 |  | 1289 |
|  | 1228 |  | 1238 |  | 1248 |  | 1258 |  | 1269 |  | 1279 |  | 1289 |
|  | 1228 |  | 1238 |  | 1248 |  | 1259 |  | 1269 |  | 1279 |  | 1289 |
|  | 1228 |  | 1238 |  | 1249 |  | 1259 |  | 1269 |  | 1279 |  | 1290 |
|  | 1228 |  | 1239 |  | 1249 |  | 1259 |  | 1269 |  | 1280 |  | 1290 |
|  | 1229 |  | 1239 |  | 1249 |  | 1259 |  | 1270 |  | 1280 |  | 1290 |
|  | 1229 |  | 1239 |  | 1249 |  | 1260 |  | 1270 |  | 1280 |  | 1290 |
|  | 1229 |  | 1239 |  | 1250 |  | 1260 |  | 1270 |  | 1280 |  | 1291 |
|  | 1229 |  | 1240 |  | 1250 |  | 1260 |  | 1270 |  | 1281 |  | 1291 |
|  | 1230 |  | 1240 |  | 1250 |  | 1260 |  | 1271 |  | 1281 |  | 1291 |
|  | 1230 |  | 1240 |  | 1250 |  | 1261 |  | 1271 |  | 1281 |  | 1291 |
|  | 1230 |  | 1240 |  | 1251 |  | 1261 |  | 1271 |  | 1281 |  | 1292 |
|  | 1230 |  | 1241 |  | 1251 |  | 1261 |  | 1271 |  | 1282 |  | 1292 |

SD4 \RDE $\backslash$ ENABLE
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Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | Bl nb |  | $\begin{aligned} & \mathrm{Bl} \text { n. } \end{aligned}$ | Tre | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1292 | PPD | 1302 | PPD | 1313 | PPD | 1323 | PPD | 1333 | PPD | 1343 | PPD | 1354 |
|  | 1292 |  | 1303 |  | 1313 |  | 1323 |  | 1333 |  | 1344 |  | 1354 |
|  | 1293 |  | 1303 |  | 1313 |  | 1323 |  | 1334 |  | 1344 |  | 1354 |
|  | 1293 |  | 1303 |  | 1313 |  | 1324 |  | 1334 |  | 1344 |  | 1354 |
|  | 1293 |  | 1303 |  | 1314 |  | 1324 |  | 1334 |  | 1344 |  | 1355 |
|  | 1293 |  | 1304 |  | 1314 |  | 1324 |  | 1334 |  | 1345 |  | 1355 |
|  | 1294 |  | 1304 |  | 1314 |  | 1324 |  | 1335 |  | 1345 |  | 1355 |
|  | 1294 |  | 1304 |  | 1314 |  | 1325 |  | 1335 |  | 1345 |  | 1355 |
|  | 1294 |  | 1304 |  | 1315 |  | 1325 |  | 1335 |  | 1345 |  | 1356 |
|  | 1294 |  | 1305 |  | 1315 |  | 1325 |  | 1335 |  | 1346 |  | 1356 |
|  | 1295 |  | 1305 |  | 1315 |  | 1325 |  | 1336 |  | 1346 |  | 1356 |
|  | 1295 |  | 1305 |  | 1315 |  | 1326 |  | 1336 |  | 1346 |  | 1356 |
|  | 1295 |  | 1305 |  | 1316 |  | 1326 |  | 1336 |  | 1346 |  | 1357 |
|  | 1295 |  | 1306 |  | 1316 |  | 1326 |  | 1336 |  | 1347 |  | 1357 |
|  | 1296 |  | 1306 |  | 1316 |  | 1326 |  | 1337 |  | 1347 |  | 1357 |
|  | 1296 |  | 1306 |  | 1316 |  | 1327 |  | 1337 |  | 1347 |  | 1357 |
|  | 1296 |  | 1306 |  | 1317 |  | 1327 |  | 1337 |  | 1347 |  | 1358 |
|  | 1296 |  | 1307 |  | 1317 |  | 1327 |  | 1337 |  | 1348 |  | 1358 |
|  | 1297 |  | 1307 |  | 1317 |  | 1327 |  | 1338 |  | 1348 |  | 1358 |
|  | 1297 |  | 1307 |  | 1317 |  | 1328 |  | 1338 |  | 1348 |  | 1358 |
|  | 1297 |  | 1307 |  | 1318 |  | 1328 |  | 1338 |  | 1348 |  | 1359 |
|  | 1297 |  | 1308 |  | 1318 |  | 1328 |  | 1338 |  | 1349 |  | 1359 |
|  | 1298 |  | 1308 |  | 1318 |  | 1328 |  | 1339 |  | 1349 |  | 1359 |
|  | 1298 |  | 1308 |  | 1318 |  | 1329 |  | 1339 |  | 1349 |  | 1359 |
|  | 1298 |  | 1308 |  | 1319 |  | 1329 |  | 1339 |  | 1349 |  | 1360 |
|  | 1298 |  | 1309 |  | 1319 |  | 1329 |  | 1339 |  | 1350 |  | 1360 |
|  | 1299 |  | 1309 |  | 1319 |  | 1329 |  | 1340 |  | 1350 |  | 1360 |
|  | 1299 |  | 1309 |  | 1319 |  | 1330 |  | 1340 |  | 1350 |  | 1360 |
|  | 1299 |  | 1309 |  | 1320 |  | 1330 |  | 1340 |  | 1350 |  | 1361 |
|  | 1299 |  | 1310 |  | 1320 |  | 1330 |  | 1340 |  | 1351 |  | 1361 |
|  | 1300 |  | 1310 |  | 1320 |  | 1330 |  | 1341 |  | 1351 |  | 1361 |
|  | 1300 |  | 1310 |  | 1320 |  | 1331 |  | 1341 |  | 1351 |  | 1361 |
|  | 1300 |  | 1310 |  | 1321 |  | 1331 |  | 1341 |  | 1351 |  | 1362 |
|  | 1300 |  | 1311 |  | 1321 |  | 1331 |  | 1341 |  | 1352 |  | 1362 |
|  | 1301 |  | 1311 |  | 1321 |  | 1331 |  | 1342 |  | 1352 |  | 1362 |
|  | 1301 |  | 1311 |  | 1321 |  | 1332 |  | 1342 |  | 1352 |  | 1362 |
|  | 1301 |  | 1311 |  | 1322 |  | 1332 |  | 1342 |  | 1352 |  | 1363 |
|  | 1301 |  | 1312 |  | 1322 |  | 1332 |  | 1342 |  | 1353 |  | 1363 |
|  | 1302 |  | 1312 |  | 1322 |  | 1332 |  | 1343 |  | 1353 |  | 1363 |
|  | 1302 |  | 1312 |  | 1322 |  | 1333 |  | 1343 |  | 1353 |  | 1363 |
|  | 1302 |  | 1312 |  | 1323 |  | 1333 |  | 1343 |  | 1353 |  | 1364 |

SD4 \RDE $\backslash$ ENABLE
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Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1364 | PPD | 1374 | PPD | 1384 | PPD | 1395 | PPD | 1405 | PPD | 1415 | PPD | 1425 |
|  | 1364 |  | 1374 |  | 1385 |  | 1395 |  | 1405 |  | 1415 |  | 1426 |
|  | 1364 |  | 1375 |  | 1385 |  | 1395 |  | 1405 |  | 1416 |  | 1426 |
|  | 1365 |  | 1375 |  | 1385 |  | 1395 |  | 1406 |  | 1416 |  | 1426 |
|  | 1365 |  | 1375 |  | 1385 |  | 1396 |  | 1406 |  | 1416 |  | 1426 |
|  | 1365 |  | 1375 |  | 1386 |  | 1396 |  | 1406 |  | 1416 |  | 1427 |
|  | 1365 |  | 1376 |  | 1386 |  | 1396 |  | 1406 |  | 1417 |  | 1427 |
|  | 1366 |  | 1376 |  | 1386 |  | 1396 |  | 1407 |  | 1417 |  | 1427 |
|  | 1366 |  | 1376 |  | 1386 |  | 1397 |  | 1407 |  | 1417 |  | 1427 |
|  | 1366 |  | 1376 |  | 1387 |  | 1397 |  | 1407 |  | 1417 |  | 1428 |
|  | 1366 |  | 1377 |  | 1387 |  | 1397 |  | 1407 |  | 1418 |  | 1428 |
|  | 1367 |  | 1377 |  | 1387 |  | 1397 |  | 1408 |  | 1418 |  | 1428 |
|  | 1367 |  | 1377 |  | 1387 |  | 1398 |  | 1408 |  | 1418 |  | 1428 |
|  | 1367 |  | 1377 |  | 1388 |  | 1398 |  | 1408 |  | 1418 |  | 1429 |
|  | 1367 |  | 1378 |  | 1388 |  | 1398 |  | 1408 |  | 1419 |  | 1429 |
|  | 1368 |  | 1378 |  | 1388 |  | 1398 |  | 1409 |  | 1419 |  | 1429 |
|  | 1368 |  | 1378 |  | 1388 |  | 1399 |  | 1409 |  | 1419 |  | 1429 |
|  | 1368 |  | 1378 |  | 1389 |  | 1399 |  | 1409 |  | 1419 |  | 1430 |
|  | 1368 |  | 1379 |  | 1389 |  | 1399 |  | 1409 |  | 1420 |  | 1430 |
|  | 1369 |  | 1379 |  | 1389 |  | 1399 |  | 1410 |  | 1420 |  | 1430 |
|  | 1369 |  | 1379 |  | 1389 |  | 1400 |  | 1410 |  | 1420 |  | 1430 |
|  | 1369 |  | 1379 |  | 1390 |  | 1400 |  | 1410 |  | 1420 |  | 1431 |
|  | 1369 |  | 1380 |  | 1390 |  | 1400 |  | 1410 |  | 1421 |  | 1431 |
|  | 1370 |  | 1380 |  | 1390 |  | 1400 |  | 1411 |  | 1421 |  | 1431 |
|  | 1370 |  | 1380 |  | 1390 |  | 1401 |  | 1411 |  | 1421 |  | 1431 |
|  | 1370 |  | 1380 |  | 1391 |  | 1401 |  | 1411 |  | 1421 |  | 1432 |
|  | 1370 |  | 1381 |  | 1391 |  | 1401 |  | 1411 |  | 1422 |  | 1432 |
|  | 1371 |  | 1381 |  | 1391 |  | 1401 |  | 1412 |  | 1422 |  | 1432 |
|  | 1371 |  | 1381 |  | 1391 |  | 1402 |  | 1412 |  | 1422 |  | 1432 |
|  | 1371 |  | 1381 |  | 1392 |  | 1402 |  | 1412 |  | 1422 |  | 1433 |
|  | 1371 |  | 1382 |  | 1392 |  | 1402 |  | 1412 |  | 1423 |  | 1433 |
|  | 1372 |  | 1382 |  | 1392 |  | 1402 |  | 1413 |  | 1423 |  | 1433 |
|  | 1372 |  | 1382 |  | 1392 |  | 1403 |  | 1413 |  | 1423 |  | 1433 |
|  | 1372 |  | 1382 |  | 1393 |  | 1403 |  | 1413 |  | 1423 |  | 1434 |
|  | 1372 |  | 1383 |  | 1393 |  | 1403 |  | 1413 |  | 1424 |  | 1434 |
|  | 1373 |  | 1383 |  | 1393 |  | 1403 |  | 1414 |  | 1424 |  | 1434 |
|  | 1373 |  | 1383 |  | 1393 |  | 1404 |  | 1414 |  | 1424 |  | 1434 |
|  | 1373 |  | 1383 |  | 1394 |  | 1404 |  | 1414 |  | 1424 |  | 1435 |
|  | 1373 |  | 1384 |  | 1394 |  | 1404 |  | 1414 |  | 1425 |  | 1435 |
|  | 1374 |  | 1384 |  | 1394 |  | 1404 |  | 1415 |  | 1425 |  | 1435 |
|  | 1374 |  | 1384 |  | 1394 |  | 1405 |  | 1415 |  | 1425 |  | 1435 |

SD4 \RDE $\backslash$ ENABLE
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Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD |  |  |  |  |  |  |  | PPD |  | PPD | 1487 | PPD | 1497 |
|  |  |  |  |  |  |  |  |  |  | 1487 | 1497 |  |
|  |  |  |  |  |  |  |  |  |  | 1487 | 1498 |  |
|  |  |  |  |  |  |  |  |  |  | 1488 | 1498 |  |
|  |  |  |  |  |  |  |  |  |  | 1488 | 1498 |  |
|  |  |  |  |  |  |  |  |  |  | 1488 | 1498 |  |
|  |  |  |  |  |  |  |  |  |  | 1488 | 1499 |  |
|  |  |  |  |  |  |  |  |  |  | 1489 | 1499 |  |
|  |  |  |  |  |  |  |  |  |  | 1489 | 1499 |  |
|  |  |  |  |  |  |  |  |  |  | 1489 | 1499 |  |
|  |  |  |  |  |  |  |  |  |  | 1489 | 1500 |  |
|  |  |  |  |  |  |  |  |  |  | 1490 | 1500 |  |
|  |  |  |  |  |  |  |  |  |  | 1490 | 1500 |  |
|  |  |  |  |  |  |  |  |  |  | 1490 | 1500 |  |
|  |  |  |  |  |  |  |  |  |  | 1490 | 1501 |  |
|  |  |  |  |  |  |  |  |  |  | 1491 | 1501 |  |
|  |  |  |  |  |  |  |  |  |  | 1491 | 1501 |  |
|  |  |  |  |  |  |  |  |  |  | 1491 | 1501 |  |
|  |  |  |  |  |  |  |  |  |  | 1491 | 1502 |  |
|  |  |  |  |  |  |  |  |  |  | 1492 | 1502 |  |
|  |  |  |  |  |  |  |  |  |  | 1492 | 1502 |  |
|  |  |  |  |  |  |  |  |  |  | 1492 | 1502 |  |
|  |  |  |  |  |  |  |  |  |  | 1492 | 1503 |  |
|  |  |  |  |  |  |  |  |  |  | 1493 | 1503 |  |
|  |  |  |  |  |  |  |  |  |  | 1493 | 1503 |  |
|  |  |  |  |  |  |  |  |  |  | 1493 | 1503 |  |
|  |  |  |  |  |  |  |  |  |  | 1493 | 1504 |  |
|  |  |  |  |  |  |  |  |  |  | 1494 | 1504 |  |
|  |  |  |  |  |  |  |  |  |  | 1494 | 1504 |  |
|  |  |  |  |  |  |  |  |  |  | 1494 | 1504 |  |
|  |  |  |  |  |  |  |  |  |  | 1494 | 1505 |  |
|  |  |  |  |  |  |  |  |  |  | 1495 | 1505 |  |
|  |  |  |  |  |  |  |  |  |  | 1495 | 1505 |  |
|  |  |  |  |  |  |  |  |  |  | 1495 | 1505 |  |
|  |  |  |  |  |  |  |  |  |  | 1495 | 1506 |  |
|  |  |  |  |  |  |  |  |  |  | 1496 | 1506 |  |
|  |  |  |  |  |  |  |  |  |  | 1496 | 1506 |  |
|  |  |  |  |  |  |  |  |  |  | 1496 | 1506 |  |
|  |  |  |  |  |  |  |  |  |  | 1496 | 1507 |  |
|  |  |  |  |  |  |  |  |  |  | 1497 | 1507 |  |
|  |  |  |  |  |  |  |  |  |  | 1497 | 1507 |  |

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ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. | Bl nb |  |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} \text { n. } \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1507 | PPD | 1518 | PPD | 1528 | PPD | 1538 | PPD | 1548 | PPD | 1559 | PPD | 1569 |
|  | 1508 |  | 1518 |  | 1528 |  | 1538 |  | 1549 |  | 1559 |  | 1569 |
|  | 1508 |  | 1518 |  | 1528 |  | 1539 |  | 1549 |  | 1559 |  | 1569 |
|  | 1508 |  | 1518 |  | 1529 |  | 1539 |  | 1549 |  | 1559 |  | 1570 |
|  | 1508 |  | 1519 |  | 1529 |  | 1539 |  | 1549 |  | 1560 |  | 1570 |
|  | 1509 |  | 1519 |  | 1529 |  | 1539 |  | 1550 |  | 1560 |  | 1570 |
|  | 1509 |  | 1519 |  | 1529 |  | 1540 |  | 1550 |  | 1560 |  | 1570 |
|  | 1509 |  | 1519 |  | 1530 |  | 1540 |  | 1550 |  | 1560 |  | 1571 |
|  | 1509 |  | 1520 |  | 1530 |  | 1540 |  | 1550 |  | 1561 |  | 1571 |
|  | 1510 |  | 1520 |  | 1530 |  | 1540 |  | 1551 |  | 1561 |  | 1571 |
|  | 1510 |  | 1520 |  | 1530 |  | 1541 |  | 1551 |  | 1561 |  | 1571 |
|  | 1510 |  | 1520 |  | 1531 |  | 1541 |  | 1551 |  | 1561 |  | 1572 |
|  | 1510 |  | 1521 |  | 1531 |  | 1541 |  | 1551 |  | 1562 |  | 1572 |
|  | 1511 |  | 1521 |  | 1531 |  | 1541 |  | 1552 |  | 1562 |  | 1572 |
|  | 1511 |  | 1521 |  | 1531 |  | 1542 |  | 1552 |  | 1562 |  | 1572 |
|  | 1511 |  | 1521 |  | 1532 |  | 1542 |  | 1552 |  | 1562 |  | 1573 |
|  | 1511 |  | 1522 |  | 1532 |  | 1542 |  | 1552 |  | 1563 |  | 1573 |
|  | 1512 |  | 1522 |  | 1532 |  | 1542 |  | 1553 |  | 1563 |  | 1573 |
|  | 1512 |  | 1522 |  | 1532 |  | 1543 |  | 1553 |  | 1563 |  | 1573 |
|  | 1512 |  | 1522 |  | 1533 |  | 1543 |  | 1553 |  | 1563 |  | 1574 |
|  | 1512 |  | 1523 |  | 1533 |  | 1543 |  | 1553 |  | 1564 |  | 1574 |
|  | 1513 |  | 1523 |  | 1533 |  | 1543 |  | 1554 |  | 1564 |  | 1574 |
|  | 1513 |  | 1523 |  | 1533 |  | 1544 |  | 1554 |  | 1564 |  | 1574 |
|  | 1513 |  | 1523 |  | 1534 |  | 1544 |  | 1554 |  | 1564 |  | 1575 |
|  | 1513 |  | 1524 |  | 1534 |  | 1544 |  | 1554 |  | 1565 |  | 1575 |
|  | 1514 |  | 1524 |  | 1534 |  | 1544 |  | 1555 |  | 1565 |  | 1575 |
|  | 1514 |  | 1524 |  | 1534 |  | 1545 |  | 1555 |  | 1565 |  | 1575 |
|  | 1514 |  | 1524 |  | 1535 |  | 1545 |  | 1555 |  | 1565 |  | 1576 |
|  | 1514 |  | 1525 |  | 1535 |  | 1545 |  | 1555 |  | 1566 |  | 1576 |
|  | 1515 |  | 1525 |  | 1535 |  | 1545 |  | 1556 |  | 1566 |  | 1576 |
|  | 1515 |  | 1525 |  | 1535 |  | 1546 |  | 1556 |  | 1566 |  | 1576 |
|  | 1515 |  | 1525 |  | 1536 |  | 1546 |  | 1556 |  | 1566 |  | 1577 |
|  | 1515 |  | 1526 |  | 1536 |  | 1546 |  | 1556 |  | 1567 |  | 1577 |
|  | 1516 |  | 1526 |  | 1536 |  | 1546 |  | 1557 |  | 1567 |  | 1577 |
|  | 1516 |  | 1526 |  | 1536 |  | 1547 |  | 1557 |  | 1567 |  | 1577 |
|  | 1516 |  | 1526 |  | 1537 |  | 1547 |  | 1557 |  | 1567 |  | 1578 |
|  | 1516 |  | 1527 |  | 1537 |  | 1547 |  | 1557 |  | 1568 |  | 1578 |
|  | 1517 |  | 1527 |  | 1537 |  | 1547 |  | 1558 |  | 1568 |  | 1578 |
|  | 1517 |  | 1527 |  | 1537 |  | 1548 |  | 1558 |  | 1568 |  | 1578 |
|  | 1517 |  | 1527 |  | 1538 |  | 1548 |  | 1558 |  | 1568 |  | 1579 |
|  | 1517 |  | 1528 |  | 1538 |  | 1548 |  | 1558 |  | 1569 |  | 1579 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \text { Trt } \\ \mathrm{N} \end{array}$ | Bl. |  | Bl. |  |  |  |  |  |  |  | Bl. | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1579 | PPD | 1589 | PPD | 1600 | PPD | 1610 | PPD | 1620 | PPD | 1630 | PPD | 1641 |
|  | 1579 |  | 1590 |  | 1600 |  | 1610 |  | 1620 |  | 1631 |  | 1641 |
|  | 1580 |  | 1590 |  | 1600 |  | 1610 |  | 1621 |  | 1631 |  | 1641 |
|  | 1580 |  | 1590 |  | 1600 |  | 1611 |  | 1621 |  | 1631 |  | 1641 |
|  | 1580 |  | 1590 |  | 1601 |  | 1611 |  | 1621 |  | 1631 |  | 1642 |
|  | 1580 |  | 1591 |  | 1601 |  | 1611 |  | 1621 |  | 1632 |  | 1642 |
|  | 1581 |  | 1591 |  | 1601 |  | 1611 |  | 1622 |  | 1632 |  | 1642 |
|  | 1581 |  | 1591 |  | 1601 |  | 1612 |  | 1622 |  | 1632 |  | 1642 |
|  | 1581 |  | 1591 |  | 1602 |  | 1612 |  | 1622 |  | 1632 |  | 1643 |
|  | 1581 |  | 1592 |  | 1602 |  | 1612 |  | 1622 |  | 1633 |  | 1643 |
|  | 1582 |  | 1592 |  | 1602 |  | 1612 |  | 1623 |  | 1633 |  | 1643 |
|  | 1582 |  | 1592 |  | 1602 |  | 1613 |  | 1623 |  | 1633 |  | 1643 |
|  | 1582 |  | 1592 |  | 1603 |  | 1613 |  | 1623 |  | 1633 |  | 1644 |
|  | 1582 |  | 1593 |  | 1603 |  | 1613 |  | 1623 |  | 1634 |  | 1644 |
|  | 1583 |  | 1593 |  | 1603 |  | 1613 |  | 1624 |  | 1634 |  | 1644 |
|  | 1583 |  | 1593 |  | 1603 |  | 1614 |  | 1624 |  | 1634 |  | 1644 |
|  | 1583 |  | 1593 |  | 1604 |  | 1614 |  | 1624 |  | 1634 |  | 1645 |
|  | 1583 |  | 1594 |  | 1604 |  | 1614 |  | 1624 |  | 1635 |  | 1645 |
|  | 1584 |  | 1594 |  | 1604 |  | 1614 |  | 1625 |  | 1635 |  | 1645 |
|  | 1584 |  | 1594 |  | 1604 |  | 1615 |  | 1625 |  | 1635 |  | 1645 |
|  | 1584 |  | 1594 |  | 1605 |  | 1615 |  | 1625 |  | 1635 |  | 1646 |
|  | 1584 |  | 1595 |  | 1605 |  | 1615 |  | 1625 |  | 1636 |  | 1646 |
|  | 1585 |  | 1595 |  | 1605 |  | 1615 |  | 1626 |  | 1636 |  | 1646 |
|  | 1585 |  | 1595 |  | 1605 |  | 1616 |  | 1626 |  | 1636 |  | 1646 |
|  | 1585 |  | 1595 |  | 1606 |  | 1616 |  | 1626 |  | 1636 |  | 1647 |
|  | 1585 |  | 1596 |  | 1606 |  | 1616 |  | 1626 |  | 1637 |  | 1647 |
|  | 1586 |  | 1596 |  | 1606 |  | 1616 |  | 1627 |  | 1637 |  | 1647 |
|  | 1586 |  | 1596 |  | 1606 |  | 1617 |  | 1627 |  | 1637 |  | 1647 |
|  | 1586 |  | 1596 |  | 1607 |  | 1617 |  | 1627 |  | 1637 |  | 1648 |
|  | 1586 |  | 1597 |  | 1607 |  | 1617 |  | 1627 |  | 1638 |  | 1648 |
|  | 1587 |  | 1597 |  | 1607 |  | 1617 |  | 1628 |  | 1638 |  | 1648 |
|  | 1587 |  | 1597 |  | 1607 |  | 1618 |  | 1628 |  | 1638 |  | 1648 |
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|  | 1588 |  | 1598 |  | 1608 |  | 1619 |  | 1629 |  | 1639 |  | 1649 |
|  | 1588 |  | 1598 |  | 1609 |  | 1619 |  | 1629 |  | 1639 |  | 1650 |
|  | 1588 |  | 1599 |  | 1609 |  | 1619 |  | 1629 |  | 1640 |  | 1650 |
|  | 1589 |  | 1599 |  | 1609 |  | 1619 |  | 1630 |  | 1640 |  | 1650 |
|  | 1589 |  | 1599 |  | 1609 |  | 1620 |  | 1630 |  | 1640 |  | 1650 |
|  | 1589 |  | 1599 |  | 1610 |  | 1620 |  | 1630 |  | 1640 |  | 1651 |

SD4\RDE\ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Tre. |  |  | Bl nb |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. } \\ & \text { No nl. } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1651 | PPD | 1661 | PPD | 1671 | PPD | 1682 | PPD | 1692 | PPD | 1702 | PPD | 1712 |
|  | 1651 |  | 1661 |  | 1672 |  | 1682 |  | 1692 |  | 1702 |  | 1713 |
|  | 1651 |  | 1662 |  | 1672 |  | 1682 |  | 1692 |  | 1703 |  | 1713 |
|  | 1652 |  | 1662 |  | 1672 |  | 1682 |  | 1693 |  | 1703 |  | 1713 |
|  | 1652 |  | 1662 |  | 1672 |  | 1683 |  | 1693 |  | 1703 |  | 1713 |
|  | 1652 |  | 1662 |  | 1673 |  | 1683 |  | 1693 |  | 1703 |  | 1714 |
|  | 1652 |  | 1663 |  | 1673 |  | 1683 |  | 1693 |  | 1704 |  | 1714 |
|  | 1653 |  | 1663 |  | 1673 |  | 1683 |  | 1694 |  | 1704 |  | 1714 |
|  | 1653 |  | 1663 |  | 1673 |  | 1684 |  | 1694 |  | 1704 |  | 1714 |
|  | 1653 |  | 1663 |  | 1674 |  | 1684 |  | 1694 |  | 1704 |  | 1715 |
|  | 1653 |  | 1664 |  | 1674 |  | 1684 |  | 1694 |  | 1705 |  | 1715 |
|  | 1654 |  | 1664 |  | 1674 |  | 1684 |  | 1695 |  | 1705 |  | 1715 |
|  | 1654 |  | 1664 |  | 1674 |  | 1685 |  | 1695 |  | 1705 |  | 1715 |
|  | 1654 |  | 1664 |  | 1675 |  | 1685 |  | 1695 |  | 1705 |  | 1716 |
|  | 1654 |  | 1665 |  | 1675 |  | 1685 |  | 1695 |  | 1706 |  | 1716 |
|  | 1655 |  | 1665 |  | 1675 |  | 1685 |  | 1696 |  | 1706 |  | 1716 |
|  | 1655 |  | 1665 |  | 1675 |  | 1686 |  | 1696 |  | 1706 |  | 1716 |
|  | 1655 |  | 1665 |  | 1676 |  | 1686 |  | 1696 |  | 1706 |  | 1717 |
|  | 1655 |  | 1666 |  | 1676 |  | 1686 |  | 1696 |  | 1707 |  | 1717 |
|  | 1656 |  | 1666 |  | 1676 |  | 1686 |  | 1697 |  | 1707 |  | 1717 |
|  | 1656 |  | 1666 |  | 1676 |  | 1687 |  | 1697 |  | 1707 |  | 1717 |
|  | 1656 |  | 1666 |  | 1677 |  | 1687 |  | 1697 |  | 1707 |  | 1718 |
|  | 1656 |  | 1667 |  | 1677 |  | 1687 |  | 1697 |  | 1708 |  | 1718 |
|  | 1657 |  | 1667 |  | 1677 |  | 1687 |  | 1698 |  | 1708 |  | 1718 |
|  | 1657 |  | 1667 |  | 1677 |  | 1688 |  | 1698 |  | 1708 |  | 1718 |
|  | 1657 |  | 1667 |  | 1678 |  | 1688 |  | 1698 |  | 1708 |  | 1719 |
|  | 1657 |  | 1668 |  | 1678 |  | 1688 |  | 1698 |  | 1709 |  | 1719 |
|  | 1658 |  | 1668 |  | 1678 |  | 1688 |  | 1699 |  | 1709 |  | 1719 |
|  | 1658 |  | 1668 |  | 1678 |  | 1689 |  | 1699 |  | 1709 |  | 1719 |
|  | 1658 |  | 1668 |  | 1679 |  | 1689 |  | 1699 |  | 1709 |  | 1720 |
|  | 1658 |  | 1669 |  | 1679 |  | 1689 |  | 1699 |  | 1710 |  | 1720 |
|  | 1659 |  | 1669 |  | 1679 |  | 1689 |  | 1700 |  | 1710 |  | 1720 |
|  | 1659 |  | 1669 |  | 1679 |  | 1690 |  | 1700 |  | 1710 |  | 1720 |
|  | 1659 |  | 1669 |  | 1680 |  | 1690 |  | 1700 |  | 1710 |  | 1721 |
|  | 1659 |  | 1670 |  | 1680 |  | 1690 |  | 1700 |  | 1711 |  | 1721 |
|  | 1660 |  | 1670 |  | 1680 |  | 1690 |  | 1701 |  | 1711 |  | 1721 |
|  | 1660 |  | 1670 |  | 1680 |  | 1691 |  | 1701 |  | 1711 |  | 1721 |
|  | 1660 |  | 1670 |  | 1681 |  | 1691 |  | 1701 |  | 1711 |  | 1722 |
|  | 1660 |  | 1671 |  | 1681 |  | 1691 |  | 1701 |  | 1712 |  | 1722 |
|  | 1661 |  | 1671 |  | 1681 |  | 1691 |  | 1702 |  | 1712 |  | 1722 |
|  | 1661 |  | 1671 |  | 1681 |  | 1692 |  | 1702 |  | 1712 |  | 1722 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. |  | $\begin{aligned} & \text { Tre. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{gathered} \text { Trt. Bl. } \\ \text { No nb } \end{gathered}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1723 | PPD | 1733 | PPD | 1743 | PPD | 1753 | PPD | 1764 | PPD | 1774 | PPD | 1784 |
|  | 1723 |  | 1733 |  | 1743 |  | 1754 |  | 1764 |  | 1774 |  | 1784 |
|  | 1723 |  | 1733 |  | 1744 |  | 1754 |  | 1764 |  | 1774 |  | 1785 |
|  | 1723 |  | 1734 |  | 1744 |  | 1754 |  | 1764 |  | 1775 |  | 1785 |
|  | 1724 |  | 1734 |  | 1744 |  | 1754 |  | 1765 |  | 1775 |  | 1785 |
|  | 1724 |  | 1734 |  | 1744 |  | 1755 |  | 1765 |  | 1775 |  | 1785 |
|  | 1724 |  | 1734 |  | 1745 |  | 1755 |  | 1765 |  | 1775 |  | 1786 |
|  | 1724 |  | 1735 |  | 1745 |  | 1755 |  | 1765 |  | 1776 |  | 1786 |
|  | 1725 |  | 1735 |  | 1745 |  | 1755 |  | 1766 |  | 1776 |  | 1786 |
|  | 1725 |  | 1735 |  | 1745 |  | 1756 |  | 1766 |  | 1776 |  | 1786 |
|  | 1725 |  | 1735 |  | 1746 |  | 1756 |  | 1766 |  | 1776 |  | 1787 |
|  | 1725 |  | 1736 |  | 1746 |  | 1756 |  | 1766 |  | 1777 |  | 1787 |
|  | 1726 |  | 1736 |  | 1746 |  | 1756 |  | 1767 |  | 1777 |  | 1787 |
|  | 1726 |  | 1736 |  | 1746 |  | 1757 |  | 1767 |  | 1777 |  | 1787 |
|  | 1726 |  | 1736 |  | 1747 |  | 1757 |  | 1767 |  | 1777 |  | 1788 |
|  | 1726 |  | 1737 |  | 1747 |  | 1757 |  | 1767 |  | 1778 |  | 1788 |
|  | 1727 |  | 1737 |  | 1747 |  | 1757 |  | 1768 |  | 1778 |  | 1788 |
|  | 1727 |  | 1737 |  | 1747 |  | 1758 |  | 1768 |  | 1778 |  | 1788 |
|  | 1727 |  | 1737 |  | 1748 |  | 1758 |  | 1768 |  | 1778 |  | 1789 |
|  | 1727 |  | 1738 |  | 1748 |  | 1758 |  | 1768 |  | 1779 |  | 1789 |
|  | 1728 |  | 1738 |  | 1748 |  | 1758 |  | 1769 |  | 1779 |  | 1789 |
|  | 1728 |  | 1738 |  | 1748 |  | 1759 |  | 1769 |  | 1779 |  | 1789 |
|  | 1728 |  | 1738 |  | 1749 |  | 1759 |  | 1769 |  | 1779 |  | 1790 |
|  | 1728 |  | 1739 |  | 1749 |  | 1759 |  | 1769 |  | 1780 |  | 1790 |
|  | 1729 |  | 1739 |  | 1749 |  | 1759 |  | 1770 |  | 1780 |  | 1790 |
|  | 1729 |  | 1739 |  | 1749 |  | 1760 |  | 1770 |  | 1780 |  | 1790 |
|  | 1729 |  | 1739 |  | 1750 |  | 1760 |  | 1770 |  | 1780 |  | 1791 |
|  | 1729 |  | 1740 |  | 1750 |  | 1760 |  | 1770 |  | 1781 |  | 1791 |
|  | 1730 |  | 1740 |  | 1750 |  | 1760 |  | 1771 |  | 1781 |  | 1791 |
|  | 1730 |  | 1740 |  | 1750 |  | 1761 |  | 1771 |  | 1781 |  | 1791 |
|  | 1730 |  | 1740 |  | 1751 |  | 1761 |  | 1771 |  | 1781 |  | 1792 |
|  | 1730 |  | 1741 |  | 1751 |  | 1761 |  | 1771 |  | 1782 |  | 1792 |
|  | 1731 |  | 1741 |  | 1751 |  | 1761 |  | 1772 |  | 1782 |  | 1792 |
|  | 1731 |  | 1741 |  | 1751 |  | 1762 |  | 1772 |  | 1782 |  | 1792 |
|  | 1731 |  | 1741 |  | 1752 |  | 1762 |  | 1772 |  | 1782 |  | 1793 |
|  | 1731 |  | 1742 |  | 1752 |  | 1762 |  | 1772 |  | 1783 |  | 1793 |
|  | 1732 |  | 1742 |  | 1752 |  | 1762 |  | 1773 |  | 1783 |  | 1793 |
|  | 1732 |  | 1742 |  | 1752 |  | 1763 |  | 1773 |  | 1783 |  | 1793 |
|  | 1732 |  | 1742 |  | 1753 |  | 1763 |  | 1773 |  | 1783 |  | 1794 |
|  | 1732 |  | 1743 |  | 1753 |  | 1763 |  | 1773 |  | 1784 |  | 1794 |
|  | 1733 |  | 1743 |  | 1753 |  | 1763 |  | 1774 |  | 1784 |  | 1794 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. |  |  | Bl nb |  | $\mathrm{Bl} \mathrm{nb}^{\text {nb }}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1794 | PPD | 1805 | PPD | 1815 | PPD | 1825 | PPD | 1835 | PPD | 1846 | PPD | 1856 |
|  | 1795 |  | 1805 |  | 1815 |  | 1825 |  | 1836 |  | 1846 |  | 1856 |
|  | 1795 |  | 1805 |  | 1815 |  | 1826 |  | 1836 |  | 1846 |  | 1856 |
|  | 1795 |  | 1805 |  | 1816 |  | 1826 |  | 1836 |  | 1846 |  | 1857 |
|  | 1795 |  | 1806 |  | 1816 |  | 1826 |  | 1836 |  | 1847 |  | 1857 |
|  | 1796 |  | 1806 |  | 1816 |  | 1826 |  | 1837 |  | 1847 |  | 1857 |
|  | 1796 |  | 1806 |  | 1816 |  | 1827 |  | 1837 |  | 1847 |  | 1857 |
|  | 1796 |  | 1806 |  | 1817 |  | 1827 |  | 1837 |  | 1847 |  | 1858 |
|  | 1796 |  | 1807 |  | 1817 |  | 1827 |  | 1837 |  | 1848 |  | 1858 |
|  | 1797 |  | 1807 |  | 1817 |  | 1827 |  | 1838 |  | 1848 |  | 1858 |
|  | 1797 |  | 1807 |  | 1817 |  | 1828 |  | 1838 |  | 1848 |  | 1858 |
|  | 1797 |  | 1807 |  | 1818 |  | 1828 |  | 1838 |  | 1848 |  | 1859 |
|  | 1797 |  | 1808 |  | 1818 |  | 1828 |  | 1838 |  | 1849 |  | 1859 |
|  | 1798 |  | 1808 |  | 1818 |  | 1828 |  | 1839 |  | 1849 |  | 1859 |
|  | 1798 |  | 1808 |  | 1818 |  | 1829 |  | 1839 |  | 1849 |  | 1859 |
|  | 1798 |  | 1808 |  | 1819 |  | 1829 |  | 1839 |  | 1849 |  | 1860 |
|  | 1798 |  | 1809 |  | 1819 |  | 1829 |  | 1839 |  | 1850 |  | 1860 |
|  | 1799 |  | 1809 |  | 1819 |  | 1829 |  | 1840 |  | 1850 |  | 1860 |
|  | 1799 |  | 1809 |  | 1819 |  | 1830 |  | 1840 |  | 1850 |  | 1860 |
|  | 1799 |  | 1809 |  | 1820 |  | 1830 |  | 1840 |  | 1850 |  | 1861 |
|  | 1799 |  | 1810 |  | 1820 |  | 1830 |  | 1840 |  | 1851 |  | 1861 |
|  | 1800 |  | 1810 |  | 1820 |  | 1830 |  | 1841 |  | 1851 |  | 1861 |
|  | 1800 |  | 1810 |  | 1820 |  | 1831 |  | 1841 |  | 1851 |  | 1861 |
|  | 1800 |  | 1810 |  | 1821 |  | 1831 |  | 1841 |  | 1851 |  | 1862 |
|  | 1800 |  | 1811 |  | 1821 |  | 1831 |  | 1841 |  | 1852 |  | 1862 |
|  | 1801 |  | 1811 |  | 1821 |  | 1831 |  | 1842 |  | 1852 |  | 1862 |
|  | 1801 |  | 1811 |  | 1821 |  | 1832 |  | 1842 |  | 1852 |  | 1862 |
|  | 1801 |  | 1811 |  | 1822 |  | 1832 |  | 1842 |  | 1852 |  | 1863 |
|  | 1801 |  | 1812 |  | 1822 |  | 1832 |  | 1842 |  | 1853 |  | 1863 |
|  | 1802 |  | 1812 |  | 1822 |  | 1832 |  | 1843 |  | 1853 |  | 1863 |
|  | 1802 |  | 1812 |  | 1822 |  | 1833 |  | 1843 |  | 1853 |  | 1863 |
|  | 1802 |  | 1812 |  | 1823 |  | 1833 |  | 1843 |  | 1853 |  | 1864 |
|  | 1802 |  | 1813 |  | 1823 |  | 1833 |  | 1843 |  | 1854 |  | 1864 |
|  | 1803 |  | 1813 |  | 1823 |  | 1833 |  | 1844 |  | 1854 |  | 1864 |
|  | 1803 |  | 1813 |  | 1823 |  | 1834 |  | 1844 |  | 1854 |  | 1864 |
|  | 1803 |  | 1813 |  | 1824 |  | 1834 |  | 1844 |  | 1854 |  | 1865 |
|  | 1803 |  | 1814 |  | 1824 |  | 1834 |  | 1844 |  | 1855 |  | 1865 |
|  | 1804 |  | 1814 |  | 1824 |  | 1834 |  | 1845 |  | 1855 |  | 1865 |
|  | 1804 |  | 1814 |  | 1824 |  | 1835 |  | 1845 |  | 1855 |  | 1865 |
|  | 1804 |  | 1814 |  | 1825 |  | 1835 |  | 1845 |  | 1855 |  | 1866 |
|  | 1804 |  | 1815 |  | 1825 |  | 1835 |  | 1845 |  | 1856 |  | 1866 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | Bl nb |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{gathered} \text { Trt. } \\ \text { No nb. } \end{gathered}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1866 | PPD | 1876 | PPD | 1887 | PPD | 1897 | PPD | 1907 | PPD | 1917 | PPD | 1928 |
|  | 1866 |  | 1877 |  | 1887 |  | 1897 |  | 1907 |  | 1918 |  | 1928 |
|  | 1867 |  | 1877 |  | 1887 |  | 1897 |  | 1908 |  | 1918 |  | 1928 |
|  | 1867 |  | 1877 |  | 1887 |  | 1898 |  | 1908 |  | 1918 |  | 1928 |
|  | 1867 |  | 1877 |  | 1888 |  | 1898 |  | 1908 |  | 1918 |  | 1929 |
|  | 1867 |  | 1878 |  | 1888 |  | 1898 |  | 1908 |  | 1919 |  | 1929 |
|  | 1868 |  | 1878 |  | 1888 |  | 1898 |  | 1909 |  | 1919 |  | 1929 |
|  | 1868 |  | 1878 |  | 1888 |  | 1899 |  | 1909 |  | 1919 |  | 1929 |
|  | 1868 |  | 1878 |  | 1889 |  | 1899 |  | 1909 |  | 1919 |  | 1930 |
|  | 1868 |  | 1879 |  | 1889 |  | 1899 |  | 1909 |  | 1920 |  | 1930 |
|  | 1869 |  | 1879 |  | 1889 |  | 1899 |  | 1910 |  | 1920 |  | 1930 |
|  | 1869 |  | 1879 |  | 1889 |  | 1900 |  | 1910 |  | 1920 |  | 1930 |
|  | 1869 |  | 1879 |  | 1890 |  | 1900 |  | 1910 |  | 1920 |  | 1931 |
|  | 1869 |  | 1880 |  | 1890 |  | 1900 |  | 1910 |  | 1921 |  | 1931 |
|  | 1870 |  | 1880 |  | 1890 |  | 1900 |  | 1911 |  | 1921 |  | 1931 |
|  | 1870 |  | 1880 |  | 1890 |  | 1901 |  | 1911 |  | 1921 |  | 1931 |
|  | 1870 |  | 1880 |  | 1891 |  | 1901 |  | 1911 |  | 1921 |  | 1932 |
|  | 1870 |  | 1881 |  | 1891 |  | 1901 |  | 1911 |  | 1922 |  | 1932 |
|  | 1871 |  | 1881 |  | 1891 |  | 1901 |  | 1912 |  | 1922 |  | 1932 |
|  | 1871 |  | 1881 |  | 1891 |  | 1902 |  | 1912 |  | 1922 |  | 1932 |
|  | 1871 |  | 1881 |  | 1892 |  | 1902 |  | 1912 |  | 1922 |  | 1933 |
|  | 1871 |  | 1882 |  | 1892 |  | 1902 |  | 1912 |  | 1923 |  | 1933 |
|  | 1872 |  | 1882 |  | 1892 |  | 1902 |  | 1913 |  | 1923 |  | 1933 |
|  | 1872 |  | 1882 |  | 1892 |  | 1903 |  | 1913 |  | 1923 |  | 1933 |
|  | 1872 |  | 1882 |  | 1893 |  | 1903 |  | 1913 |  | 1923 |  | 1934 |
|  | 1872 |  | 1883 |  | 1893 |  | 1903 |  | 1913 |  | 1924 |  | 1934 |
|  | 1873 |  | 1883 |  | 1893 |  | 1903 |  | 1914 |  | 1924 |  | 1934 |
|  | 1873 |  | 1883 |  | 1893 |  | 1904 |  | 1914 |  | 1924 |  | 1934 |
|  | 1873 |  | 1883 |  | 1894 |  | 1904 |  | 1914 |  | 1924 |  | 1935 |
|  | 1873 |  | 1884 |  | 1894 |  | 1904 |  | 1914 |  | 1925 |  | 1935 |
|  | 1874 |  | 1884 |  | 1894 |  | 1904 |  | 1915 |  | 1925 |  | 1935 |
|  | 1874 |  | 1884 |  | 1894 |  | 1905 |  | 1915 |  | 1925 |  | 1935 |
|  | 1874 |  | 1884 |  | 1895 |  | 1905 |  | 1915 |  | 1925 |  | 1936 |
|  | 1874 |  | 1885 |  | 1895 |  | 1905 |  | 1915 |  | 1926 |  | 1936 |
|  | 1875 |  | 1885 |  | 1895 |  | 1905 |  | 1916 |  | 1926 |  | 1936 |
|  | 1875 |  | 1885 |  | 1895 |  | 1906 |  | 1916 |  | 1926 |  | 1936 |
|  | 1875 |  | 1885 |  | 1896 |  | 1906 |  | 1916 |  | 1926 |  | 1937 |
|  | 1875 |  | 1886 |  | 1896 |  | 1906 |  | 1916 |  | 1927 |  | 1937 |
|  | 1876 |  | 1886 |  | 1896 |  | 1906 |  | 1917 |  | 1927 |  | 1937 |
|  | 1876 |  | 1886 |  | 1896 |  | 1907 |  | 1917 |  | 1927 |  | 1937 |
|  | 1876 |  | 1886 |  | 1897 |  | 1907 |  | 1917 |  | 1927 |  | 1938 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1938 | PPD | 1948 | PPD | 1958 | PPD | 1969 | PPD | 1979 | PPD | 1989 | PPD | 1999 |
|  | 1938 |  | 1948 |  | 1959 |  | 1969 |  | 1979 |  | 1989 |  | 2000 |
|  | 1938 |  | 1949 |  | 1959 |  | 1969 |  | 1979 |  | 1990 |  | 2000 |
|  | 1939 |  | 1949 |  | 1959 |  | 1969 |  | 1980 |  | 1990 |  | 2000 |
|  | 1939 |  | 1949 |  | 1959 |  | 1970 |  | 1980 |  | 1990 |  | 2000 |
|  | 1939 |  | 1949 |  | 1960 |  | 1970 |  | 1980 |  | 1990 |  | 2001 |
|  | 1939 |  | 1950 |  | 1960 |  | 1970 |  | 1980 |  | 1991 |  | 2001 |
|  | 1940 |  | 1950 |  | 1960 |  | 1970 |  | 1981 |  | 1991 |  | 2001 |
|  | 1940 |  | 1950 |  | 1960 |  | 1971 |  | 1981 |  | 1991 |  | 2001 |
|  | 1940 |  | 1950 |  | 1961 |  | 1971 |  | 1981 |  | 1991 |  | 2002 |
|  | 1940 |  | 1951 |  | 1961 |  | 1971 |  | 1981 |  | 1992 |  | 2002 |
|  | 1941 |  | 1951 |  | 1961 |  | 1971 |  | 1982 |  | 1992 |  | 2002 |
|  | 1941 |  | 1951 |  | 1961 |  | 1972 |  | 1982 |  | 1992 |  | 2002 |
|  | 1941 |  | 1951 |  | 1962 |  | 1972 |  | 1982 |  | 1992 |  | 2003 |
|  | 1941 |  | 1952 |  | 1962 |  | 1972 |  | 1982 |  | 1993 |  | 2003 |
|  | 1942 |  | 1952 |  | 1962 |  | 1972 |  | 1983 |  | 1993 |  | 2003 |
|  | 1942 |  | 1952 |  | 1962 |  | 1973 |  | 1983 |  | 1993 |  | 2003 |
|  | 1942 |  | 1952 |  | 1963 |  | 1973 |  | 1983 |  | 1993 |  | 2004 |
|  | 1942 |  | 1953 |  | 1963 |  | 1973 |  | 1983 |  | 1994 |  | 2004 |
|  | 1943 |  | 1953 |  | 1963 |  | 1973 |  | 1984 |  | 1994 |  | 2004 |
|  | 1943 |  | 1953 |  | 1963 |  | 1974 |  | 1984 |  | 1994 |  | 2004 |
|  | 1943 |  | 1953 |  | 1964 |  | 1974 |  | 1984 |  | 1994 |  | 2005 |
|  | 1943 |  | 1954 |  | 1964 |  | 1974 |  | 1984 |  | 1995 |  | 2005 |
|  | 1944 |  | 1954 |  | 1964 |  | 1974 |  | 1985 |  | 1995 |  | 2005 |
|  | 1944 |  | 1954 |  | 1964 |  | 1975 |  | 1985 |  | 1995 |  | 2005 |
|  | 1944 |  | 1954 |  | 1965 |  | 1975 |  | 1985 |  | 1995 |  | 2006 |
|  | 1944 |  | 1955 |  | 1965 |  | 1975 |  | 1985 |  | 1996 |  | 2006 |
|  | 1945 |  | 1955 |  | 1965 |  | 1975 |  | 1986 |  | 1996 |  | 2006 |
|  | 1945 |  | 1955 |  | 1965 |  | 1976 |  | 1986 |  | 1996 |  | 2006 |
|  | 1945 |  | 1955 |  | 1966 |  | 1976 |  | 1986 |  | 1996 |  | 2007 |
|  | 1945 |  | 1956 |  | 1966 |  | 1976 |  | 1986 |  | 1997 |  | 2007 |
|  | 1946 |  | 1956 |  | 1966 |  | 1976 |  | 1987 |  | 1997 |  | 2007 |
|  | 1946 |  | 1956 |  | 1966 |  | 1977 |  | 1987 |  | 1997 |  | 2007 |
|  | 1946 |  | 1956 |  | 1967 |  | 1977 |  | 1987 |  | 1997 |  | 2008 |
|  | 1946 |  | 1957 |  | 1967 |  | 1977 |  | 1987 |  | 1998 |  | 2008 |
|  | 1947 |  | 1957 |  | 1967 |  | 1977 |  | 1988 |  | 1998 |  | 2008 |
|  | 1947 |  | 1957 |  | 1967 |  | 1978 |  | 1988 |  | 1998 |  | 2008 |
|  | 1947 |  | 1957 |  | 1968 |  | 1978 |  | 1988 |  | 1998 |  | 2009 |
|  | 1947 |  | 1958 |  | 1968 |  | 1978 |  | 1988 |  | 1999 |  | 2009 |
|  | 1948 |  | 1958 |  | 1968 |  | 1978 |  | 1989 |  | 1999 |  | 2009 |
|  | 1948 |  | 1958 |  | 1968 |  | 1979 |  | 1989 |  | 1999 |  | 2009 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo


SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl nb | Trt | Bl. | Trt | Bl. | Trt | Bl nb |  | Bl nb |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2081 | PPD | 2092 | PPD | 2102 | PPD | 2112 | PPD | 2122 | PPD | 2133 | PPD | 2143 |
|  | 2082 |  | 2092 |  | 2102 |  | 2112 |  | 2123 |  | 2133 |  | 2143 |
|  | 2082 |  | 2092 |  | 2102 |  | 2113 |  | 2123 |  | 2133 |  | 2143 |
|  | 2082 |  | 2092 |  | 2103 |  | 2113 |  | 2123 |  | 2133 |  | 2144 |
|  | 2082 |  | 2093 |  | 2103 |  | 2113 |  | 2123 |  | 2134 |  | 2144 |
|  | 2083 |  | 2093 |  | 2103 |  | 2113 |  | 2124 |  | 2134 |  | 2144 |
|  | 2083 |  | 2093 |  | 2103 |  | 2114 |  | 2124 |  | 2134 |  | 2144 |
|  | 2083 |  | 2093 |  | 2104 |  | 2114 |  | 2124 |  | 2134 |  | 2145 |
|  | 2083 |  | 2094 |  | 2104 |  | 2114 |  | 2124 |  | 2135 |  | 2145 |
|  | 2084 |  | 2094 |  | 2104 |  | 2114 |  | 2125 |  | 2135 |  | 2145 |
|  | 2084 |  | 2094 |  | 2104 |  | 2115 |  | 2125 |  | 2135 |  | 2145 |
|  | 2084 |  | 2094 |  | 2105 |  | 2115 |  | 2125 |  | 2135 |  | 2146 |
|  | 2084 |  | 2095 |  | 2105 |  | 2115 |  | 2125 |  | 2136 |  | 2146 |
|  | 2085 |  | 2095 |  | 2105 |  | 2115 |  | 2126 |  | 2136 |  | 2146 |
|  | 2085 |  | 2095 |  | 2105 |  | 2116 |  | 2126 |  | 2136 |  | 2146 |
|  | 2085 |  | 2095 |  | 2106 |  | 2116 |  | 2126 |  | 2136 |  | 2147 |
|  | 2085 |  | 2096 |  | 2106 |  | 2116 |  | 2126 |  | 2137 |  | 2147 |
|  | 2086 |  | 2096 |  | 2106 |  | 2116 |  | 2127 |  | 2137 |  | 2147 |
|  | 2086 |  | 2096 |  | 2106 |  | 2117 |  | 2127 |  | 2137 |  | 2147 |
|  | 2086 |  | 2096 |  | 2107 |  | 2117 |  | 2127 |  | 2137 |  | 2148 |
|  | 2086 |  | 2097 |  | 2107 |  | 2117 |  | 2127 |  | 2138 |  | 2148 |
|  | 2087 |  | 2097 |  | 2107 |  | 2117 |  | 2128 |  | 2138 |  | 2148 |
|  | 2087 |  | 2097 |  | 2107 |  | 2118 |  | 2128 |  | 2138 |  | 2148 |
|  | 2087 |  | 2097 |  | 2108 |  | 2118 |  | 2128 |  | 2138 |  | 2149 |
|  | 2087 |  | 2098 |  | 2108 |  | 2118 |  | 2128 |  | 2139 |  | 2149 |
|  | 2088 |  | 2098 |  | 2108 |  | 2118 |  | 2129 |  | 2139 |  | 2149 |
|  | 2088 |  | 2098 |  | 2108 |  | 2119 |  | 2129 |  | 2139 |  | 2149 |
|  | 2088 |  | 2098 |  | 2109 |  | 2119 |  | 2129 |  | 2139 |  | 2150 |
|  | 2088 |  | 2099 |  | 2109 |  | 2119 |  | 2129 |  | 2140 |  | 2150 |
|  | 2089 |  | 2099 |  | 2109 |  | 2119 |  | 2130 |  | 2140 |  | 2150 |
|  | 2089 |  | 2099 |  | 2109 |  | 2120 |  | 2130 |  | 2140 |  | 2150 |
|  | 2089 |  | 2099 |  | 2110 |  | 2120 |  | 2130 |  | 2140 |  | 2151 |
|  | 2089 |  | 2100 |  | 2110 |  | 2120 |  | 2130 |  | 2141 |  | 2151 |
|  | 2090 |  | 2100 |  | 2110 |  | 2120 |  | 2131 |  | 2141 |  | 2151 |
|  | 2090 |  | 2100 |  | 2110 |  | 2121 |  | 2131 |  | 2141 |  | 2151 |
|  | 2090 |  | 2100 |  | 2111 |  | 2121 |  | 2131 |  | 2141 |  | 2152 |
|  | 2090 |  | 2101 |  | 2111 |  | 2121 |  | 2131 |  | 2142 |  | 2152 |
|  | 2091 |  | 2101 |  | 2111 |  | 2121 |  | 2132 |  | 2142 |  | 2152 |
|  | 2091 |  | 2101 |  | 2111 |  | 2122 |  | 2132 |  | 2142 |  | 2152 |
|  | 2091 |  | 2101 |  | 2112 |  | 2122 |  | 2132 |  | 2142 |  | 2153 |
|  | 2091 |  | 2102 |  | 2112 |  | 2122 |  | 2132 |  | 2143 |  | 2153 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)


SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2225 | PPD | 2235 | PPD | 2245 | PPD | 2256 | PPD | 2266 | PPD | 2276 | PPD | 2286 |
|  | 2225 |  | 2235 |  | 2246 |  | 2256 |  | 2266 |  | 2276 |  | 2287 |
|  | 2225 |  | 2236 |  | 2246 |  | 2256 |  | 2266 |  | 2277 |  | 2287 |
|  | 2226 |  | 2236 |  | 2246 |  | 2256 |  | 2267 |  | 2277 |  | 2287 |
|  | 2226 |  | 2236 |  | 2246 |  | 2257 |  | 2267 |  | 2277 |  | 2287 |
|  | 2226 |  | 2236 |  | 2247 |  | 2257 |  | 2267 |  | 2277 |  | 2288 |
|  | 2226 |  | 2237 |  | 2247 |  | 2257 |  | 2267 |  | 2278 |  | 2288 |
|  | 2227 |  | 2237 |  | 2247 |  | 2257 |  | 2268 |  | 2278 |  | 2288 |
|  | 2227 |  | 2237 |  | 2247 |  | 2258 |  | 2268 |  | 2278 |  | 2288 |
|  | 2227 |  | 2237 |  | 2248 |  | 2258 |  | 2268 |  | 2278 |  | 2289 |
|  | 2227 |  | 2238 |  | 2248 |  | 2258 |  | 2268 |  | 2279 |  | 2289 |
|  | 2228 |  | 2238 |  | 2248 |  | 2258 |  | 2269 |  | 2279 |  | 2289 |
|  | 2228 |  | 2238 |  | 2248 |  | 2259 |  | 2269 |  | 2279 |  | 2289 |
|  | 2228 |  | 2238 |  | 2249 |  | 2259 |  | 2269 |  | 2279 |  | 2290 |
|  | 2228 |  | 2239 |  | 2249 |  | 2259 |  | 2269 |  | 2280 |  | 2290 |
|  | 2229 |  | 2239 |  | 2249 |  | 2259 |  | 2270 |  | 2280 |  | 2290 |
|  | 2229 |  | 2239 |  | 2249 |  | 2260 |  | 2270 |  | 2280 |  | 2290 |
|  | 2229 |  | 2239 |  | 2250 |  | 2260 |  | 2270 |  | 2280 |  | 2291 |
|  | 2229 |  | 2240 |  | 2250 |  | 2260 |  | 2270 |  | 2281 |  | 2291 |
|  | 2230 |  | 2240 |  | 2250 |  | 2260 |  | 2271 |  | 2281 |  | 2291 |
|  | 2230 |  | 2240 |  | 2250 |  | 2261 |  | 2271 |  | 2281 |  | 2291 |
|  | 2230 |  | 2240 |  | 2251 |  | 2261 |  | 2271 |  | 2281 |  | 2292 |
|  | 2230 |  | 2241 |  | 2251 |  | 2261 |  | 2271 |  | 2282 |  | 2292 |
|  | 2231 |  | 2241 |  | 2251 |  | 2261 |  | 2272 |  | 2282 |  | 2292 |
|  | 2231 |  | 2241 |  | 2251 |  | 2262 |  | 2272 |  | 2282 |  | 2292 |
|  | 2231 |  | 2241 |  | 2252 |  | 2262 |  | 2272 |  | 2282 |  | 2293 |
|  | 2231 |  | 2242 |  | 2252 |  | 2262 |  | 2272 |  | 2283 |  | 2293 |
|  | 2232 |  | 2242 |  | 2252 |  | 2262 |  | 2273 |  | 2283 |  | 2293 |
|  | 2232 |  | 2242 |  | 2252 |  | 2263 |  | 2273 |  | 2283 |  | 2293 |
|  | 2232 |  | 2242 |  | 2253 |  | 2263 |  | 2273 |  | 2283 |  | 2294 |
|  | 2232 |  | 2243 |  | 2253 |  | 2263 |  | 2273 |  | 2284 |  | 2294 |
|  | 2233 |  | 2243 |  | 2253 |  | 2263 |  | 2274 |  | 2284 |  | 2294 |
|  | 2233 |  | 2243 |  | 2253 |  | 2264 |  | 2274 |  | 2284 |  | 2294 |
|  | 2233 |  | 2243 |  | 2254 |  | 2264 |  | 2274 |  | 2284 |  | 2295 |
|  | 2233 |  | 2244 |  | 2254 |  | 2264 |  | 2274 |  | 2285 |  | 2295 |
|  | 2234 |  | 2244 |  | 2254 |  | 2264 |  | 2275 |  | 2285 |  | 2295 |
|  | 2234 |  | 2244 |  | 2254 |  | 2265 |  | 2275 |  | 2285 |  | 2295 |
|  | 2234 |  | 2244 |  | 2255 |  | 2265 |  | 2275 |  | 2285 |  | 2296 |
|  | 2234 |  | 2245 |  | 2255 |  | 2265 |  | 2275 |  | 2286 |  | 2296 |
|  | 2235 |  | 2245 |  | 2255 |  | 2265 |  | 2276 |  | 2286 |  | 2296 |
|  | 2235 |  | 2245 |  | 2255 |  | 2266 |  | 2276 |  | 2286 |  | 2296 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)


SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. |  |  |  |  |  |  |  | Trt |  |  |  | $\begin{aligned} & \text { Trt. } \\ & \text { No nl. } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2368 | PPD | 2379 | PPD | 2389 | PPD | 2399 | PPD | 2409 | PPD | 2420 | PPD | 2430 |
|  | 2369 |  | 2379 |  | 2389 |  | 2399 |  | 2410 |  | 2420 |  | 2430 |
|  | 2369 |  | 2379 |  | 2389 |  | 2400 |  | 2410 |  | 2420 |  | 2430 |
|  | 2369 |  | 2379 |  | 2390 |  | 2400 |  | 2410 |  | 2420 |  | 2431 |
|  | 2369 |  | 2380 |  | 2390 |  | 2400 |  | 2410 |  | 2421 |  | 2431 |
|  | 2370 |  | 2380 |  | 2390 |  | 2400 |  | 2411 |  | 2421 |  | 2431 |
|  | 2370 |  | 2380 |  | 2390 |  | 2401 |  | 2411 |  | 2421 |  | 2431 |
|  | 2370 |  | 2380 |  | 2391 |  | 2401 |  | 2411 |  | 2421 |  | 2432 |
|  | 2370 |  | 2381 |  | 2391 |  | 2401 |  | 2411 |  | 2422 |  | 2432 |
|  | 2371 |  | 2381 |  | 2391 |  | 2401 |  | 2412 |  | 2422 |  | 2432 |
|  | 2371 |  | 2381 |  | 2391 |  | 2402 |  | 2412 |  | 2422 |  | 2432 |
|  | 2371 |  | 2381 |  | 2392 |  | 2402 |  | 2412 |  | 2422 |  | 2433 |
|  | 2371 |  | 2382 |  | 2392 |  | 2402 |  | 2412 |  | 2423 |  | 2433 |
|  | 2372 |  | 2382 |  | 2392 |  | 2402 |  | 2413 |  | 2423 |  | 2433 |
|  | 2372 |  | 2382 |  | 2392 |  | 2403 |  | 2413 |  | 2423 |  | 2433 |
|  | 2372 |  | 2382 |  | 2393 |  | 2403 |  | 2413 |  | 2423 |  | 2434 |
|  | 2372 |  | 2383 |  | 2393 |  | 2403 |  | 2413 |  | 2424 |  | 2434 |
|  | 2373 |  | 2383 |  | 2393 |  | 2403 |  | 2414 |  | 2424 |  | 2434 |
|  | 2373 |  | 2383 |  | 2393 |  | 2404 |  | 2414 |  | 2424 |  | 2434 |
|  | 2373 |  | 2383 |  | 2394 |  | 2404 |  | 2414 |  | 2424 |  | 2435 |
|  | 2373 |  | 2384 |  | 2394 |  | 2404 |  | 2414 |  | 2425 |  | 2435 |
|  | 2374 |  | 2384 |  | 2394 |  | 2404 |  | 2415 |  | 2425 |  | 2435 |
|  | 2374 |  | 2384 |  | 2394 |  | 2405 |  | 2415 |  | 2425 |  | 2435 |
|  | 2374 |  | 2384 |  | 2395 |  | 2405 |  | 2415 |  | 2425 |  | 2436 |
|  | 2374 |  | 2385 |  | 2395 |  | 2405 |  | 2415 |  | 2426 |  | 2436 |
|  | 2375 |  | 2385 |  | 2395 |  | 2405 |  | 2416 |  | 2426 |  | 2436 |
|  | 2375 |  | 2385 |  | 2395 |  | 2406 |  | 2416 |  | 2426 |  | 2436 |
|  | 2375 |  | 2385 |  | 2396 |  | 2406 |  | 2416 |  | 2426 |  | 2437 |
|  | 2375 |  | 2386 |  | 2396 |  | 2406 |  | 2416 |  | 2427 |  | 2437 |
|  | 2376 |  | 2386 |  | 2396 |  | 2406 |  | 2417 |  | 2427 |  | 2437 |
|  | 2376 |  | 2386 |  | 2396 |  | 2407 |  | 2417 |  | 2427 |  | 2437 |
|  | 2376 |  | 2386 |  | 2397 |  | 2407 |  | 2417 |  | 2427 |  | 2438 |
|  | 2376 |  | 2387 |  | 2397 |  | 2407 |  | 2417 |  | 2428 |  | 2438 |
|  | 2377 |  | 2387 |  | 2397 |  | 2407 |  | 2418 |  | 2428 |  | 2438 |
|  | 2377 |  | 2387 |  | 2397 |  | 2408 |  | 2418 |  | 2428 |  | 2438 |
|  | 2377 |  | 2387 |  | 2398 |  | 2408 |  | 2418 |  | 2428 |  | 2439 |
|  | 2377 |  | 2388 |  | 2398 |  | 2408 |  | 2418 |  | 2429 |  | 2439 |
|  | 2378 |  | 2388 |  | 2398 |  | 2408 |  | 2419 |  | 2429 |  | 2439 |
|  | 2378 |  | 2388 |  | 2398 |  | 2409 |  | 2419 |  | 2429 |  | 2439 |
|  | 2378 |  | 2388 |  | 2399 |  | 2409 |  | 2419 |  | 2429 |  | 2440 |
|  | 2378 |  | 2389 |  | 2399 |  | 2409 |  | 2419 |  | 2430 |  | 2440 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. |  |  |  |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | Bl. | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2440 | PPD | 2450 | PPD | 2461 | PPD | 2471 | PPD | 2481 | PPD | 2491 | PPD | 2502 |
|  | 2440 |  | 2451 |  | 2461 |  | 2471 |  | 2481 |  | 2492 |  | 2502 |
|  | 2441 |  | 2451 |  | 2461 |  | 2471 |  | 2482 |  | 2492 |  | 2502 |
|  | 2441 |  | 2451 |  | 2461 |  | 2472 |  | 2482 |  | 2492 |  | 2502 |
|  | 2441 |  | 2451 |  | 2462 |  | 2472 |  | 2482 |  | 2492 |  | 2503 |
|  | 2441 |  | 2452 |  | 2462 |  | 2472 |  | 2482 |  | 2493 |  | 2503 |
|  | 2442 |  | 2452 |  | 2462 |  | 2472 |  | 2483 |  | 2493 |  | 2503 |
|  | 2442 |  | 2452 |  | 2462 |  | 2473 |  | 2483 |  | 2493 |  | 2503 |
|  | 2442 |  | 2452 |  | 2463 |  | 2473 |  | 2483 |  | 2493 |  | 2504 |
|  | 2442 |  | 2453 |  | 2463 |  | 2473 |  | 2483 |  | 2494 |  | 2504 |
|  | 2443 |  | 2453 |  | 2463 |  | 2473 |  | 2484 |  | 2494 |  | 2504 |
|  | 2443 |  | 2453 |  | 2463 |  | 2474 |  | 2484 |  | 2494 |  | 2504 |
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|  | 2444 |  | 2454 |  | 2464 |  | 2474 |  | 2485 |  | 2495 |  | 2505 |
|  | 2444 |  | 2454 |  | 2464 |  | 2475 |  | 2485 |  | 2495 |  | 2505 |
|  | 2444 |  | 2454 |  | 2465 |  | 2475 |  | 2485 |  | 2495 |  | 2506 |
|  | 2444 |  | 2455 |  | 2465 |  | 2475 |  | 2485 |  | 2496 |  | 2506 |
|  | 2445 |  | 2455 |  | 2465 |  | 2475 |  | 2486 |  | 2496 |  | 2506 |
|  | 2445 |  | 2455 |  | 2465 |  | 2476 |  | 2486 |  | 2496 |  | 2506 |
|  | 2445 |  | 2455 |  | 2466 |  | 2476 |  | 2486 |  | 2496 |  | 2507 |
|  | 2445 |  | 2456 |  | 2466 |  | 2476 |  | 2486 |  | 2497 |  | 2507 |
|  | 2446 |  | 2456 |  | 2466 |  | 2476 |  | 2487 |  | 2497 |  | 2507 |
|  | 2446 |  | 2456 |  | 2466 |  | 2477 |  | 2487 |  | 2497 |  | 2507 |
|  | 2446 |  | 2456 |  | 2467 |  | 2477 |  | 2487 |  | 2497 |  | 2508 |
|  | 2446 |  | 2457 |  | 2467 |  | 2477 |  | 2487 |  | 2498 |  | 2508 |
|  | 2447 |  | 2457 |  | 2467 |  | 2477 |  | 2488 |  | 2498 |  | 2508 |
|  | 2447 |  | 2457 |  | 2467 |  | 2478 |  | 2488 |  | 2498 |  | 2508 |
|  | 2447 |  | 2457 |  | 2468 |  | 2478 |  | 2488 |  | 2498 |  | 2509 |
|  | 2447 |  | 2458 |  | 2468 |  | 2478 |  | 2488 |  | 2499 |  | 2509 |
|  | 2448 |  | 2458 |  | 2468 |  | 2478 |  | 2489 |  | 2499 |  | 2509 |
|  | 2448 |  | 2458 |  | 2468 |  | 2479 |  | 2489 |  | 2499 |  | 2509 |
|  | 2448 |  | 2458 |  | 2469 |  | 2479 |  | 2489 |  | 2499 |  | 2510 |
|  | 2448 |  | 2459 |  | 2469 |  | 2479 |  | 2489 |  | 2500 |  | 2510 |
|  | 2449 |  | 2459 |  | 2469 |  | 2479 |  | 2490 |  | 2500 |  | 2510 |
|  | 2449 |  | 2459 |  | 2469 |  | 2480 |  | 2490 |  | 2500 |  | 2510 |
|  | 2449 |  | 2459 |  | 2470 |  | 2480 |  | 2490 |  | 2500 |  | 2511 |
|  | 2449 |  | 2460 |  | 2470 |  | 2480 |  | 2490 |  | 2501 |  | 2511 |
|  | 2450 |  | 2460 |  | 2470 |  | 2480 |  | 2491 |  | 2501 |  | 2511 |
|  | 2450 |  | 2460 |  | 2470 |  | 2481 |  | 2491 |  | 2501 |  | 2511 |
|  | 2450 |  | 2460 |  | 2471 |  | 2481 |  | 2491 |  | 2501 |  | 2512 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. | Bl nb | Trt | Bl nb | Trt | Bl nb |  | Bl nb |  | $\mathrm{Bl} \text {. }$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2512 | PPD | 2522 | PPD | 2532 | PPD | 2543 | PPD | 2553 | PPD | 2563 | PPD | 2573 |
|  | 2512 |  | 2522 |  | 2533 |  | 2543 |  | 2553 |  | 2563 |  | 2574 |
|  | 2512 |  | 2523 |  | 2533 |  | 2543 |  | 2553 |  | 2564 |  | 2574 |
|  | 2513 |  | 2523 |  | 2533 |  | 2543 |  | 2554 |  | 2564 |  | 2574 |
|  | 2513 |  | 2523 |  | 2533 |  | 2544 |  | 2554 |  | 2564 |  | 2574 |
|  | 2513 |  | 2523 |  | 2534 |  | 2544 |  | 2554 |  | 2564 |  | 2575 |
|  | 2513 |  | 2524 |  | 2534 |  | 2544 |  | 2554 |  | 2565 |  | 2575 |
|  | 2514 |  | 2524 |  | 2534 |  | 2544 |  | 2555 |  | 2565 |  | 2575 |
|  | 2514 |  | 2524 |  | 2534 |  | 2545 |  | 2555 |  | 2565 |  | 2575 |
|  | 2514 |  | 2524 |  | 2535 |  | 2545 |  | 2555 |  | 2565 |  | 2576 |
|  | 2514 |  | 2525 |  | 2535 |  | 2545 |  | 2555 |  | 2566 |  | 2576 |
|  | 2515 |  | 2525 |  | 2535 |  | 2545 |  | 2556 |  | 2566 |  | 2576 |
|  | 2515 |  | 2525 |  | 2535 |  | 2546 |  | 2556 |  | 2566 |  | 2576 |
|  | 2515 |  | 2525 |  | 2536 |  | 2546 |  | 2556 |  | 2566 |  | 2577 |
|  | 2515 |  | 2526 |  | 2536 |  | 2546 |  | 2556 |  | 2567 |  | 2577 |
|  | 2516 |  | 2526 |  | 2536 |  | 2546 |  | 2557 |  | 2567 |  | 2577 |
|  | 2516 |  | 2526 |  | 2536 |  | 2547 |  | 2557 |  | 2567 |  | 2577 |
|  | 2516 |  | 2526 |  | 2537 |  | 2547 |  | 2557 |  | 2567 |  | 2578 |
|  | 2516 |  | 2527 |  | 2537 |  | 2547 |  | 2557 |  | 2568 |  | 2578 |
|  | 2517 |  | 2527 |  | 2537 |  | 2547 |  | 2558 |  | 2568 |  | 2578 |
|  | 2517 |  | 2527 |  | 2537 |  | 2548 |  | 2558 |  | 2568 |  | 2578 |
|  | 2517 |  | 2527 |  | 2538 |  | 2548 |  | 2558 |  | 2568 |  | 2579 |
|  | 2517 |  | 2528 |  | 2538 |  | 2548 |  | 2558 |  | 2569 |  | 2579 |
|  | 2518 |  | 2528 |  | 2538 |  | 2548 |  | 2559 |  | 2569 |  | 2579 |
|  | 2518 |  | 2528 |  | 2538 |  | 2549 |  | 2559 |  | 2569 |  | 2579 |
|  | 2518 |  | 2528 |  | 2539 |  | 2549 |  | 2559 |  | 2569 |  | 2580 |
|  | 2518 |  | 2529 |  | 2539 |  | 2549 |  | 2559 |  | 2570 |  | 2580 |
|  | 2519 |  | 2529 |  | 2539 |  | 2549 |  | 2560 |  | 2570 |  | 2580 |
|  | 2519 |  | 2529 |  | 2539 |  | 2550 |  | 2560 |  | 2570 |  | 2580 |
|  | 2519 |  | 2529 |  | 2540 |  | 2550 |  | 2560 |  | 2570 |  | 2581 |
|  | 2519 |  | 2530 |  | 2540 |  | 2550 |  | 2560 |  | 2571 |  | 2581 |
|  | 2520 |  | 2530 |  | 2540 |  | 2550 |  | 2561 |  | 2571 |  | 2581 |
|  | 2520 |  | 2530 |  | 2540 |  | 2551 |  | 2561 |  | 2571 |  | 2581 |
|  | 2520 |  | 2530 |  | 2541 |  | 2551 |  | 2561 |  | 2571 |  | 2582 |
|  | 2520 |  | 2531 |  | 2541 |  | 2551 |  | 2561 |  | 2572 |  | 2582 |
|  | 2521 |  | 2531 |  | 2541 |  | 2551 |  | 2562 |  | 2572 |  | 2582 |
|  | 2521 |  | 2531 |  | 2541 |  | 2552 |  | 2562 |  | 2572 |  | 2582 |
|  | 2521 |  | 2531 |  | 2542 |  | 2552 |  | 2562 |  | 2572 |  | 2583 |
|  | 2521 |  | 2532 |  | 2542 |  | 2552 |  | 2562 |  | 2573 |  | 2583 |
|  | 2522 |  | 2532 |  | 2542 |  | 2552 |  | 2563 |  | 2573 |  | 2583 |
|  | 2522 |  | 2532 |  | 2542 |  | 2553 |  | 2563 |  | 2573 |  | 2583 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl nb |  | Bl nb |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2584 | PPD | 2594 | PPD | 2604 | PPD | 2614 | PPD | 2625 | PPD | 2635 | PPD | 2645 |
|  | 2584 |  | 2594 |  | 2604 |  | 2615 |  | 2625 |  | 2635 |  | 2645 |
|  | 2584 |  | 2594 |  | 2605 |  | 2615 |  | 2625 |  | 2635 |  | 2646 |
|  | 2584 |  | 2595 |  | 2605 |  | 2615 |  | 2625 |  | 2636 |  | 2646 |
|  | 2585 |  | 2595 |  | 2605 |  | 2615 |  | 2626 |  | 2636 |  | 2646 |
|  | 2585 |  | 2595 |  | 2605 |  | 2616 |  | 2626 |  | 2636 |  | 2646 |
|  | 2585 |  | 2595 |  | 2606 |  | 2616 |  | 2626 |  | 2636 |  | 2647 |
|  | 2585 |  | 2596 |  | 2606 |  | 2616 |  | 2626 |  | 2637 |  | 2647 |
|  | 2586 |  | 2596 |  | 2606 |  | 2616 |  | 2627 |  | 2637 |  | 2647 |
|  | 2586 |  | 2596 |  | 2606 |  | 2617 |  | 2627 |  | 2637 |  | 2647 |
|  | 2586 |  | 2596 |  | 2607 |  | 2617 |  | 2627 |  | 2637 |  | 2648 |
|  | 2586 |  | 2597 |  | 2607 |  | 2617 |  | 2627 |  | 2638 |  | 2648 |
|  | 2587 |  | 2597 |  | 2607 |  | 2617 |  | 2628 |  | 2638 |  | 2648 |
|  | 2587 |  | 2597 |  | 2607 |  | 2618 |  | 2628 |  | 2638 |  | 2648 |
|  | 2587 |  | 2597 |  | 2608 |  | 2618 |  | 2628 |  | 2638 |  | 2649 |
|  | 2587 |  | 2598 |  | 2608 |  | 2618 |  | 2628 |  | 2639 |  | 2649 |
|  | 2588 |  | 2598 |  | 2608 |  | 2618 |  | 2629 |  | 2639 |  | 2649 |
|  | 2588 |  | 2598 |  | 2608 |  | 2619 |  | 2629 |  | 2639 |  | 2649 |
|  | 2588 |  | 2598 |  | 2609 |  | 2619 |  | 2629 |  | 2639 |  | 2650 |
|  | 2588 |  | 2599 |  | 2609 |  | 2619 |  | 2629 |  | 2640 |  | 2650 |
|  | 2589 |  | 2599 |  | 2609 |  | 2619 |  | 2630 |  | 2640 |  | 2650 |
|  | 2589 |  | 2599 |  | 2609 |  | 2620 |  | 2630 |  | 2640 |  | 2650 |
|  | 2589 |  | 2599 |  | 2610 |  | 2620 |  | 2630 |  | 2640 |  | 2651 |
|  | 2589 |  | 2600 |  | 2610 |  | 2620 |  | 2630 |  | 2641 |  | 2651 |
|  | 2590 |  | 2600 |  | 2610 |  | 2620 |  | 2631 |  | 2641 |  | 2651 |
|  | 2590 |  | 2600 |  | 2610 |  | 2621 |  | 2631 |  | 2641 |  | 2651 |
|  | 2590 |  | 2600 |  | 2611 |  | 2621 |  | 2631 |  | 2641 |  | 2652 |
|  | 2590 |  | 2601 |  | 2611 |  | 2621 |  | 2631 |  | 2642 |  | 2652 |
|  | 2591 |  | 2601 |  | 2611 |  | 2621 |  | 2632 |  | 2642 |  | 2652 |
|  | 2591 |  | 2601 |  | 2611 |  | 2622 |  | 2632 |  | 2642 |  | 2652 |
|  | 2591 |  | 2601 |  | 2612 |  | 2622 |  | 2632 |  | 2642 |  | 2653 |
|  | 2591 |  | 2602 |  | 2612 |  | 2622 |  | 2632 |  | 2643 |  | 2653 |
|  | 2592 |  | 2602 |  | 2612 |  | 2622 |  | 2633 |  | 2643 |  | 2653 |
|  | 2592 |  | 2602 |  | 2612 |  | 2623 |  | 2633 |  | 2643 |  | 2653 |
|  | 2592 |  | 2602 |  | 2613 |  | 2623 |  | 2633 |  | 2643 |  | 2654 |
|  | 2592 |  | 2603 |  | 2613 |  | 2623 |  | 2633 |  | 2644 |  | 2654 |
|  | 2593 |  | 2603 |  | 2613 |  | 2623 |  | 2634 |  | 2644 |  | 2654 |
|  | 2593 |  | 2603 |  | 2613 |  | 2624 |  | 2634 |  | 2644 |  | 2654 |
|  | 2593 |  | 2603 |  | 2614 |  | 2624 |  | 2634 |  | 2644 |  | 2655 |
|  | 2593 |  | 2604 |  | 2614 |  | 2624 |  | 2634 |  | 2645 |  | 2655 |
|  | 2594 |  | 2604 |  | 2614 |  | 2624 |  | 2635 |  | 2645 |  | 2655 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Tre. |  |  |  |  |  |  | $\mathrm{Bl} \text {. }$ | Trt | Bl nb |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2655 | PPD | 2666 | PPD | 2676 | PPD | 2686 | PPD | 2696 | PPD | 2707 | PPD | 2717 |
|  | 2656 |  | 2666 |  | 2676 |  | 2686 |  | 2697 |  | 2707 |  | 2717 |
|  | 2656 |  | 2666 |  | 2676 |  | 2687 |  | 2697 |  | 2707 |  | 2717 |
|  | 2656 |  | 2666 |  | 2677 |  | 2687 |  | 2697 |  | 2707 |  | 2718 |
|  | 2656 |  | 2667 |  | 2677 |  | 2687 |  | 2697 |  | 2708 |  | 2718 |
|  | 2657 |  | 2667 |  | 2677 |  | 2687 |  | 2698 |  | 2708 |  | 2718 |
|  | 2657 |  | 2667 |  | 2677 |  | 2688 |  | 2698 |  | 2708 |  | 2718 |
|  | 2657 |  | 2667 |  | 2678 |  | 2688 |  | 2698 |  | 2708 |  | 2719 |
|  | 2657 |  | 2668 |  | 2678 |  | 2688 |  | 2698 |  | 2709 |  | 2719 |
|  | 2658 |  | 2668 |  | 2678 |  | 2688 |  | 2699 |  | 2709 |  | 2719 |
|  | 2658 |  | 2668 |  | 2678 |  | 2689 |  | 2699 |  | 2709 |  | 2719 |
|  | 2658 |  | 2668 |  | 2679 |  | 2689 |  | 2699 |  | 2709 |  | 2720 |
|  | 2658 |  | 2669 |  | 2679 |  | 2689 |  | 2699 |  | 2710 |  | 2720 |
|  | 2659 |  | 2669 |  | 2679 |  | 2689 |  | 2700 |  | 2710 |  | 2720 |
|  | 2659 |  | 2669 |  | 2679 |  | 2690 |  | 2700 |  | 2710 |  | 2720 |
|  | 2659 |  | 2669 |  | 2680 |  | 2690 |  | 2700 |  | 2710 |  | 2721 |
|  | 2659 |  | 2670 |  | 2680 |  | 2690 |  | 2700 |  | 2711 |  | 2721 |
|  | 2660 |  | 2670 |  | 2680 |  | 2690 |  | 2701 |  | 2711 |  | 2721 |
|  | 2660 |  | 2670 |  | 2680 |  | 2691 |  | 2701 |  | 2711 |  | 2721 |
|  | 2660 |  | 2670 |  | 2681 |  | 2691 |  | 2701 |  | 2711 |  | 2722 |
|  | 2660 |  | 2671 |  | 2681 |  | 2691 |  | 2701 |  | 2712 |  | 2722 |
|  | 2661 |  | 2671 |  | 2681 |  | 2691 |  | 2702 |  | 2712 |  | 2722 |
|  | 2661 |  | 2671 |  | 2681 |  | 2692 |  | 2702 |  | 2712 |  | 2722 |
|  | 2661 |  | 2671 |  | 2682 |  | 2692 |  | 2702 |  | 2712 |  | 2723 |
|  | 2661 |  | 2672 |  | 2682 |  | 2692 |  | 2702 |  | 2713 |  | 2723 |
|  | 2662 |  | 2672 |  | 2682 |  | 2692 |  | 2703 |  | 2713 |  | 2723 |
|  | 2662 |  | 2672 |  | 2682 |  | 2693 |  | 2703 |  | 2713 |  | 2723 |
|  | 2662 |  | 2672 |  | 2683 |  | 2693 |  | 2703 |  | 2713 |  | 2724 |
|  | 2662 |  | 2673 |  | 2683 |  | 2693 |  | 2703 |  | 2714 |  | 2724 |
|  | 2663 |  | 2673 |  | 2683 |  | 2693 |  | 2704 |  | 2714 |  | 2724 |
|  | 2663 |  | 2673 |  | 2683 |  | 2694 |  | 2704 |  | 2714 |  | 2724 |
|  | 2663 |  | 2673 |  | 2684 |  | 2694 |  | 2704 |  | 2714 |  | 2725 |
|  | 2663 |  | 2674 |  | 2684 |  | 2694 |  | 2704 |  | 2715 |  | 2725 |
|  | 2664 |  | 2674 |  | 2684 |  | 2694 |  | 2705 |  | 2715 |  | 2725 |
|  | 2664 |  | 2674 |  | 2684 |  | 2695 |  | 2705 |  | 2715 |  | 2725 |
|  | 2664 |  | 2674 |  | 2685 |  | 2695 |  | 2705 |  | 2715 |  | 2726 |
|  | 2664 |  | 2675 |  | 2685 |  | 2695 |  | 2705 |  | 2716 |  | 2726 |
|  | 2665 |  | 2675 |  | 2685 |  | 2695 |  | 2706 |  | 2716 |  | 2726 |
|  | 2665 |  | 2675 |  | 2685 |  | 2696 |  | 2706 |  | 2716 |  | 2726 |
|  | 2665 |  | 2675 |  | 2686 |  | 2696 |  | 2706 |  | 2716 |  | 2727 |
|  | 2665 |  | 2676 |  | 2686 |  | 2696 |  | 2706 |  | 2717 |  | 2727 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. |  | $\begin{aligned} & \text { Tret. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2727 | PPD | 2737 | PPD | 2748 | PPD | 2758 | PPD | 2768 | PPD | 2778 | PPD | 2789 |
|  | 2727 |  | 2738 |  | 2748 |  | 2758 |  | 2768 |  | 2779 |  | 2789 |
|  | 2728 |  | 2738 |  | 2748 |  | 2758 |  | 2769 |  | 2779 |  | 2789 |
|  | 2728 |  | 2738 |  | 2748 |  | 2759 |  | 2769 |  | 2779 |  | 2789 |
|  | 2728 |  | 2738 |  | 2749 |  | 2759 |  | 2769 |  | 2779 |  | 2790 |
|  | 2728 |  | 2739 |  | 2749 |  | 2759 |  | 2769 |  | 2780 |  | 2790 |
|  | 2729 |  | 2739 |  | 2749 |  | 2759 |  | 2770 |  | 2780 |  | 2790 |
|  | 2729 |  | 2739 |  | 2749 |  | 2760 |  | 2770 |  | 2780 |  | 2790 |
|  | 2729 |  | 2739 |  | 2750 |  | 2760 |  | 2770 |  | 2780 |  | 2791 |
|  | 2729 |  | 2740 |  | 2750 |  | 2760 |  | 2770 |  | 2781 |  | 2791 |
|  | 2730 |  | 2740 |  | 2750 |  | 2760 |  | 2771 |  | 2781 |  | 2791 |
|  | 2730 |  | 2740 |  | 2750 |  | 2761 |  | 2771 |  | 2781 |  | 2791 |
|  | 2730 |  | 2740 |  | 2751 |  | 2761 |  | 2771 |  | 2781 |  | 2792 |
|  | 2730 |  | 2741 |  | 2751 |  | 2761 |  | 2771 |  | 2782 |  | 2792 |
|  | 2731 |  | 2741 |  | 2751 |  | 2761 |  | 2772 |  | 2782 |  | 2792 |
|  | 2731 |  | 2741 |  | 2751 |  | 2762 |  | 2772 |  | 2782 |  | 2792 |
|  | 2731 |  | 2741 |  | 2752 |  | 2762 |  | 2772 |  | 2782 |  | 2793 |
|  | 2731 |  | 2742 |  | 2752 |  | 2762 |  | 2772 |  | 2783 |  | 2793 |
|  | 2732 |  | 2742 |  | 2752 |  | 2762 |  | 2773 |  | 2783 |  | 2793 |
|  | 2732 |  | 2742 |  | 2752 |  | 2763 |  | 2773 |  | 2783 |  | 2793 |
|  | 2732 |  | 2742 |  | 2753 |  | 2763 |  | 2773 |  | 2783 |  | 2794 |
|  | 2732 |  | 2743 |  | 2753 |  | 2763 |  | 2773 |  | 2784 |  | 2794 |
|  | 2733 |  | 2743 |  | 2753 |  | 2763 |  | 2774 |  | 2784 |  | 2794 |
|  | 2733 |  | 2743 |  | 2753 |  | 2764 |  | 2774 |  | 2784 |  | 2794 |
|  | 2733 |  | 2743 |  | 2754 |  | 2764 |  | 2774 |  | 2784 |  | 2795 |
|  | 2733 |  | 2744 |  | 2754 |  | 2764 |  | 2774 |  | 2785 |  | 2795 |
|  | 2734 |  | 2744 |  | 2754 |  | 2764 |  | 2775 |  | 2785 |  | 2795 |
|  | 2734 |  | 2744 |  | 2754 |  | 2765 |  | 2775 |  | 2785 |  | 2795 |
|  | 2734 |  | 2744 |  | 2755 |  | 2765 |  | 2775 |  | 2785 |  | 2796 |
|  | 2734 |  | 2745 |  | 2755 |  | 2765 |  | 2775 |  | 2786 |  | 2796 |
|  | 2735 |  | 2745 |  | 2755 |  | 2765 |  | 2776 |  | 2786 |  | 2796 |
|  | 2735 |  | 2745 |  | 2755 |  | 2766 |  | 2776 |  | 2786 |  | 2796 |
|  | 2735 |  | 2745 |  | 2756 |  | 2766 |  | 2776 |  | 2786 |  | 2797 |
|  | 2735 |  | 2746 |  | 2756 |  | 2766 |  | 2776 |  | 2787 |  | 2797 |
|  | 2736 |  | 2746 |  | 2756 |  | 2766 |  | 2777 |  | 2787 |  | 2797 |
|  | 2736 |  | 2746 |  | 2756 |  | 2767 |  | 2777 |  | 2787 |  | 2797 |
|  | 2736 |  | 2746 |  | 2757 |  | 2767 |  | 2777 |  | 2787 |  | 2798 |
|  | 2736 |  | 2747 |  | 2757 |  | 2767 |  | 2777 |  | 2788 |  | 2798 |
|  | 2737 |  | 2747 |  | 2757 |  | 2767 |  | 2778 |  | 2788 |  | 2798 |
|  | 2737 |  | 2747 |  | 2757 |  | 2768 |  | 2778 |  | 2788 |  | 2798 |
|  | 2737 |  | 2747 |  | 2758 |  | 2768 |  | 2778 |  | 2788 |  | 2799 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. | Bl nb | Trt. Bl.No nb |  | Trt. Bl. <br> No nb |  | Trt. Bl. |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2799 | PPD | 2809 | PPD | 2819 | PPD | 2830 | PPD | 2840 | PPD | 2850 | PPD | 2860 |
|  | 2799 |  | 2809 |  | 2820 |  | 2830 |  | 2840 |  | 2850 |  | 2861 |
|  | 2799 |  | 2810 |  | 2820 |  | 2830 |  | 2840 |  | 2851 |  | 2861 |
|  | 2800 |  | 2810 |  | 2820 |  | 2830 |  | 2841 |  | 2851 |  | 2861 |
|  | 2800 |  | 2810 |  | 2820 |  | 2831 |  | 2841 |  | 2851 |  | 2861 |
|  | 2800 |  | 2810 |  | 2821 |  | 2831 |  | 2841 |  | 2851 |  | 2862 |
|  | 2800 |  | 2811 |  | 2821 |  | 2831 |  | 2841 |  | 2852 |  | 2862 |
|  | 2801 |  | 2811 |  | 2821 |  | 2831 |  | 2842 |  | 2852 |  | 2862 |
|  | 2801 |  | 2811 |  | 2821 |  | 2832 |  | 2842 |  | 2852 |  | 2862 |
|  | 2801 |  | 2811 |  | 2822 |  | 2832 |  | 2842 |  | 2852 |  | 2863 |
|  | 2801 |  | 2812 |  | 2822 |  | 2832 |  | 2842 |  | 2853 |  | 2863 |
|  | 2802 |  | 2812 |  | 2822 |  | 2832 |  | 2843 |  | 2853 |  | 2863 |
|  | 2802 |  | 2812 |  | 2822 |  | 2833 |  | 2843 |  | 2853 |  | 2863 |
|  | 2802 |  | 2812 |  | 2823 |  | 2833 |  | 2843 |  | 2853 |  | 2864 |
|  | 2802 |  | 2813 |  | 2823 |  | 2833 |  | 2843 |  | 2854 |  | 2864 |
|  | 2803 |  | 2813 |  | 2823 |  | 2833 |  | 2844 |  | 2854 |  | 2864 |
|  | 2803 |  | 2813 |  | 2823 |  | 2834 |  | 2844 |  | 2854 |  | 2864 |
|  | 2803 |  | 2813 |  | 2824 |  | 2834 |  | 2844 |  | 2854 |  | 2865 |
|  | 2803 |  | 2814 |  | 2824 |  | 2834 |  | 2844 |  | 2855 |  | 2865 |
|  | 2804 |  | 2814 |  | 2824 |  | 2834 |  | 2845 |  | 2855 |  | 2865 |
|  | 2804 |  | 2814 |  | 2824 |  | 2835 |  | 2845 |  | 2855 |  | 2865 |
|  | 2804 |  | 2814 |  | 2825 |  | 2835 |  | 2845 |  | 2855 |  | 2866 |
|  | 2804 |  | 2815 |  | 2825 |  | 2835 |  | 2845 |  | 2856 |  | 2866 |
|  | 2805 |  | 2815 |  | 2825 |  | 2835 |  | 2846 |  | 2856 |  | 2866 |
|  | 2805 |  | 2815 |  | 2825 |  | 2836 |  | 2846 |  | 2856 |  | 2866 |
|  | 2805 |  | 2815 |  | 2826 |  | 2836 |  | 2846 |  | 2856 |  | 2867 |
|  | 2805 |  | 2816 |  | 2826 |  | 2836 |  | 2846 |  | 2857 |  | 2867 |
|  | 2806 |  | 2816 |  | 2826 |  | 2836 |  | 2847 |  | 2857 |  | 2867 |
|  | 2806 |  | 2816 |  | 2826 |  | 2837 |  | 2847 |  | 2857 |  | 2867 |
|  | 2806 |  | 2816 |  | 2827 |  | 2837 |  | 2847 |  | 2857 |  | 2868 |
|  | 2806 |  | 2817 |  | 2827 |  | 2837 |  | 2847 |  | 2858 |  | 2868 |
|  | 2807 |  | 2817 |  | 2827 |  | 2837 |  | 2848 |  | 2858 |  | 2868 |
|  | 2807 |  | 2817 |  | 2827 |  | 2838 |  | 2848 |  | 2858 |  | 2868 |
|  | 2807 |  | 2817 |  | 2828 |  | 2838 |  | 2848 |  | 2858 |  | 2869 |
|  | 2807 |  | 2818 |  | 2828 |  | 2838 |  | 2848 |  | 2859 |  | 2869 |
|  | 2808 |  | 2818 |  | 2828 |  | 2838 |  | 2849 |  | 2859 |  | 2869 |
|  | 2808 |  | 2818 |  | 2828 |  | 2839 |  | 2849 |  | 2859 |  | 2869 |
|  | 2808 |  | 2818 |  | 2829 |  | 2839 |  | 2849 |  | 2859 |  | 2870 |
|  | 2808 |  | 2819 |  | 2829 |  | 2839 |  | 2849 |  | 2860 |  | 2870 |
|  | 2809 |  | 2819 |  | 2829 |  | 2839 |  | 2850 |  | 2860 |  | 2870 |
|  | 2809 |  | 2819 |  | 2829 |  | 2840 |  | 2850 |  | 2860 |  | 2870 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | Trt | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. } \mathrm{Bl} . \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2871 | PPD | 2881 | PPD | 2891 | PPD | 2901 | PPD | 2912 | PPD | 2922 | PPD | 2932 |
|  | 2871 |  | 2881 |  | 2891 |  | 2902 |  | 2912 |  | 2922 |  | 2932 |
|  | 2871 |  | 2881 |  | 2892 |  | 2902 |  | 2912 |  | 2922 |  | 2933 |
|  | 2871 |  | 2882 |  | 2892 |  | 2902 |  | 2912 |  | 2923 |  | 2933 |
|  | 2872 |  | 2882 |  | 2892 |  | 2902 |  | 2913 |  | 2923 |  | 2933 |
|  | 2872 |  | 2882 |  | 2892 |  | 2903 |  | 2913 |  | 2923 |  | 2933 |
|  | 2872 |  | 2882 |  | 2893 |  | 2903 |  | 2913 |  | 2923 |  | 2934 |
|  | 2872 |  | 2883 |  | 2893 |  | 2903 |  | 2913 |  | 2924 |  | 2934 |
|  | 2873 |  | 2883 |  | 2893 |  | 2903 |  | 2914 |  | 2924 |  | 2934 |
|  | 2873 |  | 2883 |  | 2893 |  | 2904 |  | 2914 |  | 2924 |  | 2934 |
|  | 2873 |  | 2883 |  | 2894 |  | 2904 |  | 2914 |  | 2924 |  | 2935 |
|  | 2873 |  | 2884 |  | 2894 |  | 2904 |  | 2914 |  | 2925 |  | 2935 |
|  | 2874 |  | 2884 |  | 2894 |  | 2904 |  | 2915 |  | 2925 |  | 2935 |
|  | 2874 |  | 2884 |  | 2894 |  | 2905 |  | 2915 |  | 2925 |  | 2935 |
|  | 2874 |  | 2884 |  | 2895 |  | 2905 |  | 2915 |  | 2925 |  | 2936 |
|  | 2874 |  | 2885 |  | 2895 |  | 2905 |  | 2915 |  | 2926 |  | 2936 |
|  | 2875 |  | 2885 |  | 2895 |  | 2905 |  | 2916 |  | 2926 |  | 2936 |
|  | 2875 |  | 2885 |  | 2895 |  | 2906 |  | 2916 |  | 2926 |  | 2936 |
|  | 2875 |  | 2885 |  | 2896 |  | 2906 |  | 2916 |  | 2926 |  | 2937 |
|  | 2875 |  | 2886 |  | 2896 |  | 2906 |  | 2916 |  | 2927 |  | 2937 |
|  | 2876 |  | 2886 |  | 2896 |  | 2906 |  | 2917 |  | 2927 |  | 2937 |
|  | 2876 |  | 2886 |  | 2896 |  | 2907 |  | 2917 |  | 2927 |  | 2937 |
|  | 2876 |  | 2886 |  | 2897 |  | 2907 |  | 2917 |  | 2927 |  | 2938 |
|  | 2876 |  | 2887 |  | 2897 |  | 2907 |  | 2917 |  | 2928 |  | 2938 |
|  | 2877 |  | 2887 |  | 2897 |  | 2907 |  | 2918 |  | 2928 |  | 2938 |
|  | 2877 |  | 2887 |  | 2897 |  | 2908 |  | 2918 |  | 2928 |  | 2938 |
|  | 2877 |  | 2887 |  | 2898 |  | 2908 |  | 2918 |  | 2928 |  | 2939 |
|  | 2877 |  | 2888 |  | 2898 |  | 2908 |  | 2918 |  | 2929 |  | 2939 |
|  | 2878 |  | 2888 |  | 2898 |  | 2908 |  | 2919 |  | 2929 |  | 2939 |
|  | 2878 |  | 2888 |  | 2898 |  | 2909 |  | 2919 |  | 2929 |  | 2939 |
|  | 2878 |  | 2888 |  | 2899 |  | 2909 |  | 2919 |  | 2929 |  | 2940 |
|  | 2878 |  | 2889 |  | 2899 |  | 2909 |  | 2919 |  | 2930 |  | 2940 |
|  | 2879 |  | 2889 |  | 2899 |  | 2909 |  | 2920 |  | 2930 |  | 2940 |
|  | 2879 |  | 2889 |  | 2899 |  | 2910 |  | 2920 |  | 2930 |  | 2940 |
|  | 2879 |  | 2889 |  | 2900 |  | 2910 |  | 2920 |  | 2930 |  | 2941 |
|  | 2879 |  | 2890 |  | 2900 |  | 2910 |  | 2920 |  | 2931 |  | 2941 |
|  | 2880 |  | 2890 |  | 2900 |  | 2910 |  | 2921 |  | 2931 |  | 2941 |
|  | 2880 |  | 2890 |  | 2900 |  | 2911 |  | 2921 |  | 2931 |  | 2941 |
|  | 2880 |  | 2890 |  | 2901 |  | 2911 |  | 2921 |  | 2931 |  | 2942 |
|  | 2880 |  | 2891 |  | 2901 |  | 2911 |  | 2921 |  | 2932 |  | 2942 |
|  | 2881 |  | 2891 |  | 2901 |  | 2911 |  | 2922 |  | 2932 |  | 2942 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  | Bl nb |  | $\mathrm{Bl} \text {. }$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. } \mathrm{Bl} . \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2942 | PPD | 2953 | PPD | 2963 | PPD | 2973 | PPD | 2983 | PPD | 2994 | PPD | 3004 |
|  | 2943 |  | 2953 |  | 2963 |  | 2973 |  | 2984 |  | 2994 |  | 3004 |
|  | 2943 |  | 2953 |  | 2963 |  | 2974 |  | 2984 |  | 2994 |  | 3004 |
|  | 2943 |  | 2953 |  | 2964 |  | 2974 |  | 2984 |  | 2994 |  | 3005 |
|  | 2943 |  | 2954 |  | 2964 |  | 2974 |  | 2984 |  | 2995 |  | 3005 |
|  | 2944 |  | 2954 |  | 2964 |  | 2974 |  | 2985 |  | 2995 |  | 3005 |
|  | 2944 |  | 2954 |  | 2964 |  | 2975 |  | 2985 |  | 2995 |  | 3005 |
|  | 2944 |  | 2954 |  | 2965 |  | 2975 |  | 2985 |  | 2995 |  | 3006 |
|  | 2944 |  | 2955 |  | 2965 |  | 2975 |  | 2985 |  | 2996 |  | 3006 |
|  | 2945 |  | 2955 |  | 2965 |  | 2975 |  | 2986 |  | 2996 |  | 3006 |
|  | 2945 |  | 2955 |  | 2965 |  | 2976 |  | 2986 |  | 2996 |  | 3006 |
|  | 2945 |  | 2955 |  | 2966 |  | 2976 |  | 2986 |  | 2996 |  | 3007 |
|  | 2945 |  | 2956 |  | 2966 |  | 2976 |  | 2986 |  | 2997 |  | 3007 |
|  | 2946 |  | 2956 |  | 2966 |  | 2976 |  | 2987 |  | 2997 |  | 3007 |
|  | 2946 |  | 2956 |  | 2966 |  | 2977 |  | 2987 |  | 2997 |  | 3007 |
|  | 2946 |  | 2956 |  | 2967 |  | 2977 |  | 2987 |  | 2997 |  | 3008 |
|  | 2946 |  | 2957 |  | 2967 |  | 2977 |  | 2987 |  | 2998 |  | 3008 |
|  | 2947 |  | 2957 |  | 2967 |  | 2977 |  | 2988 |  | 2998 |  | 3008 |
|  | 2947 |  | 2957 |  | 2967 |  | 2978 |  | 2988 |  | 2998 |  | 3008 |
|  | 2947 |  | 2957 |  | 2968 |  | 2978 |  | 2988 |  | 2998 |  | 3009 |
|  | 2947 |  | 2958 |  | 2968 |  | 2978 |  | 2988 |  | 2999 |  | 3009 |
|  | 2948 |  | 2958 |  | 2968 |  | 2978 |  | 2989 |  | 2999 |  | 3009 |
|  | 2948 |  | 2958 |  | 2968 |  | 2979 |  | 2989 |  | 2999 |  | 3009 |
|  | 2948 |  | 2958 |  | 2969 |  | 2979 |  | 2989 |  | 2999 |  | 3010 |
|  | 2948 |  | 2959 |  | 2969 |  | 2979 |  | 2989 |  | 3000 |  | 3010 |
|  | 2949 |  | 2959 |  | 2969 |  | 2979 |  | 2990 |  | 3000 |  | 3010 |
|  | 2949 |  | 2959 |  | 2969 |  | 2980 |  | 2990 |  | 3000 |  | 3010 |
|  | 2949 |  | 2959 |  | 2970 |  | 2980 |  | 2990 |  | 3000 |  | 3011 |
|  | 2949 |  | 2960 |  | 2970 |  | 2980 |  | 2990 |  | 3001 |  | 3011 |
|  | 2950 |  | 2960 |  | 2970 |  | 2980 |  | 2991 |  | 3001 |  | 3011 |
|  | 2950 |  | 2960 |  | 2970 |  | 2981 |  | 2991 |  | 3001 |  | 3011 |
|  | 2950 |  | 2960 |  | 2971 |  | 2981 |  | 2991 |  | 3001 |  | 3012 |
|  | 2950 |  | 2961 |  | 2971 |  | 2981 |  | 2991 |  | 3002 |  | 3012 |
|  | 2951 |  | 2961 |  | 2971 |  | 2981 |  | 2992 |  | 3002 |  | 3012 |
|  | 2951 |  | 2961 |  | 2971 |  | 2982 |  | 2992 |  | 3002 |  | 3012 |
|  | 2951 |  | 2961 |  | 2972 |  | 2982 |  | 2992 |  | 3002 |  | 3013 |
|  | 2951 |  | 2962 |  | 2972 |  | 2982 |  | 2992 |  | 3003 |  | 3013 |
|  | 2952 |  | 2962 |  | 2972 |  | 2982 |  | 2993 |  | 3003 |  | 3013 |
|  | 2952 |  | 2962 |  | 2972 |  | 2983 |  | 2993 |  | 3003 |  | 3013 |
|  | 2952 |  | 2962 |  | 2973 |  | 2983 |  | 2993 |  | 3003 |  | 3014 |
|  | 2952 |  | 2963 |  | 2973 |  | 2983 |  | 2993 |  | 3004 |  | 3014 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. } \\ & \text { No nl. } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3014 | PPD | 3024 | PPD | 3035 | PPD | 3045 | PPD | 3055 | PPD | 3065 | PPD | 3076 |
|  | 3014 |  | 3025 |  | 3035 |  | 3045 |  | 3055 |  | 3066 |  | 3076 |
|  | 3015 |  | 3025 |  | 3035 |  | 3045 |  | 3056 |  | 3066 |  | 3076 |
|  | 3015 |  | 3025 |  | 3035 |  | 3046 |  | 3056 |  | 3066 |  | 3076 |
|  | 3015 |  | 3025 |  | 3036 |  | 3046 |  | 3056 |  | 3066 |  | 3077 |
|  | 3015 |  | 3026 |  | 3036 |  | 3046 |  | 3056 |  | 3067 |  | 3077 |
|  | 3016 |  | 3026 |  | 3036 |  | 3046 |  | 3057 |  | 3067 |  | 3077 |
|  | 3016 |  | 3026 |  | 3036 |  | 3047 |  | 3057 |  | 3067 |  | 3077 |
|  | 3016 |  | 3026 |  | 3037 |  | 3047 |  | 3057 |  | 3067 |  | 3078 |
|  | 3016 |  | 3027 |  | 3037 |  | 3047 |  | 3057 |  | 3068 |  | 3078 |
|  | 3017 |  | 3027 |  | 3037 |  | 3047 |  | 3058 |  | 3068 |  | 3078 |
|  | 3017 |  | 3027 |  | 3037 |  | 3048 |  | 3058 |  | 3068 |  | 3078 |
|  | 3017 |  | 3027 |  | 3038 |  | 3048 |  | 3058 |  | 3068 |  | 3079 |
|  | 3017 |  | 3028 |  | 3038 |  | 3048 |  | 3058 |  | 3069 |  | 3079 |
|  | 3018 |  | 3028 |  | 3038 |  | 3048 |  | 3059 |  | 3069 |  | 3079 |
|  | 3018 |  | 3028 |  | 3038 |  | 3049 |  | 3059 |  | 3069 |  | 3079 |
|  | 3018 |  | 3028 |  | 3039 |  | 3049 |  | 3059 |  | 3069 |  | 3080 |
|  | 3018 |  | 3029 |  | 3039 |  | 3049 |  | 3059 |  | 3070 |  | 3080 |
|  | 3019 |  | 3029 |  | 3039 |  | 3049 |  | 3060 |  | 3070 |  | 3080 |
|  | 3019 |  | 3029 |  | 3039 |  | 3050 |  | 3060 |  | 3070 |  | 3080 |
|  | 3019 |  | 3029 |  | 3040 |  | 3050 |  | 3060 |  | 3070 |  | 3081 |
|  | 3019 |  | 3030 |  | 3040 |  | 3050 |  | 3060 |  | 3071 |  | 3081 |
|  | 3020 |  | 3030 |  | 3040 |  | 3050 |  | 3061 |  | 3071 |  | 3081 |
|  | 3020 |  | 3030 |  | 3040 |  | 3051 |  | 3061 |  | 3071 |  | 3081 |
|  | 3020 |  | 3030 |  | 3041 |  | 3051 |  | 3061 |  | 3071 |  | 3082 |
|  | 3020 |  | 3031 |  | 3041 |  | 3051 |  | 3061 |  | 3072 |  | 3082 |
|  | 3021 |  | 3031 |  | 3041 |  | 3051 |  | 3062 |  | 3072 |  | 3082 |
|  | 3021 |  | 3031 |  | 3041 |  | 3052 |  | 3062 |  | 3072 |  | 3082 |
|  | 3021 |  | 3031 |  | 3042 |  | 3052 |  | 3062 |  | 3072 |  | 3083 |
|  | 3021 |  | 3032 |  | 3042 |  | 3052 |  | 3062 |  | 3073 |  | 3083 |
|  | 3022 |  | 3032 |  | 3042 |  | 3052 |  | 3063 |  | 3073 |  | 3083 |
|  | 3022 |  | 3032 |  | 3042 |  | 3053 |  | 3063 |  | 3073 |  | 3083 |
|  | 3022 |  | 3032 |  | 3043 |  | 3053 |  | 3063 |  | 3073 |  | 3084 |
|  | 3022 |  | 3033 |  | 3043 |  | 3053 |  | 3063 |  | 3074 |  | 3084 |
|  | 3023 |  | 3033 |  | 3043 |  | 3053 |  | 3064 |  | 3074 |  | 3084 |
|  | 3023 |  | 3033 |  | 3043 |  | 3054 |  | 3064 |  | 3074 |  | 3084 |
|  | 3023 |  | 3033 |  | 3044 |  | 3054 |  | 3064 |  | 3074 |  | 3085 |
|  | 3023 |  | 3034 |  | 3044 |  | 3054 |  | 3064 |  | 3075 |  | 3085 |
|  | 3024 |  | 3034 |  | 3044 |  | 3054 |  | 3065 |  | 3075 |  | 3085 |
|  | 3024 |  | 3034 |  | 3044 |  | 3055 |  | 3065 |  | 3075 |  | 3085 |
|  | 3024 |  | 3034 |  | 3045 |  | 3055 |  | 3065 |  | 3075 |  | 3086 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  |  | Trt |  |  | Bl nb |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3086 | PPD | 3096 | PPD | 3106 | PPD | 3117 | PPD | 3127 | PPD | 3137 | PPD | 3147 |
|  | 3086 |  | 3096 |  | 3107 |  | 3117 |  | 3127 |  | 3137 |  | 3148 |
|  | 3086 |  | 3097 |  | 3107 |  | 3117 |  | 3127 |  | 3138 |  | 3148 |
|  | 3087 |  | 3097 |  | 3107 |  | 3117 |  | 3128 |  | 3138 |  | 3148 |
|  | 3087 |  | 3097 |  | 3107 |  | 3118 |  | 3128 |  | 3138 |  | 3148 |
|  | 3087 |  | 3097 |  | 3108 |  | 3118 |  | 3128 |  | 3138 |  | 3149 |
|  | 3087 |  | 3098 |  | 3108 |  | 3118 |  | 3128 |  | 3139 |  | 3149 |
|  | 3088 |  | 3098 |  | 3108 |  | 3118 |  | 3129 |  | 3139 |  | 3149 |
|  | 3088 |  | 3098 |  | 3108 |  | 3119 |  | 3129 |  | 3139 |  | 3149 |
|  | 3088 |  | 3098 |  | 3109 |  | 3119 |  | 3129 |  | 3139 |  | 3150 |
|  | 3088 |  | 3099 |  | 3109 |  | 3119 |  | 3129 |  | 3140 |  | 3150 |
|  | 3089 |  | 3099 |  | 3109 |  | 3119 |  | 3130 |  | 3140 |  | 3150 |
|  | 3089 |  | 3099 |  | 3109 |  | 3120 |  | 3130 |  | 3140 |  | 3150 |
|  | 3089 |  | 3099 |  | 3110 |  | 3120 |  | 3130 |  | 3140 |  | 3151 |
|  | 3089 |  | 3100 |  | 3110 |  | 3120 |  | 3130 |  | 3141 |  | 3151 |
|  | 3090 |  | 3100 |  | 3110 |  | 3120 |  | 3131 |  | 3141 |  | 3151 |
|  | 3090 |  | 3100 |  | 3110 |  | 3121 |  | 3131 |  | 3141 |  | 3151 |
|  | 3090 |  | 3100 |  | 3111 |  | 3121 |  | 3131 |  | 3141 |  | 3152 |
|  | 3090 |  | 3101 |  | 3111 |  | 3121 |  | 3131 |  | 3142 |  | 3152 |
|  | 3091 |  | 3101 |  | 3111 |  | 3121 |  | 3132 |  | 3142 |  | 3152 |
|  | 3091 |  | 3101 |  | 3111 |  | 3122 |  | 3132 |  | 3142 |  | 3152 |
|  | 3091 |  | 3101 |  | 3112 |  | 3122 |  | 3132 |  | 3142 |  | 3153 |
|  | 3091 |  | 3102 |  | 3112 |  | 3122 |  | 3132 |  | 3143 |  | 3153 |
|  | 3092 |  | 3102 |  | 3112 |  | 3122 |  | 3133 |  | 3143 |  | 3153 |
|  | 3092 |  | 3102 |  | 3112 |  | 3123 |  | 3133 |  | 3143 |  | 3153 |
|  | 3092 |  | 3102 |  | 3113 |  | 3123 |  | 3133 |  | 3143 |  | 3154 |
|  | 3092 |  | 3103 |  | 3113 |  | 3123 |  | 3133 |  | 3144 |  | 3154 |
|  | 3093 |  | 3103 |  | 3113 |  | 3123 |  | 3134 |  | 3144 |  | 3154 |
|  | 3093 |  | 3103 |  | 3113 |  | 3124 |  | 3134 |  | 3144 |  | 3154 |
|  | 3093 |  | 3103 |  | 3114 |  | 3124 |  | 3134 |  | 3144 |  | 3155 |
|  | 3093 |  | 3104 |  | 3114 |  | 3124 |  | 3134 |  | 3145 |  | 3155 |
|  | 3094 |  | 3104 |  | 3114 |  | 3124 |  | 3135 |  | 3145 |  | 3155 |
|  | 3094 |  | 3104 |  | 3114 |  | 3125 |  | 3135 |  | 3145 |  | 3155 |
|  | 3094 |  | 3104 |  | 3115 |  | 3125 |  | 3135 |  | 3145 |  | 3156 |
|  | 3094 |  | 3105 |  | 3115 |  | 3125 |  | 3135 |  | 3146 |  | 3156 |
|  | 3095 |  | 3105 |  | 3115 |  | 3125 |  | 3136 |  | 3146 |  | 3156 |
|  | 3095 |  | 3105 |  | 3115 |  | 3126 |  | 3136 |  | 3146 |  | 3156 |
|  | 3095 |  | 3105 |  | 3116 |  | 3126 |  | 3136 |  | 3146 |  | 3157 |
|  | 3095 |  | 3106 |  | 3116 |  | 3126 |  | 3136 |  | 3147 |  | 3157 |
|  | 3096 |  | 3106 |  | 3116 |  | 3126 |  | 3137 |  | 3147 |  | 3157 |
|  | 3096 |  | 3106 |  | 3116 |  | 3127 |  | 3137 |  | 3147 |  | 3157 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)


SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. | Bl nb |  | Bl. |  |  |  | Bl nb |  |  |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3229 | PPD | 3240 | PPD | 3250 | PPD | 3260 | PPD | 3270 | PPD | 3281 | PPD | 3291 |
|  | 3230 |  | 3240 |  | 3250 |  | 3260 |  | 3271 |  | 3281 |  | 3291 |
|  | 3230 |  | 3240 |  | 3250 |  | 3261 |  | 3271 |  | 3281 |  | 3291 |
|  | 3230 |  | 3240 |  | 3251 |  | 3261 |  | 3271 |  | 3281 |  | 3292 |
|  | 3230 |  | 3241 |  | 3251 |  | 3261 |  | 3271 |  | 3282 |  | 3292 |
|  | 3231 |  | 3241 |  | 3251 |  | 3261 |  | 3272 |  | 3282 |  | 3292 |
|  | 3231 |  | 3241 |  | 3251 |  | 3262 |  | 3272 |  | 3282 |  | 3292 |
|  | 3231 |  | 3241 |  | 3252 |  | 3262 |  | 3272 |  | 3282 |  | 3293 |
|  | 3231 |  | 3242 |  | 3252 |  | 3262 |  | 3272 |  | 3283 |  | 3293 |
|  | 3232 |  | 3242 |  | 3252 |  | 3262 |  | 3273 |  | 3283 |  | 3293 |
|  | 3232 |  | 3242 |  | 3252 |  | 3263 |  | 3273 |  | 3283 |  | 3293 |
|  | 3232 |  | 3242 |  | 3253 |  | 3263 |  | 3273 |  | 3283 |  | 3294 |
|  | 3232 |  | 3243 |  | 3253 |  | 3263 |  | 3273 |  | 3284 |  | 3294 |
|  | 3233 |  | 3243 |  | 3253 |  | 3263 |  | 3274 |  | 3284 |  | 3294 |
|  | 3233 |  | 3243 |  | 3253 |  | 3264 |  | 3274 |  | 3284 |  | 3294 |
|  | 3233 |  | 3243 |  | 3254 |  | 3264 |  | 3274 |  | 3284 |  | 3295 |
|  | 3233 |  | 3244 |  | 3254 |  | 3264 |  | 3274 |  | 3285 |  | 3295 |
|  | 3234 |  | 3244 |  | 3254 |  | 3264 |  | 3275 |  | 3285 |  | 3295 |
|  | 3234 |  | 3244 |  | 3254 |  | 3265 |  | 3275 |  | 3285 |  | 3295 |
|  | 3234 |  | 3244 |  | 3255 |  | 3265 |  | 3275 |  | 3285 |  | 3296 |
|  | 3234 |  | 3245 |  | 3255 |  | 3265 |  | 3275 |  | 3286 |  | 3296 |
|  | 3235 |  | 3245 |  | 3255 |  | 3265 |  | 3276 |  | 3286 |  | 3296 |
|  | 3235 |  | 3245 |  | 3255 |  | 3266 |  | 3276 |  | 3286 |  | 3296 |
|  | 3235 |  | 3245 |  | 3256 |  | 3266 |  | 3276 |  | 3286 |  | 3297 |
|  | 3235 |  | 3246 |  | 3256 |  | 3266 |  | 3276 |  | 3287 |  | 3297 |
|  | 3236 |  | 3246 |  | 3256 |  | 3266 |  | 3277 |  | 3287 |  | 3297 |
|  | 3236 |  | 3246 |  | 3256 |  | 3267 |  | 3277 |  | 3287 |  | 3297 |
|  | 3236 |  | 3246 |  | 3257 |  | 3267 |  | 3277 |  | 3287 |  | 3298 |
|  | 3236 |  | 3247 |  | 3257 |  | 3267 |  | 3277 |  | 3288 |  | 3298 |
|  | 3237 |  | 3247 |  | 3257 |  | 3267 |  | 3278 |  | 3288 |  | 3298 |
|  | 3237 |  | 3247 |  | 3257 |  | 3268 |  | 3278 |  | 3288 |  | 3298 |
|  | 3237 |  | 3247 |  | 3258 |  | 3268 |  | 3278 |  | 3288 |  | 3299 |
|  | 3237 |  | 3248 |  | 3258 |  | 3268 |  | 3278 |  | 3289 |  | 3299 |
|  | 3238 |  | 3248 |  | 3258 |  | 3268 |  | 3279 |  | 3289 |  | 3299 |
|  | 3238 |  | 3248 |  | 3258 |  | 3269 |  | 3279 |  | 3289 |  | 3299 |
|  | 3238 |  | 3248 |  | 3259 |  | 3269 |  | 3279 |  | 3289 |  | 3300 |
|  | 3238 |  | 3249 |  | 3259 |  | 3269 |  | 3279 |  | 3290 |  | 3300 |
|  | 3239 |  | 3249 |  | 3259 |  | 3269 |  | 3280 |  | 3290 |  | 3300 |
|  | 3239 |  | 3249 |  | 3259 |  | 3270 |  | 3280 |  | 3290 |  | 3300 |
|  | 3239 |  | 3249 |  | 3260 |  | 3270 |  | 3280 |  | 3290 |  | 3301 |
|  | 3239 |  | 3250 |  | 3260 |  | 3270 |  | 3280 |  | 3291 |  | 3301 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. |  |  | Bl. | Trt |  |  | Bl nb |  | Bl nb | Trt | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3301 | PPD | 3311 | PPD | 3322 | PPD | 3332 | PPD | 3342 | PPD | 3352 | PPD | 3363 |
|  | 3301 |  | 3312 |  | 3322 |  | 3332 |  | 3342 |  | 3353 |  | 3363 |
|  | 3302 |  | 3312 |  | 3322 |  | 3332 |  | 3343 |  | 3353 |  | 3363 |
|  | 3302 |  | 3312 |  | 3322 |  | 3333 |  | 3343 |  | 3353 |  | 3363 |
|  | 3302 |  | 3312 |  | 3323 |  | 3333 |  | 3343 |  | 3353 |  | 3364 |
|  | 3302 |  | 3313 |  | 3323 |  | 3333 |  | 3343 |  | 3354 |  | 3364 |
|  | 3303 |  | 3313 |  | 3323 |  | 3333 |  | 3344 |  | 3354 |  | 3364 |
|  | 3303 |  | 3313 |  | 3323 |  | 3334 |  | 3344 |  | 3354 |  | 3364 |
|  | 3303 |  | 3313 |  | 3324 |  | 3334 |  | 3344 |  | 3354 |  | 3365 |
|  | 3303 |  | 3314 |  | 3324 |  | 3334 |  | 3344 |  | 3355 |  | 3365 |
|  | 3304 |  | 3314 |  | 3324 |  | 3334 |  | 3345 |  | 3355 |  | 3365 |
|  | 3304 |  | 3314 |  | 3324 |  | 3335 |  | 3345 |  | 3355 |  | 3365 |
|  | 3304 |  | 3314 |  | 3325 |  | 3335 |  | 3345 |  | 3355 |  | 3366 |
|  | 3304 |  | 3315 |  | 3325 |  | 3335 |  | 3345 |  | 3356 |  | 3366 |
|  | 3305 |  | 3315 |  | 3325 |  | 3335 |  | 3346 |  | 3356 |  | 3366 |
|  | 3305 |  | 3315 |  | 3325 |  | 3336 |  | 3346 |  | 3356 |  | 3366 |
|  | 3305 |  | 3315 |  | 3326 |  | 3336 |  | 3346 |  | 3356 |  | 3367 |
|  | 3305 |  | 3316 |  | 3326 |  | 3336 |  | 3346 |  | 3357 |  | 3367 |
|  | 3306 |  | 3316 |  | 3326 |  | 3336 |  | 3347 |  | 3357 |  | 3367 |
|  | 3306 |  | 3316 |  | 3326 |  | 3337 |  | 3347 |  | 3357 |  | 3367 |
|  | 3306 |  | 3316 |  | 3327 |  | 3337 |  | 3347 |  | 3357 |  | 3368 |
|  | 3306 |  | 3317 |  | 3327 |  | 3337 |  | 3347 |  | 3358 |  | 3368 |
|  | 3307 |  | 3317 |  | 3327 |  | 3337 |  | 3348 |  | 3358 |  | 3368 |
|  | 3307 |  | 3317 |  | 3327 |  | 3338 |  | 3348 |  | 3358 |  | 3368 |
|  | 3307 |  | 3317 |  | 3328 |  | 3338 |  | 3348 |  | 3358 |  | 3369 |
|  | 3307 |  | 3318 |  | 3328 |  | 3338 |  | 3348 |  | 3359 |  | 3369 |
|  | 3308 |  | 3318 |  | 3328 |  | 3338 |  | 3349 |  | 3359 |  | 3369 |
|  | 3308 |  | 3318 |  | 3328 |  | 3339 |  | 3349 |  | 3359 |  | 3369 |
|  | 3308 |  | 3318 |  | 3329 |  | 3339 |  | 3349 |  | 3359 |  | 3370 |
|  | 3308 |  | 3319 |  | 3329 |  | 3339 |  | 3349 |  | 3360 |  | 3370 |
|  | 3309 |  | 3319 |  | 3329 |  | 3339 |  | 3350 |  | 3360 |  | 3370 |
|  | 3309 |  | 3319 |  | 3329 |  | 3340 |  | 3350 |  | 3360 |  | 3370 |
|  | 3309 |  | 3319 |  | 3330 |  | 3340 |  | 3350 |  | 3360 |  | 3371 |
|  | 3309 |  | 3320 |  | 3330 |  | 3340 |  | 3350 |  | 3361 |  | 3371 |
|  | 3310 |  | 3320 |  | 3330 |  | 3340 |  | 3351 |  | 3361 |  | 3371 |
|  | 3310 |  | 3320 |  | 3330 |  | 3341 |  | 3351 |  | 3361 |  | 3371 |
|  | 3310 |  | 3320 |  | 3331 |  | 3341 |  | 3351 |  | 3361 |  | 3372 |
|  | 3310 |  | 3321 |  | 3331 |  | 3341 |  | 3351 |  | 3362 |  | 3372 |
|  | 3311 |  | 3321 |  | 3331 |  | 3341 |  | 3352 |  | 3362 |  | 3372 |
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|  | 3311 |  | 3321 |  | 3332 |  | 3342 |  | 3352 |  | 3362 |  | 3373 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ |  |  |  |  |  |  |  | Trt |  |  |  | $\begin{aligned} & \text { Trt. } \\ & \text { No nl. } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3373 | PPD | 3383 | PPD | 3393 | PPD | 3404 | PPD | 3414 | PPD | 3424 | PPD | 3434 |
|  | 3373 |  | 3383 |  | 3394 |  | 3404 |  | 3414 |  | 3424 |  | 3435 |
|  | 3373 |  | 3384 |  | 3394 |  | 3404 |  | 3414 |  | 3425 |  | 3435 |
|  | 3374 |  | 3384 |  | 3394 |  | 3404 |  | 3415 |  | 3425 |  | 3435 |
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|  | 3374 |  | 3384 |  | 3395 |  | 3405 |  | 3415 |  | 3425 |  | 3436 |
|  | 3374 |  | 3385 |  | 3395 |  | 3405 |  | 3415 |  | 3426 |  | 3436 |
|  | 3375 |  | 3385 |  | 3395 |  | 3405 |  | 3416 |  | 3426 |  | 3436 |
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|  | 3375 |  | 3385 |  | 3396 |  | 3406 |  | 3416 |  | 3426 |  | 3437 |
|  | 3375 |  | 3386 |  | 3396 |  | 3406 |  | 3416 |  | 3427 |  | 3437 |
|  | 3376 |  | 3386 |  | 3396 |  | 3406 |  | 3417 |  | 3427 |  | 3437 |
|  | 3376 |  | 3386 |  | 3396 |  | 3407 |  | 3417 |  | 3427 |  | 3437 |
|  | 3376 |  | 3386 |  | 3397 |  | 3407 |  | 3417 |  | 3427 |  | 3438 |
|  | 3376 |  | 3387 |  | 3397 |  | 3407 |  | 3417 |  | 3428 |  | 3438 |
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|  | 3377 |  | 3387 |  | 3397 |  | 3408 |  | 3418 |  | 3428 |  | 3438 |
|  | 3377 |  | 3387 |  | 3398 |  | 3408 |  | 3418 |  | 3428 |  | 3439 |
|  | 3377 |  | 3388 |  | 3398 |  | 3408 |  | 3418 |  | 3429 |  | 3439 |
|  | 3378 |  | 3388 |  | 3398 |  | 3408 |  | 3419 |  | 3429 |  | 3439 |
|  | 3378 |  | 3388 |  | 3398 |  | 3409 |  | 3419 |  | 3429 |  | 3439 |
|  | 3378 |  | 3388 |  | 3399 |  | 3409 |  | 3419 |  | 3429 |  | 3440 |
|  | 3378 |  | 3389 |  | 3399 |  | 3409 |  | 3419 |  | 3430 |  | 3440 |
|  | 3379 |  | 3389 |  | 3399 |  | 3409 |  | 3420 |  | 3430 |  | 3440 |
|  | 3379 |  | 3389 |  | 3399 |  | 3410 |  | 3420 |  | 3430 |  | 3440 |
|  | 3379 |  | 3389 |  | 3400 |  | 3410 |  | 3420 |  | 3430 |  | 3441 |
|  | 3379 |  | 3390 |  | 3400 |  | 3410 |  | 3420 |  | 3431 |  | 3441 |
|  | 3380 |  | 3390 |  | 3400 |  | 3410 |  | 3421 |  | 3431 |  | 3441 |
|  | 3380 |  | 3390 |  | 3400 |  | 3411 |  | 3421 |  | 3431 |  | 3441 |
|  | 3380 |  | 3390 |  | 3401 |  | 3411 |  | 3421 |  | 3431 |  | 3442 |
|  | 3380 |  | 3391 |  | 3401 |  | 3411 |  | 3421 |  | 3432 |  | 3442 |
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|  | 3381 |  | 3391 |  | 3401 |  | 3412 |  | 3422 |  | 3432 |  | 3442 |
|  | 3381 |  | 3391 |  | 3402 |  | 3412 |  | 3422 |  | 3432 |  | 3443 |
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|  | 3382 |  | 3393 |  | 3403 |  | 3413 |  | 3423 |  | 3434 |  | 3444 |
|  | 3383 |  | 3393 |  | 3403 |  | 3413 |  | 3424 |  | 3434 |  | 3444 |
|  | 3383 |  | 3393 |  | 3403 |  | 3414 |  | 3424 |  | 3434 |  | 3444 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ |  |  | Bl. |  | Bl nb |  | $\mathrm{Bl} \text {. }$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3445 | PPD | 3455 | PPD | 3465 | PPD | 3475 | PPD | 3486 | PPD | 3496 | PPD | 3506 |
|  | 3445 |  | 3455 |  | 3465 |  | 3476 |  | 3486 |  | 3496 |  | 3506 |
|  | 3445 |  | 3455 |  | 3466 |  | 3476 |  | 3486 |  | 3496 |  | 3507 |
|  | 3445 |  | 3456 |  | 3466 |  | 3476 |  | 3486 |  | 3497 |  | 3507 |
|  | 3446 |  | 3456 |  | 3466 |  | 3476 |  | 3487 |  | 3497 |  | 3507 |
|  | 3446 |  | 3456 |  | 3466 |  | 3477 |  | 3487 |  | 3497 |  | 3507 |
|  | 3446 |  | 3456 |  | 3467 |  | 3477 |  | 3487 |  | 3497 |  | 3508 |
|  | 3446 |  | 3457 |  | 3467 |  | 3477 |  | 3487 |  | 3498 |  | 3508 |
|  | 3447 |  | 3457 |  | 3467 |  | 3477 |  | 3488 |  | 3498 |  | 3508 |
|  | 3447 |  | 3457 |  | 3467 |  | 3478 |  | 3488 |  | 3498 |  | 3508 |
|  | 3447 |  | 3457 |  | 3468 |  | 3478 |  | 3488 |  | 3498 |  | 3509 |
|  | 3447 |  | 3458 |  | 3468 |  | 3478 |  | 3488 |  | 3499 |  | 3509 |
|  | 3448 |  | 3458 |  | 3468 |  | 3478 |  | 3489 |  | 3499 |  | 3509 |
|  | 3448 |  | 3458 |  | 3468 |  | 3479 |  | 3489 |  | 3499 |  | 3509 |
|  | 3448 |  | 3458 |  | 3469 |  | 3479 |  | 3489 |  | 3499 |  | 3510 |
|  | 3448 |  | 3459 |  | 3469 |  | 3479 |  | 3489 |  | 3500 |  | 3510 |
|  | 3449 |  | 3459 |  | 3469 |  | 3479 |  | 3490 |  | 3500 |  | 3510 |
|  | 3449 |  | 3459 |  | 3469 |  | 3480 |  | 3490 |  | 3500 |  | 3510 |
|  | 3449 |  | 3459 |  | 3470 |  | 3480 |  | 3490 |  | 3500 |  | 3511 |
|  | 3449 |  | 3460 |  | 3470 |  | 3480 |  | 3490 |  | 3501 |  | 3511 |
|  | 3450 |  | 3460 |  | 3470 |  | 3480 |  | 3491 |  | 3501 |  | 3511 |
|  | 3450 |  | 3460 |  | 3470 |  | 3481 |  | 3491 |  | 3501 |  | 3511 |
|  | 3450 |  | 3460 |  | 3471 |  | 3481 |  | 3491 |  | 3501 |  | 3512 |
|  | 3450 |  | 3461 |  | 3471 |  | 3481 |  | 3491 |  | 3502 |  | 3512 |
|  | 3451 |  | 3461 |  | 3471 |  | 3481 |  | 3492 |  | 3502 |  | 3512 |
|  | 3451 |  | 3461 |  | 3471 |  | 3482 |  | 3492 |  | 3502 |  | 3512 |
|  | 3451 |  | 3461 |  | 3472 |  | 3482 |  | 3492 |  | 3502 |  | 3513 |
|  | 3451 |  | 3462 |  | 3472 |  | 3482 |  | 3492 |  | 3503 |  | 3513 |
|  | 3452 |  | 3462 |  | 3472 |  | 3482 |  | 3493 |  | 3503 |  | 3513 |
|  | 3452 |  | 3462 |  | 3472 |  | 3483 |  | 3493 |  | 3503 |  | 3513 |
|  | 3452 |  | 3462 |  | 3473 |  | 3483 |  | 3493 |  | 3503 |  | 3514 |
|  | 3452 |  | 3463 |  | 3473 |  | 3483 |  | 3493 |  | 3504 |  | 3514 |
|  | 3453 |  | 3463 |  | 3473 |  | 3483 |  | 3494 |  | 3504 |  | 3514 |
|  | 3453 |  | 3463 |  | 3473 |  | 3484 |  | 3494 |  | 3504 |  | 3514 |
|  | 3453 |  | 3463 |  | 3474 |  | 3484 |  | 3494 |  | 3504 |  | 3515 |
|  | 3453 |  | 3464 |  | 3474 |  | 3484 |  | 3494 |  | 3505 |  | 3515 |
|  | 3454 |  | 3464 |  | 3474 |  | 3484 |  | 3495 |  | 3505 |  | 3515 |
|  | 3454 |  | 3464 |  | 3474 |  | 3485 |  | 3495 |  | 3505 |  | 3515 |
|  | 3454 |  | 3464 |  | 3475 |  | 3485 |  | 3495 |  | 3505 |  | 3516 |
|  | 3454 |  | 3465 |  | 3475 |  | 3485 |  | 3495 |  | 3506 |  | 3516 |
|  | 3455 |  | 3465 |  | 3475 |  | 3485 |  | 3496 |  | 3506 |  | 3516 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)


SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3588 | PPD | 3598 | PPD | 3609 | PPD | 3619 | PPD | 3629 | PPD | 3639 | PPD | 3650 |
|  | 3588 |  | 3599 |  | 3609 |  | 3619 |  | 3629 |  | 3640 |  | 3650 |
|  | 3589 |  | 3599 |  | 3609 |  | 3619 |  | 3630 |  | 3640 |  | 3650 |
|  | 3589 |  | 3599 |  | 3609 |  | 3620 |  | 3630 |  | 3640 |  | 3650 |
|  | 3589 |  | 3599 |  | 3610 |  | 3620 |  | 3630 |  | 3640 |  | 3651 |
|  | 3589 |  | 3600 |  | 3610 |  | 3620 |  | 3630 |  | 3641 |  | 3651 |
|  | 3590 |  | 3600 |  | 3610 |  | 3620 |  | 3631 |  | 3641 |  | 3651 |
|  | 3590 |  | 3600 |  | 3610 |  | 3621 |  | 3631 |  | 3641 |  | 3651 |
|  | 3590 |  | 3600 |  | 3611 |  | 3621 |  | 3631 |  | 3641 |  | 3652 |
|  | 3590 |  | 3601 |  | 3611 |  | 3621 |  | 3631 |  | 3642 |  | 3652 |
|  | 3591 |  | 3601 |  | 3611 |  | 3621 |  | 3632 |  | 3642 |  | 3652 |
|  | 3591 |  | 3601 |  | 3611 |  | 3622 |  | 3632 |  | 3642 |  | 3652 |
|  | 3591 |  | 3601 |  | 3612 |  | 3622 |  | 3632 |  | 3642 |  | 3653 |
|  | 3591 |  | 3602 |  | 3612 |  | 3622 |  | 3632 |  | 3643 |  | 3653 |
|  | 3592 |  | 3602 |  | 3612 |  | 3622 |  | 3633 |  | 3643 |  | 3653 |
|  | 3592 |  | 3602 |  | 3612 |  | 3623 |  | 3633 |  | 3643 |  | 3653 |
|  | 3592 |  | 3602 |  | 3613 |  | 3623 |  | 3633 |  | 3643 |  | 3654 |
|  | 3592 |  | 3603 |  | 3613 |  | 3623 |  | 3633 |  | 3644 |  | 3654 |
|  | 3593 |  | 3603 |  | 3613 |  | 3623 |  | 3634 |  | 3644 |  | 3654 |
|  | 3593 |  | 3603 |  | 3613 |  | 3624 |  | 3634 |  | 3644 |  | 3654 |
|  | 3593 |  | 3603 |  | 3614 |  | 3624 |  | 3634 |  | 3644 |  | 3655 |
|  | 3593 |  | 3604 |  | 3614 |  | 3624 |  | 3634 |  | 3645 |  | 3655 |
|  | 3594 |  | 3604 |  | 3614 |  | 3624 |  | 3635 |  | 3645 |  | 3655 |
|  | 3594 |  | 3604 |  | 3614 |  | 3625 |  | 3635 |  | 3645 |  | 3655 |
|  | 3594 |  | 3604 |  | 3615 |  | 3625 |  | 3635 |  | 3645 |  | 3656 |
|  | 3594 |  | 3605 |  | 3615 |  | 3625 |  | 3635 |  | 3646 |  | 3656 |
|  | 3595 |  | 3605 |  | 3615 |  | 3625 |  | 3636 |  | 3646 |  | 3656 |
|  | 3595 |  | 3605 |  | 3615 |  | 3626 |  | 3636 |  | 3646 |  | 3656 |
|  | 3595 |  | 3605 |  | 3616 |  | 3626 |  | 3636 |  | 3646 |  | 3657 |
|  | 3595 |  | 3606 |  | 3616 |  | 3626 |  | 3636 |  | 3647 |  | 3657 |
|  | 3596 |  | 3606 |  | 3616 |  | 3626 |  | 3637 |  | 3647 |  | 3657 |
|  | 3596 |  | 3606 |  | 3616 |  | 3627 |  | 3637 |  | 3647 |  | 3657 |
|  | 3596 |  | 3606 |  | 3617 |  | 3627 |  | 3637 |  | 3647 |  | 3658 |
|  | 3596 |  | 3607 |  | 3617 |  | 3627 |  | 3637 |  | 3648 |  | 3658 |
|  | 3597 |  | 3607 |  | 3617 |  | 3627 |  | 3638 |  | 3648 |  | 3658 |
|  | 3597 |  | 3607 |  | 3617 |  | 3628 |  | 3638 |  | 3648 |  | 3658 |
|  | 3597 |  | 3607 |  | 3618 |  | 3628 |  | 3638 |  | 3648 |  | 3659 |
|  | 3597 |  | 3608 |  | 3618 |  | 3628 |  | 3638 |  | 3649 |  | 3659 |
|  | 3598 |  | 3608 |  | 3618 |  | 3628 |  | 3639 |  | 3649 |  | 3659 |
|  | 3598 |  | 3608 |  | 3618 |  | 3629 |  | 3639 |  | 3649 |  | 3659 |
|  | 3598 |  | 3608 |  | 3619 |  | 3629 |  | 3639 |  | 3649 |  | 3660 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl. |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3660 | PPD | 3670 | PPD | 3680 | PPD | 3691 | PPD | 3701 | PPD | 3711 | PPD | 3721 |
|  | 3660 |  | 3670 |  | 3681 |  | 3691 |  | 3701 |  | 3711 |  | 3722 |
|  | 3660 |  | 3671 |  | 3681 |  | 3691 |  | 3701 |  | 3712 |  | 3722 |
|  | 3661 |  | 3671 |  | 3681 |  | 3691 |  | 3702 |  | 3712 |  | 3722 |
|  | 3661 |  | 3671 |  | 3681 |  | 3692 |  | 3702 |  | 3712 |  | 3722 |
|  | 3661 |  | 3671 |  | 3682 |  | 3692 |  | 3702 |  | 3712 |  | 3723 |
|  | 3661 |  | 3672 |  | 3682 |  | 3692 |  | 3702 |  | 3713 |  | 3723 |
|  | 3662 |  | 3672 |  | 3682 |  | 3692 |  | 3703 |  | 3713 |  | 3723 |
|  | 3662 |  | 3672 |  | 3682 |  | 3693 |  | 3703 |  | 3713 |  | 3723 |
|  | 3662 |  | 3672 |  | 3683 |  | 3693 |  | 3703 |  | 3713 |  | 3724 |
|  | 3662 |  | 3673 |  | 3683 |  | 3693 |  | 3703 |  | 3714 |  | 3724 |
|  | 3663 |  | 3673 |  | 3683 |  | 3693 |  | 3704 |  | 3714 |  | 3724 |
|  | 3663 |  | 3673 |  | 3683 |  | 3694 |  | 3704 |  | 3714 |  | 3724 |
|  | 3663 |  | 3673 |  | 3684 |  | 3694 |  | 3704 |  | 3714 |  | 3725 |
|  | 3663 |  | 3674 |  | 3684 |  | 3694 |  | 3704 |  | 3715 |  | 3725 |
|  | 3664 |  | 3674 |  | 3684 |  | 3694 |  | 3705 |  | 3715 |  | 3725 |
|  | 3664 |  | 3674 |  | 3684 |  | 3695 |  | 3705 |  | 3715 |  | 3725 |
|  | 3664 |  | 3674 |  | 3685 |  | 3695 |  | 3705 |  | 3715 |  | 3726 |
|  | 3664 |  | 3675 |  | 3685 |  | 3695 |  | 3705 |  | 3716 |  | 3726 |
|  | 3665 |  | 3675 |  | 3685 |  | 3695 |  | 3706 |  | 3716 |  | 3726 |
|  | 3665 |  | 3675 |  | 3685 |  | 3696 |  | 3706 |  | 3716 |  | 3726 |
|  | 3665 |  | 3675 |  | 3686 |  | 3696 |  | 3706 |  | 3716 |  | 3727 |
|  | 3665 |  | 3676 |  | 3686 |  | 3696 |  | 3706 |  | 3717 |  | 3727 |
|  | 3666 |  | 3676 |  | 3686 |  | 3696 |  | 3707 |  | 3717 |  | 3727 |
|  | 3666 |  | 3676 |  | 3686 |  | 3697 |  | 3707 |  | 3717 |  | 3727 |
|  | 3666 |  | 3676 |  | 3687 |  | 3697 |  | 3707 |  | 3717 |  | 3728 |
|  | 3666 |  | 3677 |  | 3687 |  | 3697 |  | 3707 |  | 3718 |  | 3728 |
|  | 3667 |  | 3677 |  | 3687 |  | 3697 |  | 3708 |  | 3718 |  | 3728 |
|  | 3667 |  | 3677 |  | 3687 |  | 3698 |  | 3708 |  | 3718 |  | 3728 |
|  | 3667 |  | 3677 |  | 3688 |  | 3698 |  | 3708 |  | 3718 |  | 3729 |
|  | 3667 |  | 3678 |  | 3688 |  | 3698 |  | 3708 |  | 3719 |  | 3729 |
|  | 3668 |  | 3678 |  | 3688 |  | 3698 |  | 3709 |  | 3719 |  | 3729 |
|  | 3668 |  | 3678 |  | 3688 |  | 3699 |  | 3709 |  | 3719 |  | 3729 |
|  | 3668 |  | 3678 |  | 3689 |  | 3699 |  | 3709 |  | 3719 |  | 3730 |
|  | 3668 |  | 3679 |  | 3689 |  | 3699 |  | 3709 |  | 3720 |  | 3730 |
|  | 3669 |  | 3679 |  | 3689 |  | 3699 |  | 3710 |  | 3720 |  | 3730 |
|  | 3669 |  | 3679 |  | 3689 |  | 3700 |  | 3710 |  | 3720 |  | 3730 |
|  | 3669 |  | 3679 |  | 3690 |  | 3700 |  | 3710 |  | 3720 |  | 3731 |
|  | 3669 |  | 3680 |  | 3690 |  | 3700 |  | 3710 |  | 3721 |  | 3731 |
|  | 3670 |  | 3680 |  | 3690 |  | 3700 |  | 3711 |  | 3721 |  | 3731 |
|  | 3670 |  | 3680 |  | 3690 |  | 3701 |  | 3711 |  | 3721 |  | 3731 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ |  | Bl nb |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3732 | PPD | 3742 | PPD | 3752 | PPD | 3762 | PPD | 3773 | PPD | 3783 | PPD | 3793 |
|  | 3732 |  | 3742 |  | 3752 |  | 3763 |  | 3773 |  | 3783 |  | 3793 |
|  | 3732 |  | 3742 |  | 3753 |  | 3763 |  | 3773 |  | 3783 |  | 3794 |
|  | 3732 |  | 3743 |  | 3753 |  | 3763 |  | 3773 |  | 3784 |  | 3794 |
|  | 3733 |  | 3743 |  | 3753 |  | 3763 |  | 3774 |  | 3784 |  | 3794 |
|  | 3733 |  | 3743 |  | 3753 |  | 3764 |  | 3774 |  | 3784 |  | 3794 |
|  | 3733 |  | 3743 |  | 3754 |  | 3764 |  | 3774 |  | 3784 |  | 3795 |
|  | 3733 |  | 3744 |  | 3754 |  | 3764 |  | 3774 |  | 3785 |  | 3795 |
|  | 3734 |  | 3744 |  | 3754 |  | 3764 |  | 3775 |  | 3785 |  | 3795 |
|  | 3734 |  | 3744 |  | 3754 |  | 3765 |  | 3775 |  | 3785 |  | 3795 |
|  | 3734 |  | 3744 |  | 3755 |  | 3765 |  | 3775 |  | 3785 |  | 3796 |
|  | 3734 |  | 3745 |  | 3755 |  | 3765 |  | 3775 |  | 3786 |  | 3796 |
|  | 3735 |  | 3745 |  | 3755 |  | 3765 |  | 3776 |  | 3786 |  | 3796 |
|  | 3735 |  | 3745 |  | 3755 |  | 3766 |  | 3776 |  | 3786 |  | 3796 |
|  | 3735 |  | 3745 |  | 3756 |  | 3766 |  | 3776 |  | 3786 |  | 3797 |
|  | 3735 |  | 3746 |  | 3756 |  | 3766 |  | 3776 |  | 3787 |  | 3797 |
|  | 3736 |  | 3746 |  | 3756 |  | 3766 |  | 3777 |  | 3787 |  | 3797 |
|  | 3736 |  | 3746 |  | 3756 |  | 3767 |  | 3777 |  | 3787 |  | 3797 |
|  | 3736 |  | 3746 |  | 3757 |  | 3767 |  | 3777 |  | 3787 |  | 3798 |
|  | 3736 |  | 3747 |  | 3757 |  | 3767 |  | 3777 |  | 3788 |  | 3798 |
|  | 3737 |  | 3747 |  | 3757 |  | 3767 |  | 3778 |  | 3788 |  | 3798 |
|  | 3737 |  | 3747 |  | 3757 |  | 3768 |  | 3778 |  | 3788 |  | 3798 |
|  | 3737 |  | 3747 |  | 3758 |  | 3768 |  | 3778 |  | 3788 |  | 3799 |
|  | 3737 |  | 3748 |  | 3758 |  | 3768 |  | 3778 |  | 3789 |  | 3799 |
|  | 3738 |  | 3748 |  | 3758 |  | 3768 |  | 3779 |  | 3789 |  | 3799 |
|  | 3738 |  | 3748 |  | 3758 |  | 3769 |  | 3779 |  | 3789 |  | 3799 |
|  | 3738 |  | 3748 |  | 3759 |  | 3769 |  | 3779 |  | 3789 |  | 3800 |
|  | 3738 |  | 3749 |  | 3759 |  | 3769 |  | 3779 |  | 3790 |  | 3800 |
|  | 3739 |  | 3749 |  | 3759 |  | 3769 |  | 3780 |  | 3790 |  | 3800 |
|  | 3739 |  | 3749 |  | 3759 |  | 3770 |  | 3780 |  | 3790 |  | 3800 |
|  | 3739 |  | 3749 |  | 3760 |  | 3770 |  | 3780 |  | 3790 |  | 3801 |
|  | 3739 |  | 3750 |  | 3760 |  | 3770 |  | 3780 |  | 3791 |  | 3801 |
|  | 3740 |  | 3750 |  | 3760 |  | 3770 |  | 3781 |  | 3791 |  | 3801 |
|  | 3740 |  | 3750 |  | 3760 |  | 3771 |  | 3781 |  | 3791 |  | 3801 |
|  | 3740 |  | 3750 |  | 3761 |  | 3771 |  | 3781 |  | 3791 |  | 3802 |
|  | 3740 |  | 3751 |  | 3761 |  | 3771 |  | 3781 |  | 3792 |  | 3802 |
|  | 3741 |  | 3751 |  | 3761 |  | 3771 |  | 3782 |  | 3792 |  | 3802 |
|  | 3741 |  | 3751 |  | 3761 |  | 3772 |  | 3782 |  | 3792 |  | 3802 |
|  | 3741 |  | 3751 |  | 3762 |  | 3772 |  | 3782 |  | 3792 |  | 3803 |
|  | 3741 |  | 3752 |  | 3762 |  | 3772 |  | 3782 |  | 3793 |  | 3803 |
|  | 3742 |  | 3752 |  | 3762 |  | 3772 |  | 3783 |  | 3793 |  | 3803 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. |  | $\begin{aligned} & \text { Tret. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3803 | PPD | 3814 | PPD | 3824 | PPD | 3834 | PPD | 3844 | PPD | 3855 | PPD | 3865 |
|  | 3804 |  | 3814 |  | 3824 |  | 3834 |  | 3845 |  | 3855 |  | 3865 |
|  | 3804 |  | 3814 |  | 3824 |  | 3835 |  | 3845 |  | 3855 |  | 3865 |
|  | 3804 |  | 3814 |  | 3825 |  | 3835 |  | 3845 |  | 3855 |  | 3866 |
|  | 3804 |  | 3815 |  | 3825 |  | 3835 |  | 3845 |  | 3856 |  | 3866 |
|  | 3805 |  | 3815 |  | 3825 |  | 3835 |  | 3846 |  | 3856 |  | 3866 |
|  | 3805 |  | 3815 |  | 3825 |  | 3836 |  | 3846 |  | 3856 |  | 3866 |
|  | 3805 |  | 3815 |  | 3826 |  | 3836 |  | 3846 |  | 3856 |  | 3867 |
|  | 3805 |  | 3816 |  | 3826 |  | 3836 |  | 3846 |  | 3857 |  | 3867 |
|  | 3806 |  | 3816 |  | 3826 |  | 3836 |  | 3847 |  | 3857 |  | 3867 |
|  | 3806 |  | 3816 |  | 3826 |  | 3837 |  | 3847 |  | 3857 |  | 3867 |
|  | 3806 |  | 3816 |  | 3827 |  | 3837 |  | 3847 |  | 3857 |  | 3868 |
|  | 3806 |  | 3817 |  | 3827 |  | 3837 |  | 3847 |  | 3858 |  | 3868 |
|  | 3807 |  | 3817 |  | 3827 |  | 3837 |  | 3848 |  | 3858 |  | 3868 |
|  | 3807 |  | 3817 |  | 3827 |  | 3838 |  | 3848 |  | 3858 |  | 3868 |
|  | 3807 |  | 3817 |  | 3828 |  | 3838 |  | 3848 |  | 3858 |  | 3869 |
|  | 3807 |  | 3818 |  | 3828 |  | 3838 |  | 3848 |  | 3859 |  | 3869 |
|  | 3808 |  | 3818 |  | 3828 |  | 3838 |  | 3849 |  | 3859 |  | 3869 |
|  | 3808 |  | 3818 |  | 3828 |  | 3839 |  | 3849 |  | 3859 |  | 3869 |
|  | 3808 |  | 3818 |  | 3829 |  | 3839 |  | 3849 |  | 3859 |  | 3870 |
|  | 3808 |  | 3819 |  | 3829 |  | 3839 |  | 3849 |  | 3860 |  | 3870 |
|  | 3809 |  | 3819 |  | 3829 |  | 3839 |  | 3850 |  | 3860 |  | 3870 |
|  | 3809 |  | 3819 |  | 3829 |  | 3840 |  | 3850 |  | 3860 |  | 3870 |
|  | 3809 |  | 3819 |  | 3830 |  | 3840 |  | 3850 |  | 3860 |  | 3871 |
|  | 3809 |  | 3820 |  | 3830 |  | 3840 |  | 3850 |  | 3861 |  | 3871 |
|  | 3810 |  | 3820 |  | 3830 |  | 3840 |  | 3851 |  | 3861 |  | 3871 |
|  | 3810 |  | 3820 |  | 3830 |  | 3841 |  | 3851 |  | 3861 |  | 3871 |
|  | 3810 |  | 3820 |  | 3831 |  | 3841 |  | 3851 |  | 3861 |  | 3872 |
|  | 3810 |  | 3821 |  | 3831 |  | 3841 |  | 3851 |  | 3862 |  | 3872 |
|  | 3811 |  | 3821 |  | 3831 |  | 3841 |  | 3852 |  | 3862 |  | 3872 |
|  | 3811 |  | 3821 |  | 3831 |  | 3842 |  | 3852 |  | 3862 |  | 3872 |
|  | 3811 |  | 3821 |  | 3832 |  | 3842 |  | 3852 |  | 3862 |  | 3873 |
|  | 3811 |  | 3822 |  | 3832 |  | 3842 |  | 3852 |  | 3863 |  | 3873 |
|  | 3812 |  | 3822 |  | 3832 |  | 3842 |  | 3853 |  | 3863 |  | 3873 |
|  | 3812 |  | 3822 |  | 3832 |  | 3843 |  | 3853 |  | 3863 |  | 3873 |
|  | 3812 |  | 3822 |  | 3833 |  | 3843 |  | 3853 |  | 3863 |  | 3874 |
|  | 3812 |  | 3823 |  | 3833 |  | 3843 |  | 3853 |  | 3864 |  | 3874 |
|  | 3813 |  | 3823 |  | 3833 |  | 3843 |  | 3854 |  | 3864 |  | 3874 |
|  | 3813 |  | 3823 |  | 3833 |  | 3844 |  | 3854 |  | 3864 |  | 3874 |
|  | 3813 |  | 3823 |  | 3834 |  | 3844 |  | 3854 |  | 3864 |  | 3875 |
|  | 3813 |  | 3824 |  | 3834 |  | 3844 |  | 3854 |  | 3865 |  | 3875 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3875 | PPD | 3885 | PPD | 3896 | PPD | 3906 | PPD | 3916 | PPD | 3926 | PPD | 3937 |
|  | 3875 |  | 3886 |  | 3896 |  | 3906 |  | 3916 |  | 3927 |  | 3937 |
|  | 3876 |  | 3886 |  | 3896 |  | 3906 |  | 3917 |  | 3927 |  | 3937 |
|  | 3876 |  | 3886 |  | 3896 |  | 3907 |  | 3917 |  | 3927 |  | 3937 |
|  | 3876 |  | 3886 |  | 3897 |  | 3907 |  | 3917 |  | 3927 |  | 3938 |
|  | 3876 |  | 3887 |  | 3897 |  | 3907 |  | 3917 |  | 3928 |  | 3938 |
|  | 3877 |  | 3887 |  | 3897 |  | 3907 |  | 3918 |  | 3928 |  | 3938 |
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|  | 3877 |  | 3887 |  | 3898 |  | 3908 |  | 3918 |  | 3928 |  | 3939 |
|  | 3877 |  | 3888 |  | 3898 |  | 3908 |  | 3918 |  | 3929 |  | 3939 |
|  | 3878 |  | 3888 |  | 3898 |  | 3908 |  | 3919 |  | 3929 |  | 3939 |
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|  | 3878 |  | 3888 |  | 3899 |  | 3909 |  | 3919 |  | 3929 |  | 3940 |
|  | 3878 |  | 3889 |  | 3899 |  | 3909 |  | 3919 |  | 3930 |  | 3940 |
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|  | 3879 |  | 3889 |  | 3900 |  | 3910 |  | 3920 |  | 3930 |  | 3941 |
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|  | 3880 |  | 3890 |  | 3900 |  | 3910 |  | 3921 |  | 3931 |  | 3941 |
|  | 3880 |  | 3890 |  | 3900 |  | 3911 |  | 3921 |  | 3931 |  | 3941 |
|  | 3880 |  | 3890 |  | 3901 |  | 3911 |  | 3921 |  | 3931 |  | 3942 |
|  | 3880 |  | 3891 |  | 3901 |  | 3911 |  | 3921 |  | 3932 |  | 3942 |
|  | 3881 |  | 3891 |  | 3901 |  | 3911 |  | 3922 |  | 3932 |  | 3942 |
|  | 3881 |  | 3891 |  | 3901 |  | 3912 |  | 3922 |  | 3932 |  | 3942 |
|  | 3881 |  | 3891 |  | 3902 |  | 3912 |  | 3922 |  | 3932 |  | 3943 |
|  | 3881 |  | 3892 |  | 3902 |  | 3912 |  | 3922 |  | 3933 |  | 3943 |
|  | 3882 |  | 3892 |  | 3902 |  | 3912 |  | 3923 |  | 3933 |  | 3943 |
|  | 3882 |  | 3892 |  | 3902 |  | 3913 |  | 3923 |  | 3933 |  | 3943 |
|  | 3882 |  | 3892 |  | 3903 |  | 3913 |  | 3923 |  | 3933 |  | 3944 |
|  | 3882 |  | 3893 |  | 3903 |  | 3913 |  | 3923 |  | 3934 |  | 3944 |
|  | 3883 |  | 3893 |  | 3903 |  | 3913 |  | 3924 |  | 3934 |  | 3944 |
|  | 3883 |  | 3893 |  | 3903 |  | 3914 |  | 3924 |  | 3934 |  | 3944 |
|  | 3883 |  | 3893 |  | 3904 |  | 3914 |  | 3924 |  | 3934 |  | 3945 |
|  | 3883 |  | 3894 |  | 3904 |  | 3914 |  | 3924 |  | 3935 |  | 3945 |
|  | 3884 |  | 3894 |  | 3904 |  | 3914 |  | 3925 |  | 3935 |  | 3945 |
|  | 3884 |  | 3894 |  | 3904 |  | 3915 |  | 3925 |  | 3935 |  | 3945 |
|  | 3884 |  | 3894 |  | 3905 |  | 3915 |  | 3925 |  | 3935 |  | 3946 |
|  | 3884 |  | 3895 |  | 3905 |  | 3915 |  | 3925 |  | 3936 |  | 3946 |
|  | 3885 |  | 3895 |  | 3905 |  | 3915 |  | 3926 |  | 3936 |  | 3946 |
|  | 3885 |  | 3895 |  | 3905 |  | 3916 |  | 3926 |  | 3936 |  | 3946 |
|  | 3885 |  | 3895 |  | 3906 |  | 3916 |  | 3926 |  | 3936 |  | 3947 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ |  |  | Bl nb |  | Bl nb |  | Bl nb |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3947 | PPD | 3957 | PPD | 3967 | PPD | 3978 | PPD | 3988 | PPD | 3998 | PPD | 4008 |
|  | 3947 |  | 3957 |  | 3968 |  | 3978 |  | 3988 |  | 3998 |  | 4009 |
|  | 3947 |  | 3958 |  | 3968 |  | 3978 |  | 3988 |  | 3999 |  | 4009 |
|  | 3948 |  | 3958 |  | 3968 |  | 3978 |  | 3989 |  | 3999 |  | 4009 |
|  | 3948 |  | 3958 |  | 3968 |  | 3979 |  | 3989 |  | 3999 |  | 4009 |
|  | 3948 |  | 3958 |  | 3969 |  | 3979 |  | 3989 |  | 3999 |  | 4010 |
|  | 3948 |  | 3959 |  | 3969 |  | 3979 |  | 3989 |  | 4000 |  | 4010 |
|  | 3949 |  | 3959 |  | 3969 |  | 3979 |  | 3990 |  | 4000 |  | 4010 |
|  | 3949 |  | 3959 |  | 3969 |  | 3980 |  | 3990 |  | 4000 |  | 4010 |
|  | 3949 |  | 3959 |  | 3970 |  | 3980 |  | 3990 |  | 4000 |  | 4011 |
|  | 3949 |  | 3960 |  | 3970 |  | 3980 |  | 3990 |  | 4001 |  | 4011 |
|  | 3950 |  | 3960 |  | 3970 |  | 3980 |  | 3991 |  | 4001 |  | 4011 |
|  | 3950 |  | 3960 |  | 3970 |  | 3981 |  | 3991 |  | 4001 |  | 4011 |
|  | 3950 |  | 3960 |  | 3971 |  | 3981 |  | 3991 |  | 4001 |  | 4012 |
|  | 3950 |  | 3961 |  | 3971 |  | 3981 |  | 3991 |  | 4002 |  | 4012 |
|  | 3951 |  | 3961 |  | 3971 |  | 3981 |  | 3992 |  | 4002 |  | 4012 |
|  | 3951 |  | 3961 |  | 3971 |  | 3982 |  | 3992 |  | 4002 |  | 4012 |
|  | 3951 |  | 3961 |  | 3972 |  | 3982 |  | 3992 |  | 4002 |  | 4013 |
|  | 3951 |  | 3962 |  | 3972 |  | 3982 |  | 3992 |  | 4003 |  | 4013 |
|  | 3952 |  | 3962 |  | 3972 |  | 3982 |  | 3993 |  | 4003 |  | 4013 |
|  | 3952 |  | 3962 |  | 3972 |  | 3983 |  | 3993 |  | 4003 |  | 4013 |
|  | 3952 |  | 3962 |  | 3973 |  | 3983 |  | 3993 |  | 4003 |  | 4014 |
|  | 3952 |  | 3963 |  | 3973 |  | 3983 |  | 3993 |  | 4004 |  | 4014 |
|  | 3953 |  | 3963 |  | 3973 |  | 3983 |  | 3994 |  | 4004 |  | 4014 |
|  | 3953 |  | 3963 |  | 3973 |  | 3984 |  | 3994 |  | 4004 |  | 4014 |
|  | 3953 |  | 3963 |  | 3974 |  | 3984 |  | 3994 |  | 4004 |  | 4015 |
|  | 3953 |  | 3964 |  | 3974 |  | 3984 |  | 3994 |  | 4005 |  | 4015 |
|  | 3954 |  | 3964 |  | 3974 |  | 3984 |  | 3995 |  | 4005 |  | 4015 |
|  | 3954 |  | 3964 |  | 3974 |  | 3985 |  | 3995 |  | 4005 |  | 4015 |
|  | 3954 |  | 3964 |  | 3975 |  | 3985 |  | 3995 |  | 4005 |  | 4016 |
|  | 3954 |  | 3965 |  | 3975 |  | 3985 |  | 3995 |  | 4006 |  | 4016 |
|  | 3955 |  | 3965 |  | 3975 |  | 3985 |  | 3996 |  | 4006 |  | 4016 |
|  | 3955 |  | 3965 |  | 3975 |  | 3986 |  | 3996 |  | 4006 |  | 4016 |
|  | 3955 |  | 3965 |  | 3976 |  | 3986 |  | 3996 |  | 4006 |  | 4017 |
|  | 3955 |  | 3966 |  | 3976 |  | 3986 |  | 3996 |  | 4007 |  | 4017 |
|  | 3956 |  | 3966 |  | 3976 |  | 3986 |  | 3997 |  | 4007 |  | 4017 |
|  | 3956 |  | 3966 |  | 3976 |  | 3987 |  | 3997 |  | 4007 |  | 4017 |
|  | 3956 |  | 3966 |  | 3977 |  | 3987 |  | 3997 |  | 4007 |  | 4018 |
|  | 3956 |  | 3967 |  | 3977 |  | 3987 |  | 3997 |  | 4008 |  | 4018 |
|  | 3957 |  | 3967 |  | 3977 |  | 3987 |  | 3998 |  | 4008 |  | 4018 |
|  | 3957 |  | 3967 |  | 3977 |  | 3988 |  | 3998 |  | 4008 |  | 4018 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ |  |  |  |  |  |  | Bl nb | Trt | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. } \\ & \text { No nl. } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4019 | PPD | 4029 | PPD | 4039 | PPD | 4049 | PPD | 4060 | PPD | 4070 | PPD | 4080 |
|  | 4019 |  | 4029 |  | 4039 |  | 4050 |  | 4060 |  | 4070 |  | 4080 |
|  | 4019 |  | 4029 |  | 4040 |  | 4050 |  | 4060 |  | 4070 |  | 4081 |
|  | 4019 |  | 4030 |  | 4040 |  | 4050 |  | 4060 |  | 4071 |  | 4081 |
|  | 4020 |  | 4030 |  | 4040 |  | 4050 |  | 4061 |  | 4071 |  | 4081 |
|  | 4020 |  | 4030 |  | 4040 |  | 4051 |  | 4061 |  | 4071 |  | 4081 |
|  | 4020 |  | 4030 |  | 4041 |  | 4051 |  | 4061 |  | 4071 |  | 4082 |
|  | 4020 |  | 4031 |  | 4041 |  | 4051 |  | 4061 |  | 4072 |  | 4082 |
|  | 4021 |  | 4031 |  | 4041 |  | 4051 |  | 4062 |  | 4072 |  | 4082 |
|  | 4021 |  | 4031 |  | 4041 |  | 4052 |  | 4062 |  | 4072 |  | 4082 |
|  | 4021 |  | 4031 |  | 4042 |  | 4052 |  | 4062 |  | 4072 |  | 4083 |
|  | 4021 |  | 4032 |  | 4042 |  | 4052 |  | 4062 |  | 4073 |  | 4083 |
|  | 4022 |  | 4032 |  | 4042 |  | 4052 |  | 4063 |  | 4073 |  | 4083 |
|  | 4022 |  | 4032 |  | 4042 |  | 4053 |  | 4063 |  | 4073 |  | 4083 |
|  | 4022 |  | 4032 |  | 4043 |  | 4053 |  | 4063 |  | 4073 |  | 4084 |
|  | 4022 |  | 4033 |  | 4043 |  | 4053 |  | 4063 |  | 4074 |  | 4084 |
|  | 4023 |  | 4033 |  | 4043 |  | 4053 |  | 4064 |  | 4074 |  | 4084 |
|  | 4023 |  | 4033 |  | 4043 |  | 4054 |  | 4064 |  | 4074 |  | 4084 |
|  | 4023 |  | 4033 |  | 4044 |  | 4054 |  | 4064 |  | 4074 |  | 4085 |
|  | 4023 |  | 4034 |  | 4044 |  | 4054 |  | 4064 |  | 4075 |  | 4085 |
|  | 4024 |  | 4034 |  | 4044 |  | 4054 |  | 4065 |  | 4075 |  | 4085 |
|  | 4024 |  | 4034 |  | 4044 |  | 4055 |  | 4065 |  | 4075 |  | 4085 |
|  | 4024 |  | 4034 |  | 4045 |  | 4055 |  | 4065 |  | 4075 |  | 4086 |
|  | 4024 |  | 4035 |  | 4045 |  | 4055 |  | 4065 |  | 4076 |  | 4086 |
|  | 4025 |  | 4035 |  | 4045 |  | 4055 |  | 4066 |  | 4076 |  | 4086 |
|  | 4025 |  | 4035 |  | 4045 |  | 4056 |  | 4066 |  | 4076 |  | 4086 |
|  | 4025 |  | 4035 |  | 4046 |  | 4056 |  | 4066 |  | 4076 |  | 4087 |
|  | 4025 |  | 4036 |  | 4046 |  | 4056 |  | 4066 |  | 4077 |  | 4087 |
|  | 4026 |  | 4036 |  | 4046 |  | 4056 |  | 4067 |  | 4077 |  | 4087 |
|  | 4026 |  | 4036 |  | 4046 |  | 4057 |  | 4067 |  | 4077 |  | 4087 |
|  | 4026 |  | 4036 |  | 4047 |  | 4057 |  | 4067 |  | 4077 |  | 4088 |
|  | 4026 |  | 4037 |  | 4047 |  | 4057 |  | 4067 |  | 4078 |  | 4088 |
|  | 4027 |  | 4037 |  | 4047 |  | 4057 |  | 4068 |  | 4078 |  | 4088 |
|  | 4027 |  | 4037 |  | 4047 |  | 4058 |  | 4068 |  | 4078 |  | 4088 |
|  | 4027 |  | 4037 |  | 4048 |  | 4058 |  | 4068 |  | 4078 |  | 4089 |
|  | 4027 |  | 4038 |  | 4048 |  | 4058 |  | 4068 |  | 4079 |  | 4089 |
|  | 4028 |  | 4038 |  | 4048 |  | 4058 |  | 4069 |  | 4079 |  | 4089 |
|  | 4028 |  | 4038 |  | 4048 |  | 4059 |  | 4069 |  | 4079 |  | 4089 |
|  | 4028 |  | 4038 |  | 4049 |  | 4059 |  | 4069 |  | 4079 |  | 4090 |
|  | 4028 |  | 4039 |  | 4049 |  | 4059 |  | 4069 |  | 4080 |  | 4090 |
|  | 4029 |  | 4039 |  | 4049 |  | 4059 |  | 4070 |  | 4080 |  | 4090 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl. | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | Trt. Bl. No nb |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4090 | PPD | 4101 | PPD | 4111 | PPD | 4121 | PPD | 4131 | PPD | 4142 | PPD | 4152 |
|  | 4091 |  | 4101 |  | 4111 |  | 4121 |  | 4132 |  | 4142 |  | 4152 |
|  | 4091 |  | 4101 |  | 4111 |  | 4122 |  | 4132 |  | 4142 |  | 4152 |
|  | 4091 |  | 4101 |  | 4112 |  | 4122 |  | 4132 |  | 4142 |  | 4153 |
|  | 4091 |  | 4102 |  | 4112 |  | 4122 |  | 4132 |  | 4143 |  | 4153 |
|  | 4092 |  | 4102 |  | 4112 |  | 4122 |  | 4133 |  | 4143 |  | 4153 |
|  | 4092 |  | 4102 |  | 4112 |  | 4123 |  | 4133 |  | 4143 |  | 4153 |
|  | 4092 |  | 4102 |  | 4113 |  | 4123 |  | 4133 |  | 4143 |  | 4154 |
|  | 4092 |  | 4103 |  | 4113 |  | 4123 |  | 4133 |  | 4144 |  | 4154 |
|  | 4093 |  | 4103 |  | 4113 |  | 4123 |  | 4134 |  | 4144 |  | 4154 |
|  | 4093 |  | 4103 |  | 4113 |  | 4124 |  | 4134 |  | 4144 |  | 4154 |
|  | 4093 |  | 4103 |  | 4114 |  | 4124 |  | 4134 |  | 4144 |  | 4155 |
|  | 4093 |  | 4104 |  | 4114 |  | 4124 |  | 4134 |  | 4145 |  | 4155 |
|  | 4094 |  | 4104 |  | 4114 |  | 4124 |  | 4135 |  | 4145 |  | 4155 |
|  | 4094 |  | 4104 |  | 4114 |  | 4125 |  | 4135 |  | 4145 |  | 4155 |
|  | 4094 |  | 4104 |  | 4115 |  | 4125 |  | 4135 |  | 4145 |  | 4156 |
|  | 4094 |  | 4105 |  | 4115 |  | 4125 |  | 4135 |  | 4146 |  | 4156 |
|  | 4095 |  | 4105 |  | 4115 |  | 4125 |  | 4136 |  | 4146 |  | 4156 |
|  | 4095 |  | 4105 |  | 4115 |  | 4126 |  | 4136 |  | 4146 |  | 4156 |
|  | 4095 |  | 4105 |  | 4116 |  | 4126 |  | 4136 |  | 4146 |  | 4157 |
|  | 4095 |  | 4106 |  | 4116 |  | 4126 |  | 4136 |  | 4147 |  | 4157 |
|  | 4096 |  | 4106 |  | 4116 |  | 4126 |  | 4137 |  | 4147 |  | 4157 |
|  | 4096 |  | 4106 |  | 4116 |  | 4127 |  | 4137 |  | 4147 |  | 4157 |
|  | 4096 |  | 4106 |  | 4117 |  | 4127 |  | 4137 |  | 4147 |  | 4158 |
|  | 4096 |  | 4107 |  | 4117 |  | 4127 |  | 4137 |  | 4148 |  | 4158 |
|  | 4097 |  | 4107 |  | 4117 |  | 4127 |  | 4138 |  | 4148 |  | 4158 |
|  | 4097 |  | 4107 |  | 4117 |  | 4128 |  | 4138 |  | 4148 |  | 4158 |
|  | 4097 |  | 4107 |  | 4118 |  | 4128 |  | 4138 |  | 4148 |  | 4159 |
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|  | 4098 |  | 4108 |  | 4118 |  | 4128 |  | 4139 |  | 4149 |  | 4159 |
|  | 4098 |  | 4108 |  | 4118 |  | 4129 |  | 4139 |  | 4149 |  | 4159 |
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|  | 4098 |  | 4109 |  | 4119 |  | 4129 |  | 4139 |  | 4150 |  | 4160 |
|  | 4099 |  | 4109 |  | 4119 |  | 4129 |  | 4140 |  | 4150 |  | 4160 |
|  | 4099 |  | 4109 |  | 4119 |  | 4130 |  | 4140 |  | 4150 |  | 4160 |
|  | 4099 |  | 4109 |  | 4120 |  | 4130 |  | 4140 |  | 4150 |  | 4161 |
|  | 4099 |  | 4110 |  | 4120 |  | 4130 |  | 4140 |  | 4151 |  | 4161 |
|  | 4100 |  | 4110 |  | 4120 |  | 4130 |  | 4141 |  | 4151 |  | 4161 |
|  | 4100 |  | 4110 |  | 4120 |  | 4131 |  | 4141 |  | 4151 |  | 4161 |
|  | 4100 |  | 4110 |  | 4121 |  | 4131 |  | 4141 |  | 4151 |  | 4162 |
|  | 4100 |  | 4111 |  | 4121 |  | 4131 |  | 4141 |  | 4152 |  | 4162 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  |  |  |  |  | Bl nb |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4162 | PPD | 4172 | PPD | 4183 | PPD | 4193 | PPD | 4203 | PPD | 4213 | PPD | 4224 |
|  | 4162 |  | 4173 |  | 4183 |  | 4193 |  | 4203 |  | 4214 |  | 4224 |
|  | 4163 |  | 4173 |  | 4183 |  | 4193 |  | 4204 |  | 4214 |  | 4224 |
|  | 4163 |  | 4173 |  | 4183 |  | 4194 |  | 4204 |  | 4214 |  | 4224 |
|  | 4163 |  | 4173 |  | 4184 |  | 4194 |  | 4204 |  | 4214 |  | 4225 |
|  | 4163 |  | 4174 |  | 4184 |  | 4194 |  | 4204 |  | 4215 |  | 4225 |
|  | 4164 |  | 4174 |  | 4184 |  | 4194 |  | 4205 |  | 4215 |  | 4225 |
|  | 4164 |  | 4174 |  | 4184 |  | 4195 |  | 4205 |  | 4215 |  | 4225 |
|  | 4164 |  | 4174 |  | 4185 |  | 4195 |  | 4205 |  | 4215 |  | 4226 |
|  | 4164 |  | 4175 |  | 4185 |  | 4195 |  | 4205 |  | 4216 |  | 4226 |
|  | 4165 |  | 4175 |  | 4185 |  | 4195 |  | 4206 |  | 4216 |  | 4226 |
|  | 4165 |  | 4175 |  | 4185 |  | 4196 |  | 4206 |  | 4216 |  | 4226 |
|  | 4165 |  | 4175 |  | 4186 |  | 4196 |  | 4206 |  | 4216 |  | 4227 |
|  | 4165 |  | 4176 |  | 4186 |  | 4196 |  | 4206 |  | 4217 |  | 4227 |
|  | 4166 |  | 4176 |  | 4186 |  | 4196 |  | 4207 |  | 4217 |  | 4227 |
|  | 4166 |  | 4176 |  | 4186 |  | 4197 |  | 4207 |  | 4217 |  | 4227 |
|  | 4166 |  | 4176 |  | 4187 |  | 4197 |  | 4207 |  | 4217 |  | 4228 |
|  | 4166 |  | 4177 |  | 4187 |  | 4197 |  | 4207 |  | 4218 |  | 4228 |
|  | 4167 |  | 4177 |  | 4187 |  | 4197 |  | 4208 |  | 4218 |  | 4228 |
|  | 4167 |  | 4177 |  | 4187 |  | 4198 |  | 4208 |  | 4218 |  | 4228 |
|  | 4167 |  | 4177 |  | 4188 |  | 4198 |  | 4208 |  | 4218 |  | 4229 |
|  | 4167 |  | 4178 |  | 4188 |  | 4198 |  | 4208 |  | 4219 |  | 4229 |
|  | 4168 |  | 4178 |  | 4188 |  | 4198 |  | 4209 |  | 4219 |  | 4229 |
|  | 4168 |  | 4178 |  | 4188 |  | 4199 |  | 4209 |  | 4219 |  | 4229 |
|  | 4168 |  | 4178 |  | 4189 |  | 4199 |  | 4209 |  | 4219 |  | 4230 |
|  | 4168 |  | 4179 |  | 4189 |  | 4199 |  | 4209 |  | 4220 |  | 4230 |
|  | 4169 |  | 4179 |  | 4189 |  | 4199 |  | 4210 |  | 4220 |  | 4230 |
|  | 4169 |  | 4179 |  | 4189 |  | 4200 |  | 4210 |  | 4220 |  | 4230 |
|  | 4169 |  | 4179 |  | 4190 |  | 4200 |  | 4210 |  | 4220 |  | 4231 |
|  | 4169 |  | 4180 |  | 4190 |  | 4200 |  | 4210 |  | 4221 |  | 4231 |
|  | 4170 |  | 4180 |  | 4190 |  | 4200 |  | 4211 |  | 4221 |  | 4231 |
|  | 4170 |  | 4180 |  | 4190 |  | 4201 |  | 4211 |  | 4221 |  | 4231 |
|  | 4170 |  | 4180 |  | 4191 |  | 4201 |  | 4211 |  | 4221 |  | 4232 |
|  | 4170 |  | 4181 |  | 4191 |  | 4201 |  | 4211 |  | 4222 |  | 4232 |
|  | 4171 |  | 4181 |  | 4191 |  | 4201 |  | 4212 |  | 4222 |  | 4232 |
|  | 4171 |  | 4181 |  | 4191 |  | 4202 |  | 4212 |  | 4222 |  | 4232 |
|  | 4171 |  | 4181 |  | 4192 |  | 4202 |  | 4212 |  | 4222 |  | 4233 |
|  | 4171 |  | 4182 |  | 4192 |  | 4202 |  | 4212 |  | 4223 |  | 4233 |
|  | 4172 |  | 4182 |  | 4192 |  | 4202 |  | 4213 |  | 4223 |  | 4233 |
|  | 4172 |  | 4182 |  | 4192 |  | 4203 |  | 4213 |  | 4223 |  | 4233 |
|  | 4172 |  | 4182 |  | 4193 |  | 4203 |  | 4213 |  | 4223 |  | 4234 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. |  |  | Bl nb |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. } \\ & \text { No nl. } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4234 | PPD | 4244 | PPD | 4254 | PPD | 4265 | PPD | 4275 | PPD | 4285 | PPD | 4295 |
|  | 4234 |  | 4244 |  | 4255 |  | 4265 |  | 4275 |  | 4285 |  | 4296 |
|  | 4234 |  | 4245 |  | 4255 |  | 4265 |  | 4275 |  | 4286 |  | 4296 |
|  | 4235 |  | 4245 |  | 4255 |  | 4265 |  | 4276 |  | 4286 |  | 4296 |
|  | 4235 |  | 4245 |  | 4255 |  | 4266 |  | 4276 |  | 4286 |  | 4296 |
|  | 4235 |  | 4245 |  | 4256 |  | 4266 |  | 4276 |  | 4286 |  | 4297 |
|  | 4235 |  | 4246 |  | 4256 |  | 4266 |  | 4276 |  | 4287 |  | 4297 |
|  | 4236 |  | 4246 |  | 4256 |  | 4266 |  | 4277 |  | 4287 |  | 4297 |
|  | 4236 |  | 4246 |  | 4256 |  | 4267 |  | 4277 |  | 4287 |  | 4297 |
|  | 4236 |  | 4246 |  | 4257 |  | 4267 |  | 4277 |  | 4287 |  | 4298 |
|  | 4236 |  | 4247 |  | 4257 |  | 4267 |  | 4277 |  | 4288 |  | 4298 |
|  | 4237 |  | 4247 |  | 4257 |  | 4267 |  | 4278 |  | 4288 |  | 4298 |
|  | 4237 |  | 4247 |  | 4257 |  | 4268 |  | 4278 |  | 4288 |  | 4298 |
|  | 4237 |  | 4247 |  | 4258 |  | 4268 |  | 4278 |  | 4288 |  | 4299 |
|  | 4237 |  | 4248 |  | 4258 |  | 4268 |  | 4278 |  | 4289 |  | 4299 |
|  | 4238 |  | 4248 |  | 4258 |  | 4268 |  | 4279 |  | 4289 |  | 4299 |
|  | 4238 |  | 4248 |  | 4258 |  | 4269 |  | 4279 |  | 4289 |  | 4299 |
|  | 4238 |  | 4248 |  | 4259 |  | 4269 |  | 4279 |  | 4289 |  | 4300 |
|  | 4238 |  | 4249 |  | 4259 |  | 4269 |  | 4279 |  | 4290 |  | 4300 |
|  | 4239 |  | 4249 |  | 4259 |  | 4269 |  | 4280 |  | 4290 |  | 4300 |
|  | 4239 |  | 4249 |  | 4259 |  | 4270 |  | 4280 |  | 4290 |  | 4300 |
|  | 4239 |  | 4249 |  | 4260 |  | 4270 |  | 4280 |  | 4290 |  | 4301 |
|  | 4239 |  | 4250 |  | 4260 |  | 4270 |  | 4280 |  | 4291 |  | 4301 |
|  | 4240 |  | 4250 |  | 4260 |  | 4270 |  | 4281 |  | 4291 |  | 4301 |
|  | 4240 |  | 4250 |  | 4260 |  | 4271 |  | 4281 |  | 4291 |  | 4301 |
|  | 4240 |  | 4250 |  | 4261 |  | 4271 |  | 4281 |  | 4291 |  | 4302 |
|  | 4240 |  | 4251 |  | 4261 |  | 4271 |  | 4281 |  | 4292 |  | 4302 |
|  | 4241 |  | 4251 |  | 4261 |  | 4271 |  | 4282 |  | 4292 |  | 4302 |
|  | 4241 |  | 4251 |  | 4261 |  | 4272 |  | 4282 |  | 4292 |  | 4302 |
|  | 4241 |  | 4251 |  | 4262 |  | 4272 |  | 4282 |  | 4292 |  | 4303 |
|  | 4241 |  | 4252 |  | 4262 |  | 4272 |  | 4282 |  | 4293 |  | 4303 |
|  | 4242 |  | 4252 |  | 4262 |  | 4272 |  | 4283 |  | 4293 |  | 4303 |
|  | 4242 |  | 4252 |  | 4262 |  | 4273 |  | 4283 |  | 4293 |  | 4303 |
|  | 4242 |  | 4252 |  | 4263 |  | 4273 |  | 4283 |  | 4293 |  | 4304 |
|  | 4242 |  | 4253 |  | 4263 |  | 4273 |  | 4283 |  | 4294 |  | 4304 |
|  | 4243 |  | 4253 |  | 4263 |  | 4273 |  | 4284 |  | 4294 |  | 4304 |
|  | 4243 |  | 4253 |  | 4263 |  | 4274 |  | 4284 |  | 4294 |  | 4304 |
|  | 4243 |  | 4253 |  | 4264 |  | 4274 |  | 4284 |  | 4294 |  | 4305 |
|  | 4243 |  | 4254 |  | 4264 |  | 4274 |  | 4284 |  | 4295 |  | 4305 |
|  | 4244 |  | 4254 |  | 4264 |  | 4274 |  | 4285 |  | 4295 |  | 4305 |
|  | 4244 |  | 4254 |  | 4264 |  | 4275 |  | 4285 |  | 4295 |  | 4305 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. | Bl nb |  | Bl. | Trt | Bl. |  | Bl nb |  | Bl nb |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4306 | PPD | 4316 | PPD | 4326 | PPD | 4336 | PPD | 4347 | PPD | 4357 | PPD | 4367 |
|  | 4306 |  | 4316 |  | 4326 |  | 4337 |  | 4347 |  | 4357 |  | 4367 |
|  | 4306 |  | 4316 |  | 4327 |  | 4337 |  | 4347 |  | 4357 |  | 4368 |
|  | 4306 |  | 4317 |  | 4327 |  | 4337 |  | 4347 |  | 4358 |  | 4368 |
|  | 4307 |  | 4317 |  | 4327 |  | 4337 |  | 4348 |  | 4358 |  | 4368 |
|  | 4307 |  | 4317 |  | 4327 |  | 4338 |  | 4348 |  | 4358 |  | 4368 |
|  | 4307 |  | 4317 |  | 4328 |  | 4338 |  | 4348 |  | 4358 |  | 4369 |
|  | 4307 |  | 4318 |  | 4328 |  | 4338 |  | 4348 |  | 4359 |  | 4369 |
|  | 4308 |  | 4318 |  | 4328 |  | 4338 |  | 4349 |  | 4359 |  | 4369 |
|  | 4308 |  | 4318 |  | 4328 |  | 4339 |  | 4349 |  | 4359 |  | 4369 |
|  | 4308 |  | 4318 |  | 4329 |  | 4339 |  | 4349 |  | 4359 |  | 4370 |
|  | 4308 |  | 4319 |  | 4329 |  | 4339 |  | 4349 |  | 4360 |  | 4370 |
|  | 4309 |  | 4319 |  | 4329 |  | 4339 |  | 4350 |  | 4360 |  | 4370 |
|  | 4309 |  | 4319 |  | 4329 |  | 4340 |  | 4350 |  | 4360 |  | 4370 |
|  | 4309 |  | 4319 |  | 4330 |  | 4340 |  | 4350 |  | 4360 |  | 4371 |
|  | 4309 |  | 4320 |  | 4330 |  | 4340 |  | 4350 |  | 4361 |  | 4371 |
|  | 4310 |  | 4320 |  | 4330 |  | 4340 |  | 4351 |  | 4361 |  | 4371 |
|  | 4310 |  | 4320 |  | 4330 |  | 4341 |  | 4351 |  | 4361 |  | 4371 |
|  | 4310 |  | 4320 |  | 4331 |  | 4341 |  | 4351 |  | 4361 |  | 4372 |
|  | 4310 |  | 4321 |  | 4331 |  | 4341 |  | 4351 |  | 4362 |  | 4372 |
|  | 4311 |  | 4321 |  | 4331 |  | 4341 |  | 4352 |  | 4362 |  | 4372 |
|  | 4311 |  | 4321 |  | 4331 |  | 4342 |  | 4352 |  | 4362 |  | 4372 |
|  | 4311 |  | 4321 |  | 4332 |  | 4342 |  | 4352 |  | 4362 |  | 4373 |
|  | 4311 |  | 4322 |  | 4332 |  | 4342 |  | 4352 |  | 4363 |  | 4373 |
|  | 4312 |  | 4322 |  | 4332 |  | 4342 |  | 4353 |  | 4363 |  | 4373 |
|  | 4312 |  | 4322 |  | 4332 |  | 4343 |  | 4353 |  | 4363 |  | 4373 |
|  | 4312 |  | 4322 |  | 4333 |  | 4343 |  | 4353 |  | 4363 |  | 4374 |
|  | 4312 |  | 4323 |  | 4333 |  | 4343 |  | 4353 |  | 4364 |  | 4374 |
|  | 4313 |  | 4323 |  | 4333 |  | 4343 |  | 4354 |  | 4364 |  | 4374 |
|  | 4313 |  | 4323 |  | 4333 |  | 4344 |  | 4354 |  | 4364 |  | 4374 |
|  | 4313 |  | 4323 |  | 4334 |  | 4344 |  | 4354 |  | 4364 |  | 4375 |
|  | 4313 |  | 4324 |  | 4334 |  | 4344 |  | 4354 |  | 4365 |  | 4375 |
|  | 4314 |  | 4324 |  | 4334 |  | 4344 |  | 4355 |  | 4365 |  | 4375 |
|  | 4314 |  | 4324 |  | 4334 |  | 4345 |  | 4355 |  | 4365 |  | 4375 |
|  | 4314 |  | 4324 |  | 4335 |  | 4345 |  | 4355 |  | 4365 |  | 4376 |
|  | 4314 |  | 4325 |  | 4335 |  | 4345 |  | 4355 |  | 4366 |  | 4376 |
|  | 4315 |  | 4325 |  | 4335 |  | 4345 |  | 4356 |  | 4366 |  | 4376 |
|  | 4315 |  | 4325 |  | 4335 |  | 4346 |  | 4356 |  | 4366 |  | 4376 |
|  | 4315 |  | 4325 |  | 4336 |  | 4346 |  | 4356 |  | 4366 |  | 4377 |
|  | 4315 |  | 4326 |  | 4336 |  | 4346 |  | 4356 |  | 4367 |  | 4377 |
|  | 4316 |  | 4326 |  | 4336 |  | 4346 |  | 4357 |  | 4367 |  | 4377 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. No |  |  |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4377 | PPD | 4388 | PPD | 4398 | PPD | 4408 | PPD | 4418 | PPD | 4429 | PPD | 4439 |
|  | 4378 |  | 4388 |  | 4398 |  | 4408 |  | 4419 |  | 4429 |  | 4439 |
|  | 4378 |  | 4388 |  | 4398 |  | 4409 |  | 4419 |  | 4429 |  | 4439 |
|  | 4378 |  | 4388 |  | 4399 |  | 4409 |  | 4419 |  | 4429 |  | 4440 |
|  | 4378 |  | 4389 |  | 4399 |  | 4409 |  | 4419 |  | 4430 |  | 4440 |
|  | 4379 |  | 4389 |  | 4399 |  | 4409 |  | 4420 |  | 4430 |  | 4440 |
|  | 4379 |  | 4389 |  | 4399 |  | 4410 |  | 4420 |  | 4430 |  | 4440 |
|  | 4379 |  | 4389 |  | 4400 |  | 4410 |  | 4420 |  | 4430 |  | 4441 |
|  | 4379 |  | 4390 |  | 4400 |  | 4410 |  | 4420 |  | 4431 |  | 4441 |
|  | 4380 |  | 4390 |  | 4400 |  | 4410 |  | 4421 |  | 4431 |  | 4441 |
|  | 4380 |  | 4390 |  | 4400 |  | 4411 |  | 4421 |  | 4431 |  | 4441 |
|  | 4380 |  | 4390 |  | 4401 |  | 4411 |  | 4421 |  | 4431 |  | 4442 |
|  | 4380 |  | 4391 |  | 4401 |  | 4411 |  | 4421 |  | 4432 |  | 4442 |
|  | 4381 |  | 4391 |  | 4401 |  | 4411 |  | 4422 |  | 4432 |  | 4442 |
|  | 4381 |  | 4391 |  | 4401 |  | 4412 |  | 4422 |  | 4432 |  | 4442 |
|  | 4381 |  | 4391 |  | 4402 |  | 4412 |  | 4422 |  | 4432 |  | 4443 |
|  | 4381 |  | 4392 |  | 4402 |  | 4412 |  | 4422 |  | 4433 |  | 4443 |
|  | 4382 |  | 4392 |  | 4402 |  | 4412 |  | 4423 |  | 4433 |  | 4443 |
|  | 4382 |  | 4392 |  | 4402 |  | 4413 |  | 4423 |  | 4433 |  | 4443 |
|  | 4382 |  | 4392 |  | 4403 |  | 4413 |  | 4423 |  | 4433 |  | 4444 |
|  | 4382 |  | 4393 |  | 4403 |  | 4413 |  | 4423 |  | 4434 |  | 4444 |
|  | 4383 |  | 4393 |  | 4403 |  | 4413 |  | 4424 |  | 4434 |  | 4444 |
|  | 4383 |  | 4393 |  | 4403 |  | 4414 |  | 4424 |  | 4434 |  | 4444 |
|  | 4383 |  | 4393 |  | 4404 |  | 4414 |  | 4424 |  | 4434 |  | 4445 |
|  | 4383 |  | 4394 |  | 4404 |  | 4414 |  | 4424 |  | 4435 |  | 4445 |
|  | 4384 |  | 4394 |  | 4404 |  | 4414 |  | 4425 |  | 4435 |  | 4445 |
|  | 4384 |  | 4394 |  | 4404 |  | 4415 |  | 4425 |  | 4435 |  | 4445 |
|  | 4384 |  | 4394 |  | 4405 |  | 4415 |  | 4425 |  | 4435 |  | 4446 |
|  | 4384 |  | 4395 |  | 4405 |  | 4415 |  | 4425 |  | 4436 |  | 4446 |
|  | 4385 |  | 4395 |  | 4405 |  | 4415 |  | 4426 |  | 4436 |  | 4446 |
|  | 4385 |  | 4395 |  | 4405 |  | 4416 |  | 4426 |  | 4436 |  | 4446 |
|  | 4385 |  | 4395 |  | 4406 |  | 4416 |  | 4426 |  | 4436 |  | 4447 |
|  | 4385 |  | 4396 |  | 4406 |  | 4416 |  | 4426 |  | 4437 |  | 4447 |
|  | 4386 |  | 4396 |  | 4406 |  | 4416 |  | 4427 |  | 4437 |  | 4447 |
|  | 4386 |  | 4396 |  | 4406 |  | 4417 |  | 4427 |  | 4437 |  | 4447 |
|  | 4386 |  | 4396 |  | 4407 |  | 4417 |  | 4427 |  | 4437 |  | 4448 |
|  | 4386 |  | 4397 |  | 4407 |  | 4417 |  | 4427 |  | 4438 |  | 4448 |
|  | 4387 |  | 4397 |  | 4407 |  | 4417 |  | 4428 |  | 4438 |  | 4448 |
|  | 4387 |  | 4397 |  | 4407 |  | 4418 |  | 4428 |  | 4438 |  | 4448 |
|  | 4387 |  | 4397 |  | 4408 |  | 4418 |  | 4428 |  | 4438 |  | 4449 |
|  | 4387 |  | 4398 |  | 4408 |  | 4418 |  | 4428 |  | 4439 |  | 4449 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ |  |  | Bl. |  |  |  |  |  |  |  | Bl. | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4449 | PPD | 4459 | PPD | 4470 | PPD | 4480 | PPD | 4490 | PPD | 4500 | PPD | 4511 |
|  | 4449 |  | 4460 |  | 4470 |  | 4480 |  | 4490 |  | 4501 |  | 4511 |
|  | 4450 |  | 4460 |  | 4470 |  | 4480 |  | 4491 |  | 4501 |  | 4511 |
|  | 4450 |  | 4460 |  | 4470 |  | 4481 |  | 4491 |  | 4501 |  | 4511 |
|  | 4450 |  | 4460 |  | 4471 |  | 4481 |  | 4491 |  | 4501 |  | 4512 |
|  | 4450 |  | 4461 |  | 4471 |  | 4481 |  | 4491 |  | 4502 |  | 4512 |
|  | 4451 |  | 4461 |  | 4471 |  | 4481 |  | 4492 |  | 4502 |  | 4512 |
|  | 4451 |  | 4461 |  | 4471 |  | 4482 |  | 4492 |  | 4502 |  | 4512 |
|  | 4451 |  | 4461 |  | 4472 |  | 4482 |  | 4492 |  | 4502 |  | 4513 |
|  | 4451 |  | 4462 |  | 4472 |  | 4482 |  | 4492 |  | 4503 |  | 4513 |
|  | 4452 |  | 4462 |  | 4472 |  | 4482 |  | 4493 |  | 4503 |  | 4513 |
|  | 4452 |  | 4462 |  | 4472 |  | 4483 |  | 4493 |  | 4503 |  | 4513 |
|  | 4452 |  | 4462 |  | 4473 |  | 4483 |  | 4493 |  | 4503 |  | 4514 |
|  | 4452 |  | 4463 |  | 4473 |  | 4483 |  | 4493 |  | 4504 |  | 4514 |
|  | 4453 |  | 4463 |  | 4473 |  | 4483 |  | 4494 |  | 4504 |  | 4514 |
|  | 4453 |  | 4463 |  | 4473 |  | 4484 |  | 4494 |  | 4504 |  | 4514 |
|  | 4453 |  | 4463 |  | 4474 |  | 4484 |  | 4494 |  | 4504 |  | 4515 |
|  | 4453 |  | 4464 |  | 4474 |  | 4484 |  | 4494 |  | 4505 |  | 4515 |
|  | 4454 |  | 4464 |  | 4474 |  | 4484 |  | 4495 |  | 4505 |  | 4515 |
|  | 4454 |  | 4464 |  | 4474 |  | 4485 |  | 4495 |  | 4505 |  | 4515 |
|  | 4454 |  | 4464 |  | 4475 |  | 4485 |  | 4495 |  | 4505 |  | 4516 |
|  | 4454 |  | 4465 |  | 4475 |  | 4485 |  | 4495 |  | 4506 |  | 4516 |
|  | 4455 |  | 4465 |  | 4475 |  | 4485 |  | 4496 |  | 4506 |  | 4516 |
|  | 4455 |  | 4465 |  | 4475 |  | 4486 |  | 4496 |  | 4506 |  | 4516 |
|  | 4455 |  | 4465 |  | 4476 |  | 4486 |  | 4496 |  | 4506 |  | 4517 |
|  | 4455 |  | 4466 |  | 4476 |  | 4486 |  | 4496 |  | 4507 |  | 4517 |
|  | 4456 |  | 4466 |  | 4476 |  | 4486 |  | 4497 |  | 4507 |  | 4517 |
|  | 4456 |  | 4466 |  | 4476 |  | 4487 |  | 4497 |  | 4507 |  | 4517 |
|  | 4456 |  | 4466 |  | 4477 |  | 4487 |  | 4497 |  | 4507 |  | 4518 |
|  | 4456 |  | 4467 |  | 4477 |  | 4487 |  | 4497 |  | 4508 |  | 4518 |
|  | 4457 |  | 4467 |  | 4477 |  | 4487 |  | 4498 |  | 4508 |  | 4518 |
|  | 4457 |  | 4467 |  | 4477 |  | 4488 |  | 4498 |  | 4508 |  | 4518 |
|  | 4457 |  | 4467 |  | 4478 |  | 4488 |  | 4498 |  | 4508 |  | 4519 |
|  | 4457 |  | 4468 |  | 4478 |  | 4488 |  | 4498 |  | 4509 |  | 4519 |
|  | 4458 |  | 4468 |  | 4478 |  | 4488 |  | 4499 |  | 4509 |  | 4519 |
|  | 4458 |  | 4468 |  | 4478 |  | 4489 |  | 4499 |  | 4509 |  | 4519 |
|  | 4458 |  | 4468 |  | 4479 |  | 4489 |  | 4499 |  | 4509 |  | 4520 |
|  | 4458 |  | 4469 |  | 4479 |  | 4489 |  | 4499 |  | 4510 |  | 4520 |
|  | 4459 |  | 4469 |  | 4479 |  | 4489 |  | 4500 |  | 4510 |  | 4520 |
|  | 4459 |  | 4469 |  | 4479 |  | 4490 |  | 4500 |  | 4510 |  | 4520 |
|  | 4459 |  | 4469 |  | 4480 |  | 4490 |  | 4500 |  | 4510 |  | 4521 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Tre. |  |  | Bl nb |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. | $\begin{gathered} \text { Trt. } \\ \text { No nb. } \end{gathered}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4521 | PPD | 4531 | PPD | 4541 | PPD | 4552 | PPD | 4562 | PPD | 4572 | PPD | 4582 |
|  | 4521 |  | 4531 |  | 4542 |  | 4552 |  | 4562 |  | 4572 |  | 4583 |
|  | 4521 |  | 4532 |  | 4542 |  | 4552 |  | 4562 |  | 4573 |  | 4583 |
|  | 4522 |  | 4532 |  | 4542 |  | 4552 |  | 4563 |  | 4573 |  | 4583 |
|  | 4522 |  | 4532 |  | 4542 |  | 4553 |  | 4563 |  | 4573 |  | 4583 |
|  | 4522 |  | 4532 |  | 4543 |  | 4553 |  | 4563 |  | 4573 |  | 4584 |
|  | 4522 |  | 4533 |  | 4543 |  | 4553 |  | 4563 |  | 4574 |  | 4584 |
|  | 4523 |  | 4533 |  | 4543 |  | 4553 |  | 4564 |  | 4574 |  | 4584 |
|  | 4523 |  | 4533 |  | 4543 |  | 4554 |  | 4564 |  | 4574 |  | 4584 |
|  | 4523 |  | 4533 |  | 4544 |  | 4554 |  | 4564 |  | 4574 |  | 4585 |
|  | 4523 |  | 4534 |  | 4544 |  | 4554 |  | 4564 |  | 4575 |  | 4585 |
|  | 4524 |  | 4534 |  | 4544 |  | 4554 |  | 4565 |  | 4575 |  | 4585 |
|  | 4524 |  | 4534 |  | 4544 |  | 4555 |  | 4565 |  | 4575 |  | 4585 |
|  | 4524 |  | 4534 |  | 4545 |  | 4555 |  | 4565 |  | 4575 |  | 4586 |
|  | 4524 |  | 4535 |  | 4545 |  | 4555 |  | 4565 |  | 4576 |  | 4586 |
|  | 4525 |  | 4535 |  | 4545 |  | 4555 |  | 4566 |  | 4576 |  | 4586 |
|  | 4525 |  | 4535 |  | 4545 |  | 4556 |  | 4566 |  | 4576 |  | 4586 |
|  | 4525 |  | 4535 |  | 4546 |  | 4556 |  | 4566 |  | 4576 |  | 4587 |
|  | 4525 |  | 4536 |  | 4546 |  | 4556 |  | 4566 |  | 4577 |  | 4587 |
|  | 4526 |  | 4536 |  | 4546 |  | 4556 |  | 4567 |  | 4577 |  | 4587 |
|  | 4526 |  | 4536 |  | 4546 |  | 4557 |  | 4567 |  | 4577 |  | 4587 |
|  | 4526 |  | 4536 |  | 4547 |  | 4557 |  | 4567 |  | 4577 |  | 4588 |
|  | 4526 |  | 4537 |  | 4547 |  | 4557 |  | 4567 |  | 4578 |  | 4588 |
|  | 4527 |  | 4537 |  | 4547 |  | 4557 |  | 4568 |  | 4578 |  | 4588 |
|  | 4527 |  | 4537 |  | 4547 |  | 4558 |  | 4568 |  | 4578 |  | 4588 |
|  | 4527 |  | 4537 |  | 4548 |  | 4558 |  | 4568 |  | 4578 |  | 4589 |
|  | 4527 |  | 4538 |  | 4548 |  | 4558 |  | 4568 |  | 4579 |  | 4589 |
|  | 4528 |  | 4538 |  | 4548 |  | 4558 |  | 4569 |  | 4579 |  | 4589 |
|  | 4528 |  | 4538 |  | 4548 |  | 4559 |  | 4569 |  | 4579 |  | 4589 |
|  | 4528 |  | 4538 |  | 4549 |  | 4559 |  | 4569 |  | 4579 |  | 4590 |
|  | 4528 |  | 4539 |  | 4549 |  | 4559 |  | 4569 |  | 4580 |  | 4590 |
|  | 4529 |  | 4539 |  | 4549 |  | 4559 |  | 4570 |  | 4580 |  | 4590 |
|  | 4529 |  | 4539 |  | 4549 |  | 4560 |  | 4570 |  | 4580 |  | 4590 |
|  | 4529 |  | 4539 |  | 4550 |  | 4560 |  | 4570 |  | 4580 |  | 4591 |
|  | 4529 |  | 4540 |  | 4550 |  | 4560 |  | 4570 |  | 4581 |  | 4591 |
|  | 4530 |  | 4540 |  | 4550 |  | 4560 |  | 4571 |  | 4581 |  | 4591 |
|  | 4530 |  | 4540 |  | 4550 |  | 4561 |  | 4571 |  | 4581 |  | 4591 |
|  | 4530 |  | 4540 |  | 4551 |  | 4561 |  | 4571 |  | 4581 |  | 4592 |
|  | 4530 |  | 4541 |  | 4551 |  | 4561 |  | 4571 |  | 4582 |  | 4592 |
|  | 4531 |  | 4541 |  | 4551 |  | 4561 |  | 4572 |  | 4582 |  | 4592 |
|  | 4531 |  | 4541 |  | 4551 |  | 4562 |  | 4572 |  | 4582 |  | 4592 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text { n. } \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4593 | PPD | 4603 | PPD | 4613 | PPD | 4623 | PPD | 4634 | PPD | 4644 | PPD | 4654 |
|  | 4593 |  | 4603 |  | 4613 |  | 4624 |  | 4634 |  | 4644 |  | 4654 |
|  | 4593 |  | 4603 |  | 4614 |  | 4624 |  | 4634 |  | 4644 |  | 4655 |
|  | 4593 |  | 4604 |  | 4614 |  | 4624 |  | 4634 |  | 4645 |  | 4655 |
|  | 4594 |  | 4604 |  | 4614 |  | 4624 |  | 4635 |  | 4645 |  | 4655 |
|  | 4594 |  | 4604 |  | 4614 |  | 4625 |  | 4635 |  | 4645 |  | 4655 |
|  | 4594 |  | 4604 |  | 4615 |  | 4625 |  | 4635 |  | 4645 |  | 4656 |
|  | 4594 |  | 4605 |  | 4615 |  | 4625 |  | 4635 |  | 4646 |  | 4656 |
|  | 4595 |  | 4605 |  | 4615 |  | 4625 |  | 4636 |  | 4646 |  | 4656 |
|  | 4595 |  | 4605 |  | 4615 |  | 4626 |  | 4636 |  | 4646 |  | 4656 |
|  | 4595 |  | 4605 |  | 4616 |  | 4626 |  | 4636 |  | 4646 |  | 4657 |
|  | 4595 |  | 4606 |  | 4616 |  | 4626 |  | 4636 |  | 4647 |  | 4657 |
|  | 4596 |  | 4606 |  | 4616 |  | 4626 |  | 4637 |  | 4647 |  | 4657 |
|  | 4596 |  | 4606 |  | 4616 |  | 4627 |  | 4637 |  | 4647 |  | 4657 |
|  | 4596 |  | 4606 |  | 4617 |  | 4627 |  | 4637 |  | 4647 |  | 4658 |
|  | 4596 |  | 4607 |  | 4617 |  | 4627 |  | 4637 |  | 4648 |  | 4658 |
|  | 4597 |  | 4607 |  | 4617 |  | 4627 |  | 4638 |  | 4648 |  | 4658 |
|  | 4597 |  | 4607 |  | 4617 |  | 4628 |  | 4638 |  | 4648 |  | 4658 |
|  | 4597 |  | 4607 |  | 4618 |  | 4628 |  | 4638 |  | 4648 |  | 4659 |
|  | 4597 |  | 4608 |  | 4618 |  | 4628 |  | 4638 |  | 4649 |  | 4659 |
|  | 4598 |  | 4608 |  | 4618 |  | 4628 |  | 4639 |  | 4649 |  | 4659 |
|  | 4598 |  | 4608 |  | 4618 |  | 4629 |  | 4639 |  | 4649 |  | 4659 |
|  | 4598 |  | 4608 |  | 4619 |  | 4629 |  | 4639 |  | 4649 |  | 4660 |
|  | 4598 |  | 4609 |  | 4619 |  | 4629 |  | 4639 |  | 4650 |  | 4660 |
|  | 4599 |  | 4609 |  | 4619 |  | 4629 |  | 4640 |  | 4650 |  | 4660 |
|  | 4599 |  | 4609 |  | 4619 |  | 4630 |  | 4640 |  | 4650 |  | 4660 |
|  | 4599 |  | 4609 |  | 4620 |  | 4630 |  | 4640 |  | 4650 |  | 4661 |
|  | 4599 |  | 4610 |  | 4620 |  | 4630 |  | 4640 |  | 4651 |  | 4661 |
|  | 4600 |  | 4610 |  | 4620 |  | 4630 |  | 4641 |  | 4651 |  | 4661 |
|  | 4600 |  | 4610 |  | 4620 |  | 4631 |  | 4641 |  | 4651 |  | 4661 |
|  | 4600 |  | 4610 |  | 4621 |  | 4631 |  | 4641 |  | 4651 |  | 4662 |
|  | 4600 |  | 4611 |  | 4621 |  | 4631 |  | 4641 |  | 4652 |  | 4662 |
|  | 4601 |  | 4611 |  | 4621 |  | 4631 |  | 4642 |  | 4652 |  | 4662 |
|  | 4601 |  | 4611 |  | 4621 |  | 4632 |  | 4642 |  | 4652 |  | 4662 |
|  | 4601 |  | 4611 |  | 4622 |  | 4632 |  | 4642 |  | 4652 |  | 4663 |
|  | 4601 |  | 4612 |  | 4622 |  | 4632 |  | 4642 |  | 4653 |  | 4663 |
|  | 4602 |  | 4612 |  | 4622 |  | 4632 |  | 4643 |  | 4653 |  | 4663 |
|  | 4602 |  | 4612 |  | 4622 |  | 4633 |  | 4643 |  | 4653 |  | 4663 |
|  | 4602 |  | 4612 |  | 4623 |  | 4633 |  | 4643 |  | 4653 |  | 4664 |
|  | 4602 |  | 4613 |  | 4623 |  | 4633 |  | 4643 |  | 4654 |  | 4664 |
|  | 4603 |  | 4613 |  | 4623 |  | 4633 |  | 4644 |  | 4654 |  | 4664 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text { n. } \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4664 | PPD | 4675 | PPD | 4685 | PPD | 4695 | PPD | 4705 | PPD | 4716 | PPD | 4726 |
|  | 4665 |  | 4675 |  | 4685 |  | 4695 |  | 4706 |  | 4716 |  | 4726 |
|  | 4665 |  | 4675 |  | 4685 |  | 4696 |  | 4706 |  | 4716 |  | 4726 |
|  | 4665 |  | 4675 |  | 4686 |  | 4696 |  | 4706 |  | 4716 |  | 4727 |
|  | 4665 |  | 4676 |  | 4686 |  | 4696 |  | 4706 |  | 4717 |  | 4727 |
|  | 4666 |  | 4676 |  | 4686 |  | 4696 |  | 4707 |  | 4717 |  | 4727 |
|  | 4666 |  | 4676 |  | 4686 |  | 4697 |  | 4707 |  | 4717 |  | 4727 |
|  | 4666 |  | 4676 |  | 4687 |  | 4697 |  | 4707 |  | 4717 |  | 4728 |
|  | 4666 |  | 4677 |  | 4687 |  | 4697 |  | 4707 |  | 4718 |  | 4728 |
|  | 4667 |  | 4677 |  | 4687 |  | 4697 |  | 4708 |  | 4718 |  | 4728 |
|  | 4667 |  | 4677 |  | 4687 |  | 4698 |  | 4708 |  | 4718 |  | 4728 |
|  | 4667 |  | 4677 |  | 4688 |  | 4698 |  | 4708 |  | 4718 |  | 4729 |
|  | 4667 |  | 4678 |  | 4688 |  | 4698 |  | 4708 |  | 4719 |  | 4729 |
|  | 4668 |  | 4678 |  | 4688 |  | 4698 |  | 4709 |  | 4719 |  | 4729 |
|  | 4668 |  | 4678 |  | 4688 |  | 4699 |  | 4709 |  | 4719 |  | 4729 |
|  | 4668 |  | 4678 |  | 4689 |  | 4699 |  | 4709 |  | 4719 |  | 4730 |
|  | 4668 |  | 4679 |  | 4689 |  | 4699 |  | 4709 |  | 4720 |  | 4730 |
|  | 4669 |  | 4679 |  | 4689 |  | 4699 |  | 4710 |  | 4720 |  | 4730 |
|  | 4669 |  | 4679 |  | 4689 |  | 4700 |  | 4710 |  | 4720 |  | 4730 |
|  | 4669 |  | 4679 |  | 4690 |  | 4700 |  | 4710 |  | 4720 |  | 4731 |
|  | 4669 |  | 4680 |  | 4690 |  | 4700 |  | 4710 |  | 4721 |  | 4731 |
|  | 4670 |  | 4680 |  | 4690 |  | 4700 |  | 4711 |  | 4721 |  | 4731 |
|  | 4670 |  | 4680 |  | 4690 |  | 4701 |  | 4711 |  | 4721 |  | 4731 |
|  | 4670 |  | 4680 |  | 4691 |  | 4701 |  | 4711 |  | 4721 |  | 4732 |
|  | 4670 |  | 4681 |  | 4691 |  | 4701 |  | 4711 |  | 4722 |  | 4732 |
|  | 4671 |  | 4681 |  | 4691 |  | 4701 |  | 4712 |  | 4722 |  | 4732 |
|  | 4671 |  | 4681 |  | 4691 |  | 4702 |  | 4712 |  | 4722 |  | 4732 |
|  | 4671 |  | 4681 |  | 4692 |  | 4702 |  | 4712 |  | 4722 |  | 4733 |
|  | 4671 |  | 4682 |  | 4692 |  | 4702 |  | 4712 |  | 4723 |  | 4733 |
|  | 4672 |  | 4682 |  | 4692 |  | 4702 |  | 4713 |  | 4723 |  | 4733 |
|  | 4672 |  | 4682 |  | 4692 |  | 4703 |  | 4713 |  | 4723 |  | 4733 |
|  | 4672 |  | 4682 |  | 4693 |  | 4703 |  | 4713 |  | 4723 |  | 4734 |
|  | 4672 |  | 4683 |  | 4693 |  | 4703 |  | 4713 |  | 4724 |  | 4734 |
|  | 4673 |  | 4683 |  | 4693 |  | 4703 |  | 4714 |  | 4724 |  | 4734 |
|  | 4673 |  | 4683 |  | 4693 |  | 4704 |  | 4714 |  | 4724 |  | 4734 |
|  | 4673 |  | 4683 |  | 4694 |  | 4704 |  | 4714 |  | 4724 |  | 4735 |
|  | 4673 |  | 4684 |  | 4694 |  | 4704 |  | 4714 |  | 4725 |  | 4735 |
|  | 4674 |  | 4684 |  | 4694 |  | 4704 |  | 4715 |  | 4725 |  | 4735 |
|  | 4674 |  | 4684 |  | 4694 |  | 4705 |  | 4715 |  | 4725 |  | 4735 |
|  | 4674 |  | 4684 |  | 4695 |  | 4705 |  | 4715 |  | 4725 |  | 4736 |
|  | 4674 |  | 4685 |  | 4695 |  | 4705 |  | 4715 |  | 4726 |  | 4736 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4736 | PPD | 4746 | PPD | 4757 | PPD | 4767 | PPD | 4777 | PPD | 4787 | PPD | 4798 |
|  | 4736 |  | 4747 |  | 4757 |  | 4767 |  | 4777 |  | 4788 |  | 4798 |
|  | 4737 |  | 4747 |  | 4757 |  | 4767 |  | 4778 |  | 4788 |  | 4798 |
|  | 4737 |  | 4747 |  | 4757 |  | 4768 |  | 4778 |  | 4788 |  | 4798 |
|  | 4737 |  | 4747 |  | 4758 |  | 4768 |  | 4778 |  | 4788 |  | 4799 |
|  | 4737 |  | 4748 |  | 4758 |  | 4768 |  | 4778 |  | 4789 |  | 4799 |
|  | 4738 |  | 4748 |  | 4758 |  | 4768 |  | 4779 |  | 4789 |  | 4799 |
|  | 4738 |  | 4748 |  | 4758 |  | 4769 |  | 4779 |  | 4789 |  | 4799 |
|  | 4738 |  | 4748 |  | 4759 |  | 4769 |  | 4779 |  | 4789 |  | 4800 |
|  | 4738 |  | 4749 |  | 4759 |  | 4769 |  | 4779 |  | 4790 |  | 4800 |
|  | 4739 |  | 4749 |  | 4759 |  | 4769 |  | 4780 |  | 4790 |  | 4800 |
|  | 4739 |  | 4749 |  | 4759 |  | 4770 |  | 4780 |  | 4790 |  | 4800 |
|  | 4739 |  | 4749 |  | 4760 |  | 4770 |  | 4780 |  | 4790 |  | 4801 |
|  | 4739 |  | 4750 |  | 4760 |  | 4770 |  | 4780 |  | 4791 |  | 4801 |
|  | 4740 |  | 4750 |  | 4760 |  | 4770 |  | 4781 |  | 4791 |  | 4801 |
|  | 4740 |  | 4750 |  | 4760 |  | 4771 |  | 4781 |  | 4791 |  | 4801 |
|  | 4740 |  | 4750 |  | 4761 |  | 4771 |  | 4781 |  | 4791 |  | 4802 |
|  | 4740 |  | 4751 |  | 4761 |  | 4771 |  | 4781 |  | 4792 |  | 4802 |
|  | 4741 |  | 4751 |  | 4761 |  | 4771 |  | 4782 |  | 4792 |  | 4802 |
|  | 4741 |  | 4751 |  | 4761 |  | 4772 |  | 4782 |  | 4792 |  | 4802 |
|  | 4741 |  | 4751 |  | 4762 |  | 4772 |  | 4782 |  | 4792 |  | 4803 |
|  | 4741 |  | 4752 |  | 4762 |  | 4772 |  | 4782 |  | 4793 |  | 4803 |
|  | 4742 |  | 4752 |  | 4762 |  | 4772 |  | 4783 |  | 4793 |  | 4803 |
|  | 4742 |  | 4752 |  | 4762 |  | 4773 |  | 4783 |  | 4793 |  | 4803 |
|  | 4742 |  | 4752 |  | 4763 |  | 4773 |  | 4783 |  | 4793 |  | 4804 |
|  | 4742 |  | 4753 |  | 4763 |  | 4773 |  | 4783 |  | 4794 |  | 4804 |
|  | 4743 |  | 4753 |  | 4763 |  | 4773 |  | 4784 |  | 4794 |  | 4804 |
|  | 4743 |  | 4753 |  | 4763 |  | 4774 |  | 4784 |  | 4794 |  | 4804 |
|  | 4743 |  | 4753 |  | 4764 |  | 4774 |  | 4784 |  | 4794 |  | 4805 |
|  | 4743 |  | 4754 |  | 4764 |  | 4774 |  | 4784 |  | 4795 |  | 4805 |
|  | 4744 |  | 4754 |  | 4764 |  | 4774 |  | 4785 |  | 4795 |  | 4805 |
|  | 4744 |  | 4754 |  | 4764 |  | 4775 |  | 4785 |  | 4795 |  | 4805 |
|  | 4744 |  | 4754 |  | 4765 |  | 4775 |  | 4785 |  | 4795 |  | 4806 |
|  | 4744 |  | 4755 |  | 4765 |  | 4775 |  | 4785 |  | 4796 |  | 4806 |
|  | 4745 |  | 4755 |  | 4765 |  | 4775 |  | 4786 |  | 4796 |  | 4806 |
|  | 4745 |  | 4755 |  | 4765 |  | 4776 |  | 4786 |  | 4796 |  | 4806 |
|  | 4745 |  | 4755 |  | 4766 |  | 4776 |  | 4786 |  | 4796 |  | 4807 |
|  | 4745 |  | 4756 |  | 4766 |  | 4776 |  | 4786 |  | 4797 |  | 4807 |
|  | 4746 |  | 4756 |  | 4766 |  | 4776 |  | 4787 |  | 4797 |  | 4807 |
|  | 4746 |  | 4756 |  | 4766 |  | 4777 |  | 4787 |  | 4797 |  | 4807 |
|  | 4746 |  | 4756 |  | 4767 |  | 4777 |  | 4787 |  | 4797 |  | 4808 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ | Bl. |  | Bl nb |  | Bl nb |  |  | Trt | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4808 | PPD | 4818 | PPD | 4828 | PPD | 4839 | PPD | 4849 | PPD | 4859 | PPD | 4869 |
|  | 4808 |  | 4818 |  | 4829 |  | 4839 |  | 4849 |  | 4859 |  | 4870 |
|  | 4808 |  | 4819 |  | 4829 |  | 4839 |  | 4849 |  | 4860 |  | 4870 |
|  | 4809 |  | 4819 |  | 4829 |  | 4839 |  | 4850 |  | 4860 |  | 4870 |
|  | 4809 |  | 4819 |  | 4829 |  | 4840 |  | 4850 |  | 4860 |  | 4870 |
|  | 4809 |  | 4819 |  | 4830 |  | 4840 |  | 4850 |  | 4860 |  | 4871 |
|  | 4809 |  | 4820 |  | 4830 |  | 4840 |  | 4850 |  | 4861 |  | 4871 |
|  | 4810 |  | 4820 |  | 4830 |  | 4840 |  | 4851 |  | 4861 |  | 4871 |
|  | 4810 |  | 4820 |  | 4830 |  | 4841 |  | 4851 |  | 4861 |  | 4871 |
|  | 4810 |  | 4820 |  | 4831 |  | 4841 |  | 4851 |  | 4861 |  | 4872 |
|  | 4810 |  | 4821 |  | 4831 |  | 4841 |  | 4851 |  | 4862 |  | 4872 |
|  | 4811 |  | 4821 |  | 4831 |  | 4841 |  | 4852 |  | 4862 |  | 4872 |
|  | 4811 |  | 4821 |  | 4831 |  | 4842 |  | 4852 |  | 4862 |  | 4872 |
|  | 4811 |  | 4821 |  | 4832 |  | 4842 |  | 4852 |  | 4862 |  | 4873 |
|  | 4811 |  | 4822 |  | 4832 |  | 4842 |  | 4852 |  | 4863 |  | 4873 |
|  | 4812 |  | 4822 |  | 4832 |  | 4842 |  | 4853 |  | 4863 |  | 4873 |
|  | 4812 |  | 4822 |  | 4832 |  | 4843 |  | 4853 |  | 4863 |  | 4873 |
|  | 4812 |  | 4822 |  | 4833 |  | 4843 |  | 4853 |  | 4863 |  | 4874 |
|  | 4812 |  | 4823 |  | 4833 |  | 4843 |  | 4853 |  | 4864 |  | 4874 |
|  | 4813 |  | 4823 |  | 4833 |  | 4843 |  | 4854 |  | 4864 |  | 4874 |
|  | 4813 |  | 4823 |  | 4833 |  | 4844 |  | 4854 |  | 4864 |  | 4874 |
|  | 4813 |  | 4823 |  | 4834 |  | 4844 |  | 4854 |  | 4864 |  | 4875 |
|  | 4813 |  | 4824 |  | 4834 |  | 4844 |  | 4854 |  | 4865 |  | 4875 |
|  | 4814 |  | 4824 |  | 4834 |  | 4844 |  | 4855 |  | 4865 |  | 4875 |
|  | 4814 |  | 4824 |  | 4834 |  | 4845 |  | 4855 |  | 4865 |  | 4875 |
|  | 4814 |  | 4824 |  | 4835 |  | 4845 |  | 4855 |  | 4865 |  | 4876 |
|  | 4814 |  | 4825 |  | 4835 |  | 4845 |  | 4855 |  | 4866 |  | 4876 |
|  | 4815 |  | 4825 |  | 4835 |  | 4845 |  | 4856 |  | 4866 |  | 4876 |
|  | 4815 |  | 4825 |  | 4835 |  | 4846 |  | 4856 |  | 4866 |  | 4876 |
|  | 4815 |  | 4825 |  | 4836 |  | 4846 |  | 4856 |  | 4866 |  | 4877 |
|  | 4815 |  | 4826 |  | 4836 |  | 4846 |  | 4856 |  | 4867 |  | 4877 |
|  | 4816 |  | 4826 |  | 4836 |  | 4846 |  | 4857 |  | 4867 |  | 4877 |
|  | 4816 |  | 4826 |  | 4836 |  | 4847 |  | 4857 |  | 4867 |  | 4877 |
|  | 4816 |  | 4826 |  | 4837 |  | 4847 |  | 4857 |  | 4867 |  | 4878 |
|  | 4816 |  | 4827 |  | 4837 |  | 4847 |  | 4857 |  | 4868 |  | 4878 |
|  | 4817 |  | 4827 |  | 4837 |  | 4847 |  | 4858 |  | 4868 |  | 4878 |
|  | 4817 |  | 4827 |  | 4837 |  | 4848 |  | 4858 |  | 4868 |  | 4878 |
|  | 4817 |  | 4827 |  | 4838 |  | 4848 |  | 4858 |  | 4868 |  | 4879 |
|  | 4817 |  | 4828 |  | 4838 |  | 4848 |  | 4858 |  | 4869 |  | 4879 |
|  | 4818 |  | 4828 |  | 4838 |  | 4848 |  | 4859 |  | 4869 |  | 4879 |
|  | 4818 |  | 4828 |  | 4838 |  | 4849 |  | 4859 |  | 4869 |  | 4879 |

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Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl. |  | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4880 | PPD | 4890 | PPD | 4900 | PPD | 4910 | PPD | 4921 | PPD | 4931 | PPD | 4941 |
|  | 4880 |  | 4890 |  | 4900 |  | 4911 |  | 4921 |  | 4931 |  | 4941 |
|  | 4880 |  | 4890 |  | 4901 |  | 4911 |  | 4921 |  | 4931 |  | 4942 |
|  | 4880 |  | 4891 |  | 4901 |  | 4911 |  | 4921 |  | 4932 |  | 4942 |
|  | 4881 |  | 4891 |  | 4901 |  | 4911 |  | 4922 |  | 4932 |  | 4942 |
|  | 4881 |  | 4891 |  | 4901 |  | 4912 |  | 4922 |  | 4932 |  | 4942 |
|  | 4881 |  | 4891 |  | 4902 |  | 4912 |  | 4922 |  | 4932 |  | 4943 |
|  | 4881 |  | 4892 |  | 4902 |  | 4912 |  | 4922 |  | 4933 |  | 4943 |
|  | 4882 |  | 4892 |  | 4902 |  | 4912 |  | 4923 |  | 4933 |  | 4943 |
|  | 4882 |  | 4892 |  | 4902 |  | 4913 |  | 4923 |  | 4933 |  | 4943 |
|  | 4882 |  | 4892 |  | 4903 |  | 4913 |  | 4923 |  | 4933 |  | 4944 |
|  | 4882 |  | 4893 |  | 4903 |  | 4913 |  | 4923 |  | 4934 |  | 4944 |
|  | 4883 |  | 4893 |  | 4903 |  | 4913 |  | 4924 |  | 4934 |  | 4944 |
|  | 4883 |  | 4893 |  | 4903 |  | 4914 |  | 4924 |  | 4934 |  | 4944 |
|  | 4883 |  | 4893 |  | 4904 |  | 4914 |  | 4924 |  | 4934 |  | 4945 |
|  | 4883 |  | 4894 |  | 4904 |  | 4914 |  | 4924 |  | 4935 |  | 4945 |
|  | 4884 |  | 4894 |  | 4904 |  | 4914 |  | 4925 |  | 4935 |  | 4945 |
|  | 4884 |  | 4894 |  | 4904 |  | 4915 |  | 4925 |  | 4935 |  | 4945 |
|  | 4884 |  | 4894 |  | 4905 |  | 4915 |  | 4925 |  | 4935 |  | 4946 |
|  | 4884 |  | 4895 |  | 4905 |  | 4915 |  | 4925 |  | 4936 |  | 4946 |
|  | 4885 |  | 4895 |  | 4905 |  | 4915 |  | 4926 |  | 4936 |  | 4946 |
|  | 4885 |  | 4895 |  | 4905 |  | 4916 |  | 4926 |  | 4936 |  | 4946 |
|  | 4885 |  | 4895 |  | 4906 |  | 4916 |  | 4926 |  | 4936 |  | 4947 |
|  | 4885 |  | 4896 |  | 4906 |  | 4916 |  | 4926 |  | 4937 |  | 4947 |
|  | 4886 |  | 4896 |  | 4906 |  | 4916 |  | 4927 |  | 4937 |  | 4947 |
|  | 4886 |  | 4896 |  | 4906 |  | 4917 |  | 4927 |  | 4937 |  | 4947 |
|  | 4886 |  | 4896 |  | 4907 |  | 4917 |  | 4927 |  | 4937 |  | 4948 |
|  | 4886 |  | 4897 |  | 4907 |  | 4917 |  | 4927 |  | 4938 |  | 4948 |
|  | 4887 |  | 4897 |  | 4907 |  | 4917 |  | 4928 |  | 4938 |  | 4948 |
|  | 4887 |  | 4897 |  | 4907 |  | 4918 |  | 4928 |  | 4938 |  | 4948 |
|  | 4887 |  | 4897 |  | 4908 |  | 4918 |  | 4928 |  | 4938 |  | 4949 |
|  | 4887 |  | 4898 |  | 4908 |  | 4918 |  | 4928 |  | 4939 |  | 4949 |
|  | 4888 |  | 4898 |  | 4908 |  | 4918 |  | 4929 |  | 4939 |  | 4949 |
|  | 4888 |  | 4898 |  | 4908 |  | 4919 |  | 4929 |  | 4939 |  | 4949 |
|  | 4888 |  | 4898 |  | 4909 |  | 4919 |  | 4929 |  | 4939 |  | 4950 |
|  | 4888 |  | 4899 |  | 4909 |  | 4919 |  | 4929 |  | 4940 |  | 4950 |
|  | 4889 |  | 4899 |  | 4909 |  | 4919 |  | 4930 |  | 4940 |  | 4950 |
|  | 4889 |  | 4899 |  | 4909 |  | 4920 |  | 4930 |  | 4940 |  | 4950 |
|  | 4889 |  | 4899 |  | 4910 |  | 4920 |  | 4930 |  | 4940 |  | 4951 |
|  | 4889 |  | 4900 |  | 4910 |  | 4920 |  | 4930 |  | 4941 |  | 4951 |
|  | 4890 |  | 4900 |  | 4910 |  | 4920 |  | 4931 |  | 4941 |  | 4951 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Tre. |  |  | Bl nb |  |  |  | Bl. |  | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4951 | PPD | 4962 | PPD | 4972 | PPD | 4982 | PPD | 4992 | PPD | 5003 | PPD | 5013 |
|  | 4952 |  | 4962 |  | 4972 |  | 4982 |  | 4993 |  | 5003 |  | 5013 |
|  | 4952 |  | 4962 |  | 4972 |  | 4983 |  | 4993 |  | 5003 |  | 5013 |
|  | 4952 |  | 4962 |  | 4973 |  | 4983 |  | 4993 |  | 5003 |  | 5014 |
|  | 4952 |  | 4963 |  | 4973 |  | 4983 |  | 4993 |  | 5004 |  | 5014 |
|  | 4953 |  | 4963 |  | 4973 |  | 4983 |  | 4994 |  | 5004 |  | 5014 |
|  | 4953 |  | 4963 |  | 4973 |  | 4984 |  | 4994 |  | 5004 |  | 5014 |
|  | 4953 |  | 4963 |  | 4974 |  | 4984 |  | 4994 |  | 5004 |  | 5015 |
|  | 4953 |  | 4964 |  | 4974 |  | 4984 |  | 4994 |  | 5005 |  | 5015 |
|  | 4954 |  | 4964 |  | 4974 |  | 4984 |  | 4995 |  | 5005 |  | 5015 |
|  | 4954 |  | 4964 |  | 4974 |  | 4985 |  | 4995 |  | 5005 |  | 5015 |
|  | 4954 |  | 4964 |  | 4975 |  | 4985 |  | 4995 |  | 5005 |  | 5016 |
|  | 4954 |  | 4965 |  | 4975 |  | 4985 |  | 4995 |  | 5006 |  | 5016 |
|  | 4955 |  | 4965 |  | 4975 |  | 4985 |  | 4996 |  | 5006 |  | 5016 |
|  | 4955 |  | 4965 |  | 4975 |  | 4986 |  | 4996 |  | 5006 |  | 5016 |
|  | 4955 |  | 4965 |  | 4976 |  | 4986 |  | 4996 |  | 5006 |  | 5017 |
|  | 4955 |  | 4966 |  | 4976 |  | 4986 |  | 4996 |  | 5007 |  | 5017 |
|  | 4956 |  | 4966 |  | 4976 |  | 4986 |  | 4997 |  | 5007 |  | 5017 |
|  | 4956 |  | 4966 |  | 4976 |  | 4987 |  | 4997 |  | 5007 |  | 5017 |
|  | 4956 |  | 4966 |  | 4977 |  | 4987 |  | 4997 |  | 5007 |  | 5018 |
|  | 4956 |  | 4967 |  | 4977 |  | 4987 |  | 4997 |  | 5008 |  | 5018 |
|  | 4957 |  | 4967 |  | 4977 |  | 4987 |  | 4998 |  | 5008 |  | 5018 |
|  | 4957 |  | 4967 |  | 4977 |  | 4988 |  | 4998 |  | 5008 |  | 5018 |
|  | 4957 |  | 4967 |  | 4978 |  | 4988 |  | 4998 |  | 5008 |  | 5019 |
|  | 4957 |  | 4968 |  | 4978 |  | 4988 |  | 4998 |  | 5009 |  | 5019 |
|  | 4958 |  | 4968 |  | 4978 |  | 4988 |  | 4999 |  | 5009 |  | 5019 |
|  | 4958 |  | 4968 |  | 4978 |  | 4989 |  | 4999 |  | 5009 |  | 5019 |
|  | 4958 |  | 4968 |  | 4979 |  | 4989 |  | 4999 |  | 5009 |  | 5020 |
|  | 4958 |  | 4969 |  | 4979 |  | 4989 |  | 4999 |  | 5010 |  | 5020 |
|  | 4959 |  | 4969 |  | 4979 |  | 4989 |  | 5000 |  | 5010 |  | 5020 |
|  | 4959 |  | 4969 |  | 4979 |  | 4990 |  | 5000 |  | 5010 |  | 5020 |
|  | 4959 |  | 4969 |  | 4980 |  | 4990 |  | 5000 |  | 5010 |  | 5021 |
|  | 4959 |  | 4970 |  | 4980 |  | 4990 |  | 5000 |  | 5011 |  | 5021 |
|  | 4960 |  | 4970 |  | 4980 |  | 4990 |  | 5001 |  | 5011 |  | 5021 |
|  | 4960 |  | 4970 |  | 4980 |  | 4991 |  | 5001 |  | 5011 |  | 5021 |
|  | 4960 |  | 4970 |  | 4981 |  | 4991 |  | 5001 |  | 5011 |  | 5022 |
|  | 4960 |  | 4971 |  | 4981 |  | 4991 |  | 5001 |  | 5012 |  | 5022 |
|  | 4961 |  | 4971 |  | 4981 |  | 4991 |  | 5002 |  | 5012 |  | 5022 |
|  | 4961 |  | 4971 |  | 4981 |  | 4992 |  | 5002 |  | 5012 |  | 5022 |
|  | 4961 |  | 4971 |  | 4982 |  | 4992 |  | 5002 |  | 5012 |  | 5023 |
|  | 4961 |  | 4972 |  | 4982 |  | 4992 |  | 5002 |  | 5013 |  | 5023 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. |  | Bl nb |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5023 | PPD | 5033 | PPD | 5044 | PPD | 5054 | PPD | 5064 | PPD | 5074 | PPD | 5085 |
|  | 5023 |  | 5034 |  | 5044 |  | 5054 |  | 5064 |  | 5075 |  | 5085 |
|  | 5024 |  | 5034 |  | 5044 |  | 5054 |  | 5065 |  | 5075 |  | 5085 |
|  | 5024 |  | 5034 |  | 5044 |  | 5055 |  | 5065 |  | 5075 |  | 5085 |
|  | 5024 |  | 5034 |  | 5045 |  | 5055 |  | 5065 |  | 5075 |  | 5086 |
|  | 5024 |  | 5035 |  | 5045 |  | 5055 |  | 5065 |  | 5076 |  | 5086 |
|  | 5025 |  | 5035 |  | 5045 |  | 5055 |  | 5066 |  | 5076 |  | 5086 |
|  | 5025 |  | 5035 |  | 5045 |  | 5056 |  | 5066 |  | 5076 |  | 5086 |
|  | 5025 |  | 5035 |  | 5046 |  | 5056 |  | 5066 |  | 5076 |  | 5087 |
|  | 5025 |  | 5036 |  | 5046 |  | 5056 |  | 5066 |  | 5077 |  | 5087 |
|  | 5026 |  | 5036 |  | 5046 |  | 5056 |  | 5067 |  | 5077 |  | 5087 |
|  | 5026 |  | 5036 |  | 5046 |  | 5057 |  | 5067 |  | 5077 |  | 5087 |
|  | 5026 |  | 5036 |  | 5047 |  | 5057 |  | 5067 |  | 5077 |  | 5088 |
|  | 5026 |  | 5037 |  | 5047 |  | 5057 |  | 5067 |  | 5078 |  | 5088 |
|  | 5027 |  | 5037 |  | 5047 |  | 5057 |  | 5068 |  | 5078 |  | 5088 |
|  | 5027 |  | 5037 |  | 5047 |  | 5058 |  | 5068 |  | 5078 |  | 5088 |
|  | 5027 |  | 5037 |  | 5048 |  | 5058 |  | 5068 |  | 5078 |  | 5089 |
|  | 5027 |  | 5038 |  | 5048 |  | 5058 |  | 5068 |  | 5079 |  | 5089 |
|  | 5028 |  | 5038 |  | 5048 |  | 5058 |  | 5069 |  | 5079 |  | 5089 |
|  | 5028 |  | 5038 |  | 5048 |  | 5059 |  | 5069 |  | 5079 |  | 5089 |
|  | 5028 |  | 5038 |  | 5049 |  | 5059 |  | 5069 |  | 5079 |  | 5090 |
|  | 5028 |  | 5039 |  | 5049 |  | 5059 |  | 5069 |  | 5080 |  | 5090 |
|  | 5029 |  | 5039 |  | 5049 |  | 5059 |  | 5070 |  | 5080 |  | 5090 |
|  | 5029 |  | 5039 |  | 5049 |  | 5060 |  | 5070 |  | 5080 |  | 5090 |
|  | 5029 |  | 5039 |  | 5050 |  | 5060 |  | 5070 |  | 5080 |  | 5091 |
|  | 5029 |  | 5040 |  | 5050 |  | 5060 |  | 5070 |  | 5081 |  | 5091 |
|  | 5030 |  | 5040 |  | 5050 |  | 5060 |  | 5071 |  | 5081 |  | 5091 |
|  | 5030 |  | 5040 |  | 5050 |  | 5061 |  | 5071 |  | 5081 |  | 5091 |
|  | 5030 |  | 5040 |  | 5051 |  | 5061 |  | 5071 |  | 5081 |  | 5092 |
|  | 5030 |  | 5041 |  | 5051 |  | 5061 |  | 5071 |  | 5082 |  | 5092 |
|  | 5031 |  | 5041 |  | 5051 |  | 5061 |  | 5072 |  | 5082 |  | 5092 |
|  | 5031 |  | 5041 |  | 5051 |  | 5062 |  | 5072 |  | 5082 |  | 5092 |
|  | 5031 |  | 5041 |  | 5052 |  | 5062 |  | 5072 |  | 5082 |  | 5093 |
|  | 5031 |  | 5042 |  | 5052 |  | 5062 |  | 5072 |  | 5083 |  | 5093 |
|  | 5032 |  | 5042 |  | 5052 |  | 5062 |  | 5073 |  | 5083 |  | 5093 |
|  | 5032 |  | 5042 |  | 5052 |  | 5063 |  | 5073 |  | 5083 |  | 5093 |
|  | 5032 |  | 5042 |  | 5053 |  | 5063 |  | 5073 |  | 5083 |  | 5094 |
|  | 5032 |  | 5043 |  | 5053 |  | 5063 |  | 5073 |  | 5084 |  | 5094 |
|  | 5033 |  | 5043 |  | 5053 |  | 5063 |  | 5074 |  | 5084 |  | 5094 |
|  | 5033 |  | 5043 |  | 5053 |  | 5064 |  | 5074 |  | 5084 |  | 5094 |
|  | 5033 |  | 5043 |  | 5054 |  | 5064 |  | 5074 |  | 5084 |  | 5095 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. |  | $\begin{aligned} & \text { Tret. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | Trit. Bl. |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5095 | PPD | 5105 | PPD | 5115 | PPD | 5126 | PPD | 5136 | PPD | 5146 | PPD | 5156 |
|  | 5095 |  | 5105 |  | 5116 |  | 5126 |  | 5136 |  | 5146 |  | 5157 |
|  | 5095 |  | 5106 |  | 5116 |  | 5126 |  | 5136 |  | 5147 |  | 5157 |
|  | 5096 |  | 5106 |  | 5116 |  | 5126 |  | 5137 |  | 5147 |  | 5157 |
|  | 5096 |  | 5106 |  | 5116 |  | 5127 |  | 5137 |  | 5147 |  | 5157 |
|  | 5096 |  | 5106 |  | 5117 |  | 5127 |  | 5137 |  | 5147 |  | 5158 |
|  | 5096 |  | 5107 |  | 5117 |  | 5127 |  | 5137 |  | 5148 |  | 5158 |
|  | 5097 |  | 5107 |  | 5117 |  | 5127 |  | 5138 |  | 5148 |  | 5158 |
|  | 5097 |  | 5107 |  | 5117 |  | 5128 |  | 5138 |  | 5148 |  | 5158 |
|  | 5097 |  | 5107 |  | 5118 |  | 5128 |  | 5138 |  | 5148 |  | 5159 |
|  | 5097 |  | 5108 |  | 5118 |  | 5128 |  | 5138 |  | 5149 |  | 5159 |
|  | 5098 |  | 5108 |  | 5118 |  | 5128 |  | 5139 |  | 5149 |  | 5159 |
|  | 5098 |  | 5108 |  | 5118 |  | 5129 |  | 5139 |  | 5149 |  | 5159 |
|  | 5098 |  | 5108 |  | 5119 |  | 5129 |  | 5139 |  | 5149 |  | 5160 |
|  | 5098 |  | 5109 |  | 5119 |  | 5129 |  | 5139 |  | 5150 |  | 5160 |
|  | 5099 |  | 5109 |  | 5119 |  | 5129 |  | 5140 |  | 5150 |  | 5160 |
|  | 5099 |  | 5109 |  | 5119 |  | 5130 |  | 5140 |  | 5150 |  | 5160 |
|  | 5099 |  | 5109 |  | 5120 |  | 5130 |  | 5140 |  | 5150 |  | 5161 |
|  | 5099 |  | 5110 |  | 5120 |  | 5130 |  | 5140 |  | 5151 |  | 5161 |
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|  | 5102 |  | 5112 |  | 5122 |  | 5133 |  | 5143 |  | 5153 |  | 5163 |
|  | 5102 |  | 5112 |  | 5123 |  | 5133 |  | 5143 |  | 5153 |  | 5164 |
|  | 5102 |  | 5113 |  | 5123 |  | 5133 |  | 5143 |  | 5154 |  | 5164 |
|  | 5103 |  | 5113 |  | 5123 |  | 5133 |  | 5144 |  | 5154 |  | 5164 |
|  | 5103 |  | 5113 |  | 5123 |  | 5134 |  | 5144 |  | 5154 |  | 5164 |
|  | 5103 |  | 5113 |  | 5124 |  | 5134 |  | 5144 |  | 5154 |  | 5165 |
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|  | 5104 |  | 5114 |  | 5124 |  | 5134 |  | 5145 |  | 5155 |  | 5165 |
|  | 5104 |  | 5114 |  | 5124 |  | 5135 |  | 5145 |  | 5155 |  | 5165 |
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SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{array}{r} \operatorname{Trt} \\ \mathrm{N} \end{array}$ | Bl nb | Trt | Bl. | Trt |  | Trt | $\mathrm{Bl} \text {. }$ | Trt | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ | Trt | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5167 | PPD | 5177 | PPD | 5187 | PPD | 5197 | PPD | 5208 | PPD | 5218 | PPD | 5228 |
|  | 5167 |  | 5177 |  | 5187 |  | 5198 |  | 5208 |  | 5218 |  | 5228 |
|  | 5167 |  | 5177 |  | 5188 |  | 5198 |  | 5208 |  | 5218 |  | 5229 |
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|  | 5177 |  | 5187 |  | 5197 |  | 5207 |  | 5218 |  | 5228 |  | 5238 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5238 | PPD | 5249 | PPD | 5259 | PPD | 5269 | PPD | 5279 | PPD | 5290 | PPD | 5300 |
|  | 5239 |  | 5249 |  | 5259 |  | 5269 |  | 5280 |  | 5290 |  | 5300 |
|  | 5239 |  | 5249 |  | 5259 |  | 5270 |  | 5280 |  | 5290 |  | 5300 |
|  | 5239 |  | 5249 |  | 5260 |  | 5270 |  | 5280 |  | 5290 |  | 5301 |
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|  | 5240 |  | 5250 |  | 5260 |  | 5271 |  | 5281 |  | 5291 |  | 5301 |
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|  | 5241 |  | 5251 |  | 5261 |  | 5271 |  | 5282 |  | 5292 |  | 5302 |
|  | 5241 |  | 5251 |  | 5261 |  | 5272 |  | 5282 |  | 5292 |  | 5302 |
|  | 5241 |  | 5251 |  | 5262 |  | 5272 |  | 5282 |  | 5292 |  | 5303 |
|  | 5241 |  | 5252 |  | 5262 |  | 5272 |  | 5282 |  | 5293 |  | 5303 |
|  | 5242 |  | 5252 |  | 5262 |  | 5272 |  | 5283 |  | 5293 |  | 5303 |
|  | 5242 |  | 5252 |  | 5262 |  | 5273 |  | 5283 |  | 5293 |  | 5303 |
|  | 5242 |  | 5252 |  | 5263 |  | 5273 |  | 5283 |  | 5293 |  | 5304 |
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|  | 5244 |  | 5255 |  | 5265 |  | 5275 |  | 5285 |  | 5296 |  | 5306 |
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|  | 5245 |  | 5255 |  | 5266 |  | 5276 |  | 5286 |  | 5296 |  | 5307 |
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|  | 5246 |  | 5256 |  | 5266 |  | 5276 |  | 5287 |  | 5297 |  | 5307 |
|  | 5246 |  | 5256 |  | 5266 |  | 5277 |  | 5287 |  | 5297 |  | 5307 |
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SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  | Bl nb |  | Bl nb |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5310 | PPD | 5320 | PPD | 5331 | PPD | 5341 | PPD | 5351 | PPD | 5361 | PPD | 5372 |
|  | 5310 |  | 5321 |  | 5331 |  | 5341 |  | 5351 |  | 5362 |  | 5372 |
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|  | 5320 |  | 5330 |  | 5341 |  | 5351 |  | 5361 |  | 5371 |  | 5382 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. } \\ & \text { No nl. } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5382 | PPD | 5392 | PPD | 5402 | PPD | 5413 | PPD | 5423 | PPD | 5433 | PPD | 5443 |
|  | 5382 |  | 5392 |  | 5403 |  | 5413 |  | 5423 |  | 5433 |  | 5444 |
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|  | 5392 |  | 5402 |  | 5412 |  | 5423 |  | 5433 |  | 5443 |  | 5453 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Trt. |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5454 | PPD | 5464 | PPD | 5474 | PPD | 5484 | PPD | 5495 | PPD | 5505 | PPD | 5515 |
|  | 5454 |  | 5464 |  | 5474 |  | 5485 |  | 5495 |  | 5505 |  | 5515 |
|  | 5454 |  | 5464 |  | 5475 |  | 5485 |  | 5495 |  | 5505 |  | 5516 |
|  | 5454 |  | 5465 |  | 5475 |  | 5485 |  | 5495 |  | 5506 |  | 5516 |
|  | 5455 |  | 5465 |  | 5475 |  | 5485 |  | 5496 |  | 5506 |  | 5516 |
|  | 5455 |  | 5465 |  | 5475 |  | 5486 |  | 5496 |  | 5506 |  | 5516 |
|  | 5455 |  | 5465 |  | 5476 |  | 5486 |  | 5496 |  | 5506 |  | 5517 |
|  | 5455 |  | 5466 |  | 5476 |  | 5486 |  | 5496 |  | 5507 |  | 5517 |
|  | 5456 |  | 5466 |  | 5476 |  | 5486 |  | 5497 |  | 5507 |  | 5517 |
|  | 5456 |  | 5466 |  | 5476 |  | 5487 |  | 5497 |  | 5507 |  | 5517 |
|  | 5456 |  | 5466 |  | 5477 |  | 5487 |  | 5497 |  | 5507 |  | 5518 |
|  | 5456 |  | 5467 |  | 5477 |  | 5487 |  | 5497 |  | 5508 |  | 5518 |
|  | 5457 |  | 5467 |  | 5477 |  | 5487 |  | 5498 |  | 5508 |  | 5518 |
|  | 5457 |  | 5467 |  | 5477 |  | 5488 |  | 5498 |  | 5508 |  | 5518 |
|  | 5457 |  | 5467 |  | 5478 |  | 5488 |  | 5498 |  | 5508 |  | 5519 |
|  | 5457 |  | 5468 |  | 5478 |  | 5488 |  | 5498 |  | 5509 |  | 5519 |
|  | 5458 |  | 5468 |  | 5478 |  | 5488 |  | 5499 |  | 5509 |  | 5519 |
|  | 5458 |  | 5468 |  | 5478 |  | 5489 |  | 5499 |  | 5509 |  | 5519 |
|  | 5458 |  | 5468 |  | 5479 |  | 5489 |  | 5499 |  | 5509 |  | 5520 |
|  | 5458 |  | 5469 |  | 5479 |  | 5489 |  | 5499 |  | 5510 |  | 5520 |
|  | 5459 |  | 5469 |  | 5479 |  | 5489 |  | 5500 |  | 5510 |  | 5520 |
|  | 5459 |  | 5469 |  | 5479 |  | 5490 |  | 5500 |  | 5510 |  | 5520 |
|  | 5459 |  | 5469 |  | 5480 |  | 5490 |  | 5500 |  | 5510 |  | 5521 |
|  | 5459 |  | 5470 |  | 5480 |  | 5490 |  | 5500 |  | 5511 |  | 5521 |
|  | 5460 |  | 5470 |  | 5480 |  | 5490 |  | 5501 |  | 5511 |  | 5521 |
|  | 5460 |  | 5470 |  | 5480 |  | 5491 |  | 5501 |  | 5511 |  | 5521 |
|  | 5460 |  | 5470 |  | 5481 |  | 5491 |  | 5501 |  | 5511 |  | 5522 |
|  | 5460 |  | 5471 |  | 5481 |  | 5491 |  | 5501 |  | 5512 |  | 5522 |
|  | 5461 |  | 5471 |  | 5481 |  | 5491 |  | 5502 |  | 5512 |  | 5522 |
|  | 5461 |  | 5471 |  | 5481 |  | 5492 |  | 5502 |  | 5512 |  | 5522 |
|  | 5461 |  | 5471 |  | 5482 |  | 5492 |  | 5502 |  | 5512 |  | 5523 |
|  | 5461 |  | 5472 |  | 5482 |  | 5492 |  | 5502 |  | 5513 |  | 5523 |
|  | 5462 |  | 5472 |  | 5482 |  | 5492 |  | 5503 |  | 5513 |  | 5523 |
|  | 5462 |  | 5472 |  | 5482 |  | 5493 |  | 5503 |  | 5513 |  | 5523 |
|  | 5462 |  | 5472 |  | 5483 |  | 5493 |  | 5503 |  | 5513 |  | 5524 |
|  | 5462 |  | 5473 |  | 5483 |  | 5493 |  | 5503 |  | 5514 |  | 5524 |
|  | 5463 |  | 5473 |  | 5483 |  | 5493 |  | 5504 |  | 5514 |  | 5524 |
|  | 5463 |  | 5473 |  | 5483 |  | 5494 |  | 5504 |  | 5514 |  | 5524 |
|  | 5463 |  | 5473 |  | 5484 |  | 5494 |  | 5504 |  | 5514 |  | 5525 |
|  | 5463 |  | 5474 |  | 5484 |  | 5494 |  | 5504 |  | 5515 |  | 5525 |
|  | 5464 |  | 5474 |  | 5484 |  | 5494 |  | 5505 |  | 5515 |  | 5525 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  |  |  | Bl. |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5525 | PPD | 5536 | PPD | 5546 | PPD | 5556 | PPD | 5566 | PPD | 5577 | PPD | 5587 |
|  | 5526 |  | 5536 |  | 5546 |  | 5556 |  | 5567 |  | 5577 |  | 5587 |
|  | 5526 |  | 5536 |  | 5546 |  | 5557 |  | 5567 |  | 5577 |  | 5587 |
|  | 5526 |  | 5536 |  | 5547 |  | 5557 |  | 5567 |  | 5577 |  | 5588 |
|  | 5526 |  | 5537 |  | 5547 |  | 5557 |  | 5567 |  | 5578 |  | 5588 |
|  | 5527 |  | 5537 |  | 5547 |  | 5557 |  | 5568 |  | 5578 |  | 5588 |
|  | 5527 |  | 5537 |  | 5547 |  | 5558 |  | 5568 |  | 5578 |  | 5588 |
|  | 5527 |  | 5537 |  | 5548 |  | 5558 |  | 5568 |  | 5578 |  | 5589 |
|  | 5527 |  | 5538 |  | 5548 |  | 5558 |  | 5568 |  | 5579 |  | 5589 |
|  | 5528 |  | 5538 |  | 5548 |  | 5558 |  | 5569 |  | 5579 |  | 5589 |
|  | 5528 |  | 5538 |  | 5548 |  | 5559 |  | 5569 |  | 5579 |  | 5589 |
|  | 5528 |  | 5538 |  | 5549 |  | 5559 |  | 5569 |  | 5579 |  | 5590 |
|  | 5528 |  | 5539 |  | 5549 |  | 5559 |  | 5569 |  | 5580 |  | 5590 |
|  | 5529 |  | 5539 |  | 5549 |  | 5559 |  | 5570 |  | 5580 |  | 5590 |
|  | 5529 |  | 5539 |  | 5549 |  | 5560 |  | 5570 |  | 5580 |  | 5590 |
|  | 5529 |  | 5539 |  | 5550 |  | 5560 |  | 5570 |  | 5580 |  | 5591 |
|  | 5529 |  | 5540 |  | 5550 |  | 5560 |  | 5570 |  | 5581 |  | 5591 |
|  | 5530 |  | 5540 |  | 5550 |  | 5560 |  | 5571 |  | 5581 |  | 5591 |
|  | 5530 |  | 5540 |  | 5550 |  | 5561 |  | 5571 |  | 5581 |  | 5591 |
|  | 5530 |  | 5540 |  | 5551 |  | 5561 |  | 5571 |  | 5581 |  | 5592 |
|  | 5530 |  | 5541 |  | 5551 |  | 5561 |  | 5571 |  | 5582 |  | 5592 |
|  | 5531 |  | 5541 |  | 5551 |  | 5561 |  | 5572 |  | 5582 |  | 5592 |
|  | 5531 |  | 5541 |  | 5551 |  | 5562 |  | 5572 |  | 5582 |  | 5592 |
|  | 5531 |  | 5541 |  | 5552 |  | 5562 |  | 5572 |  | 5582 |  | 5593 |
|  | 5531 |  | 5542 |  | 5552 |  | 5562 |  | 5572 |  | 5583 |  | 5593 |
|  | 5532 |  | 5542 |  | 5552 |  | 5562 |  | 5573 |  | 5583 |  | 5593 |
|  | 5532 |  | 5542 |  | 5552 |  | 5563 |  | 5573 |  | 5583 |  | 5593 |
|  | 5532 |  | 5542 |  | 5553 |  | 5563 |  | 5573 |  | 5583 |  | 5594 |
|  | 5532 |  | 5543 |  | 5553 |  | 5563 |  | 5573 |  | 5584 |  | 5594 |
|  | 5533 |  | 5543 |  | 5553 |  | 5563 |  | 5574 |  | 5584 |  | 5594 |
|  | 5533 |  | 5543 |  | 5553 |  | 5564 |  | 5574 |  | 5584 |  | 5594 |
|  | 5533 |  | 5543 |  | 5554 |  | 5564 |  | 5574 |  | 5584 |  | 5595 |
|  | 5533 |  | 5544 |  | 5554 |  | 5564 |  | 5574 |  | 5585 |  | 5595 |
|  | 5534 |  | 5544 |  | 5554 |  | 5564 |  | 5575 |  | 5585 |  | 5595 |
|  | 5534 |  | 5544 |  | 5554 |  | 5565 |  | 5575 |  | 5585 |  | 5595 |
|  | 5534 |  | 5544 |  | 5555 |  | 5565 |  | 5575 |  | 5585 |  | 5596 |
|  | 5534 |  | 5545 |  | 5555 |  | 5565 |  | 5575 |  | 5586 |  | 5596 |
|  | 5535 |  | 5545 |  | 5555 |  | 5565 |  | 5576 |  | 5586 |  | 5596 |
|  | 5535 |  | 5545 |  | 5555 |  | 5566 |  | 5576 |  | 5586 |  | 5596 |
|  | 5535 |  | 5545 |  | 5556 |  | 5566 |  | 5576 |  | 5586 |  | 5597 |
|  | 5535 |  | 5546 |  | 5556 |  | 5566 |  | 5576 |  | 5587 |  | 5597 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| Tre. |  |  | Bl. | Trt | Bl nb |  | Bl nb |  | $\mathrm{Bl} .$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5597 | PPD | 5607 | PPD | 5618 | PPD | 5628 | PPD | 5638 | PPD | 5648 | PPD | 5659 |
|  | 5597 |  | 5608 |  | 5618 |  | 5628 |  | 5638 |  | 5649 |  | 5659 |
|  | 5598 |  | 5608 |  | 5618 |  | 5628 |  | 5639 |  | 5649 |  | 5659 |
|  | 5598 |  | 5608 |  | 5618 |  | 5629 |  | 5639 |  | 5649 |  | 5659 |
|  | 5598 |  | 5608 |  | 5619 |  | 5629 |  | 5639 |  | 5649 |  | 5660 |
|  | 5598 |  | 5609 |  | 5619 |  | 5629 |  | 5639 |  | 5650 |  | 5660 |
|  | 5599 |  | 5609 |  | 5619 |  | 5629 |  | 5640 |  | 5650 |  | 5660 |
|  | 5599 |  | 5609 |  | 5619 |  | 5630 |  | 5640 |  | 5650 |  | 5660 |
|  | 5599 |  | 5609 |  | 5620 |  | 5630 |  | 5640 |  | 5650 |  | 5661 |
|  | 5599 |  | 5610 |  | 5620 |  | 5630 |  | 5640 |  | 5651 |  | 5661 |
|  | 5600 |  | 5610 |  | 5620 |  | 5630 |  | 5641 |  | 5651 |  | 5661 |
|  | 5600 |  | 5610 |  | 5620 |  | 5631 |  | 5641 |  | 5651 |  | 5661 |
|  | 5600 |  | 5610 |  | 5621 |  | 5631 |  | 5641 |  | 5651 |  | 5662 |
|  | 5600 |  | 5611 |  | 5621 |  | 5631 |  | 5641 |  | 5652 |  | 5662 |
|  | 5601 |  | 5611 |  | 5621 |  | 5631 |  | 5642 |  | 5652 |  | 5662 |
|  | 5601 |  | 5611 |  | 5621 |  | 5632 |  | 5642 |  | 5652 |  | 5662 |
|  | 5601 |  | 5611 |  | 5622 |  | 5632 |  | 5642 |  | 5652 |  | 5663 |
|  | 5601 |  | 5612 |  | 5622 |  | 5632 |  | 5642 |  | 5653 |  | 5663 |
|  | 5602 |  | 5612 |  | 5622 |  | 5632 |  | 5643 |  | 5653 |  | 5663 |
|  | 5602 |  | 5612 |  | 5622 |  | 5633 |  | 5643 |  | 5653 |  | 5663 |
|  | 5602 |  | 5612 |  | 5623 |  | 5633 |  | 5643 |  | 5653 |  | 5664 |
|  | 5602 |  | 5613 |  | 5623 |  | 5633 |  | 5643 |  | 5654 |  | 5664 |
|  | 5603 |  | 5613 |  | 5623 |  | 5633 |  | 5644 |  | 5654 |  | 5664 |
|  | 5603 |  | 5613 |  | 5623 |  | 5634 |  | 5644 |  | 5654 |  | 5664 |
|  | 5603 |  | 5613 |  | 5624 |  | 5634 |  | 5644 |  | 5654 |  | 5665 |
|  | 5603 |  | 5614 |  | 5624 |  | 5634 |  | 5644 |  | 5655 |  | 5665 |
|  | 5604 |  | 5614 |  | 5624 |  | 5634 |  | 5645 |  | 5655 |  | 5665 |
|  | 5604 |  | 5614 |  | 5624 |  | 5635 |  | 5645 |  | 5655 |  | 5665 |
|  | 5604 |  | 5614 |  | 5625 |  | 5635 |  | 5645 |  | 5655 |  | 5666 |
|  | 5604 |  | 5615 |  | 5625 |  | 5635 |  | 5645 |  | 5656 |  | 5666 |
|  | 5605 |  | 5615 |  | 5625 |  | 5635 |  | 5646 |  | 5656 |  | 5666 |
|  | 5605 |  | 5615 |  | 5625 |  | 5636 |  | 5646 |  | 5656 |  | 5666 |
|  | 5605 |  | 5615 |  | 5626 |  | 5636 |  | 5646 |  | 5656 |  | 5667 |
|  | 5605 |  | 5616 |  | 5626 |  | 5636 |  | 5646 |  | 5657 |  | 5667 |
|  | 5606 |  | 5616 |  | 5626 |  | 5636 |  | 5647 |  | 5657 |  | 5667 |
|  | 5606 |  | 5616 |  | 5626 |  | 5637 |  | 5647 |  | 5657 |  | 5667 |
|  | 5606 |  | 5616 |  | 5627 |  | 5637 |  | 5647 |  | 5657 |  | 5668 |
|  | 5606 |  | 5617 |  | 5627 |  | 5637 |  | 5647 |  | 5658 |  | 5668 |
|  | 5607 |  | 5617 |  | 5627 |  | 5637 |  | 5648 |  | 5658 |  | 5668 |
|  | 5607 |  | 5617 |  | 5627 |  | 5638 |  | 5648 |  | 5658 |  | 5668 |
|  | 5607 |  | 5617 |  | 5628 |  | 5638 |  | 5648 |  | 5658 |  | 5669 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} \text { n. } \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5669 | PPD | 5679 | PPD | 5689 | PPD | 5700 | PPD | 5710 | PPD | 5720 | PPD | 5730 |
|  | 5669 |  | 5679 |  | 5690 |  | 5700 |  | 5710 |  | 5720 |  | 5731 |
|  | 5669 |  | 5680 |  | 5690 |  | 5700 |  | 5710 |  | 5721 |  | 5731 |
|  | 5670 |  | 5680 |  | 5690 |  | 5700 |  | 5711 |  | 5721 |  | 5731 |
|  | 5670 |  | 5680 |  | 5690 |  | 5701 |  | 5711 |  | 5721 |  | 5731 |
|  | 5670 |  | 5680 |  | 5691 |  | 5701 |  | 5711 |  | 5721 |  | 5732 |
|  | 5670 |  | 5681 |  | 5691 |  | 5701 |  | 5711 |  | 5722 |  | 5732 |
|  | 5671 |  | 5681 |  | 5691 |  | 5701 |  | 5712 |  | 5722 |  | 5732 |
|  | 5671 |  | 5681 |  | 5691 |  | 5702 |  | 5712 |  | 5722 |  | 5732 |
|  | 5671 |  | 5681 |  | 5692 |  | 5702 |  | 5712 |  | 5722 |  | 5733 |
|  | 5671 |  | 5682 |  | 5692 |  | 5702 |  | 5712 |  | 5723 |  | 5733 |
|  | 5672 |  | 5682 |  | 5692 |  | 5702 |  | 5713 |  | 5723 |  | 5733 |
|  | 5672 |  | 5682 |  | 5692 |  | 5703 |  | 5713 |  | 5723 |  | 5733 |
|  | 5672 |  | 5682 |  | 5693 |  | 5703 |  | 5713 |  | 5723 |  | 5734 |
|  | 5672 |  | 5683 |  | 5693 |  | 5703 |  | 5713 |  | 5724 |  | 5734 |
|  | 5673 |  | 5683 |  | 5693 |  | 5703 |  | 5714 |  | 5724 |  | 5734 |
|  | 5673 |  | 5683 |  | 5693 |  | 5704 |  | 5714 |  | 5724 |  | 5734 |
|  | 5673 |  | 5683 |  | 5694 |  | 5704 |  | 5714 |  | 5724 |  | 5735 |
|  | 5673 |  | 5684 |  | 5694 |  | 5704 |  | 5714 |  | 5725 |  | 5735 |
|  | 5674 |  | 5684 |  | 5694 |  | 5704 |  | 5715 |  | 5725 |  | 5735 |
|  | 5674 |  | 5684 |  | 5694 |  | 5705 |  | 5715 |  | 5725 |  | 5735 |
|  | 5674 |  | 5684 |  | 5695 |  | 5705 |  | 5715 |  | 5725 |  | 5736 |
|  | 5674 |  | 5685 |  | 5695 |  | 5705 |  | 5715 |  | 5726 |  | 5736 |
|  | 5675 |  | 5685 |  | 5695 |  | 5705 |  | 5716 |  | 5726 |  | 5736 |
|  | 5675 |  | 5685 |  | 5695 |  | 5706 |  | 5716 |  | 5726 |  | 5736 |
|  | 5675 |  | 5685 |  | 5696 |  | 5706 |  | 5716 |  | 5726 |  | 5737 |
|  | 5675 |  | 5686 |  | 5696 |  | 5706 |  | 5716 |  | 5727 |  | 5737 |
|  | 5676 |  | 5686 |  | 5696 |  | 5706 |  | 5717 |  | 5727 |  | 5737 |
|  | 5676 |  | 5686 |  | 5696 |  | 5707 |  | 5717 |  | 5727 |  | 5737 |
|  | 5676 |  | 5686 |  | 5697 |  | 5707 |  | 5717 |  | 5727 |  | 5738 |
|  | 5676 |  | 5687 |  | 5697 |  | 5707 |  | 5717 |  | 5728 |  | 5738 |
|  | 5677 |  | 5687 |  | 5697 |  | 5707 |  | 5718 |  | 5728 |  | 5738 |
|  | 5677 |  | 5687 |  | 5697 |  | 5708 |  | 5718 |  | 5728 |  | 5738 |
|  | 5677 |  | 5687 |  | 5698 |  | 5708 |  | 5718 |  | 5728 |  | 5739 |
|  | 5677 |  | 5688 |  | 5698 |  | 5708 |  | 5718 |  | 5729 |  | 5739 |
|  | 5678 |  | 5688 |  | 5698 |  | 5708 |  | 5719 |  | 5729 |  | 5739 |
|  | 5678 |  | 5688 |  | 5698 |  | 5709 |  | 5719 |  | 5729 |  | 5739 |
|  | 5678 |  | 5688 |  | 5699 |  | 5709 |  | 5719 |  | 5729 |  | 5740 |
|  | 5678 |  | 5689 |  | 5699 |  | 5709 |  | 5719 |  | 5730 |  | 5740 |
|  | 5679 |  | 5689 |  | 5699 |  | 5709 |  | 5720 |  | 5730 |  | 5740 |
|  | 5679 |  | 5689 |  | 5699 |  | 5710 |  | 5720 |  | 5730 |  | 5740 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5741 | PPD | 5751 | PPD | 5761 | PPD | 5771 | PPD | 5782 | PPD | 5792 | PPD | 5802 |
|  | 5741 |  | 5751 |  | 5761 |  | 5772 |  | 5782 |  | 5792 |  | 5802 |
|  | 5741 |  | 5751 |  | 5762 |  | 5772 |  | 5782 |  | 5792 |  | 5803 |
|  | 5741 |  | 5752 |  | 5762 |  | 5772 |  | 5782 |  | 5793 |  | 5803 |
|  | 5742 |  | 5752 |  | 5762 |  | 5772 |  | 5783 |  | 5793 |  | 5803 |
|  | 5742 |  | 5752 |  | 5762 |  | 5773 |  | 5783 |  | 5793 |  | 5803 |
|  | 5742 |  | 5752 |  | 5763 |  | 5773 |  | 5783 |  | 5793 |  | 5804 |
|  | 5742 |  | 5753 |  | 5763 |  | 5773 |  | 5783 |  | 5794 |  | 5804 |
|  | 5743 |  | 5753 |  | 5763 |  | 5773 |  | 5784 |  | 5794 |  | 5804 |
|  | 5743 |  | 5753 |  | 5763 |  | 5774 |  | 5784 |  | 5794 |  | 5804 |
|  | 5743 |  | 5753 |  | 5764 |  | 5774 |  | 5784 |  | 5794 |  | 5805 |
|  | 5743 |  | 5754 |  | 5764 |  | 5774 |  | 5784 |  | 5795 |  | 5805 |
|  | 5744 |  | 5754 |  | 5764 |  | 5774 |  | 5785 |  | 5795 |  | 5805 |
|  | 5744 |  | 5754 |  | 5764 |  | 5775 |  | 5785 |  | 5795 |  | 5805 |
|  | 5744 |  | 5754 |  | 5765 |  | 5775 |  | 5785 |  | 5795 |  | 5806 |
|  | 5744 |  | 5755 |  | 5765 |  | 5775 |  | 5785 |  | 5796 |  | 5806 |
|  | 5745 |  | 5755 |  | 5765 |  | 5775 |  | 5786 |  | 5796 |  | 5806 |
|  | 5745 |  | 5755 |  | 5765 |  | 5776 |  | 5786 |  | 5796 |  | 5806 |
|  | 5745 |  | 5755 |  | 5766 |  | 5776 |  | 5786 |  | 5796 |  | 5807 |
|  | 5745 |  | 5756 |  | 5766 |  | 5776 |  | 5786 |  | 5797 |  | 5807 |
|  | 5746 |  | 5756 |  | 5766 |  | 5776 |  | 5787 |  | 5797 |  | 5807 |
|  | 5746 |  | 5756 |  | 5766 |  | 5777 |  | 5787 |  | 5797 |  | 5807 |
|  | 5746 |  | 5756 |  | 5767 |  | 5777 |  | 5787 |  | 5797 |  | 5808 |
|  | 5746 |  | 5757 |  | 5767 |  | 5777 |  | 5787 |  | 5798 |  | 5808 |
|  | 5747 |  | 5757 |  | 5767 |  | 5777 |  | 5788 |  | 5798 |  | 5808 |
|  | 5747 |  | 5757 |  | 5767 |  | 5778 |  | 5788 |  | 5798 |  | 5808 |
|  | 5747 |  | 5757 |  | 5768 |  | 5778 |  | 5788 |  | 5798 |  | 5809 |
|  | 5747 |  | 5758 |  | 5768 |  | 5778 |  | 5788 |  | 5799 |  | 5809 |
|  | 5748 |  | 5758 |  | 5768 |  | 5778 |  | 5789 |  | 5799 |  | 5809 |
|  | 5748 |  | 5758 |  | 5768 |  | 5779 |  | 5789 |  | 5799 |  | 5809 |
|  | 5748 |  | 5758 |  | 5769 |  | 5779 |  | 5789 |  | 5799 |  | 5810 |
|  | 5748 |  | 5759 |  | 5769 |  | 5779 |  | 5789 |  | 5800 |  | 5810 |
|  | 5749 |  | 5759 |  | 5769 |  | 5779 |  | 5790 |  | 5800 |  | 5810 |
|  | 5749 |  | 5759 |  | 5769 |  | 5780 |  | 5790 |  | 5800 |  | 5810 |
|  | 5749 |  | 5759 |  | 5770 |  | 5780 |  | 5790 |  | 5800 |  | 5811 |
|  | 5749 |  | 5760 |  | 5770 |  | 5780 |  | 5790 |  | 5801 |  | 5811 |
|  | 5750 |  | 5760 |  | 5770 |  | 5780 |  | 5791 |  | 5801 |  | 5811 |
|  | 5750 |  | 5760 |  | 5770 |  | 5781 |  | 5791 |  | 5801 |  | 5811 |
|  | 5750 |  | 5760 |  | 5771 |  | 5781 |  | 5791 |  | 5801 |  | 5812 |
|  | 5750 |  | 5761 |  | 5771 |  | 5781 |  | 5791 |  | 5802 |  | 5812 |
|  | 5751 |  | 5761 |  | 5771 |  | 5781 |  | 5792 |  | 5802 |  | 5812 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5812 | PPD | 5823 | PPD | 5833 | PPD | 5843 | PPD | 5853 | PPD | 5864 | PPD | 5874 |
|  | 5813 |  | 5823 |  | 5833 |  | 5843 |  | 5854 |  | 5864 |  | 5874 |
|  | 5813 |  | 5823 |  | 5833 |  | 5844 |  | 5854 |  | 5864 |  | 5874 |
|  | 5813 |  | 5823 |  | 5834 |  | 5844 |  | 5854 |  | 5864 |  | 5875 |
|  | 5813 |  | 5824 |  | 5834 |  | 5844 |  | 5854 |  | 5865 |  | 5875 |
|  | 5814 |  | 5824 |  | 5834 |  | 5844 |  | 5855 |  | 5865 |  | 5875 |
|  | 5814 |  | 5824 |  | 5834 |  | 5845 |  | 5855 |  | 5865 |  | 5875 |
|  | 5814 |  | 5824 |  | 5835 |  | 5845 |  | 5855 |  | 5865 |  | 5876 |
|  | 5814 |  | 5825 |  | 5835 |  | 5845 |  | 5855 |  | 5866 |  | 5876 |
|  | 5815 |  | 5825 |  | 5835 |  | 5845 |  | 5856 |  | 5866 |  | 5876 |
|  | 5815 |  | 5825 |  | 5835 |  | 5846 |  | 5856 |  | 5866 |  | 5876 |
|  | 5815 |  | 5825 |  | 5836 |  | 5846 |  | 5856 |  | 5866 |  | 5877 |
|  | 5815 |  | 5826 |  | 5836 |  | 5846 |  | 5856 |  | 5867 |  | 5877 |
|  | 5816 |  | 5826 |  | 5836 |  | 5846 |  | 5857 |  | 5867 |  | 5877 |
|  | 5816 |  | 5826 |  | 5836 |  | 5847 |  | 5857 |  | 5867 |  | 5877 |
|  | 5816 |  | 5826 |  | 5837 |  | 5847 |  | 5857 |  | 5867 |  | 5878 |
|  | 5816 |  | 5827 |  | 5837 |  | 5847 |  | 5857 |  | 5868 |  | 5878 |
|  | 5817 |  | 5827 |  | 5837 |  | 5847 |  | 5858 |  | 5868 |  | 5878 |
|  | 5817 |  | 5827 |  | 5837 |  | 5848 |  | 5858 |  | 5868 |  | 5878 |
|  | 5817 |  | 5827 |  | 5838 |  | 5848 |  | 5858 |  | 5868 |  | 5879 |
|  | 5817 |  | 5828 |  | 5838 |  | 5848 |  | 5858 |  | 5869 |  | 5879 |
|  | 5818 |  | 5828 |  | 5838 |  | 5848 |  | 5859 |  | 5869 |  | 5879 |
|  | 5818 |  | 5828 |  | 5838 |  | 5849 |  | 5859 |  | 5869 |  | 5879 |
|  | 5818 |  | 5828 |  | 5839 |  | 5849 |  | 5859 |  | 5869 |  | 5880 |
|  | 5818 |  | 5829 |  | 5839 |  | 5849 |  | 5859 |  | 5870 |  | 5880 |
|  | 5819 |  | 5829 |  | 5839 |  | 5849 |  | 5860 |  | 5870 |  | 5880 |
|  | 5819 |  | 5829 |  | 5839 |  | 5850 |  | 5860 |  | 5870 |  | 5880 |
|  | 5819 |  | 5829 |  | 5840 |  | 5850 |  | 5860 |  | 5870 |  | 5881 |
|  | 5819 |  | 5830 |  | 5840 |  | 5850 |  | 5860 |  | 5871 |  | 5881 |
|  | 5820 |  | 5830 |  | 5840 |  | 5850 |  | 5861 |  | 5871 |  | 5881 |
|  | 5820 |  | 5830 |  | 5840 |  | 5851 |  | 5861 |  | 5871 |  | 5881 |
|  | 5820 |  | 5830 |  | 5841 |  | 5851 |  | 5861 |  | 5871 |  | 5882 |
|  | 5820 |  | 5831 |  | 5841 |  | 5851 |  | 5861 |  | 5872 |  | 5882 |
|  | 5821 |  | 5831 |  | 5841 |  | 5851 |  | 5862 |  | 5872 |  | 5882 |
|  | 5821 |  | 5831 |  | 5841 |  | 5852 |  | 5862 |  | 5872 |  | 5882 |
|  | 5821 |  | 5831 |  | 5842 |  | 5852 |  | 5862 |  | 5872 |  | 5883 |
|  | 5821 |  | 5832 |  | 5842 |  | 5852 |  | 5862 |  | 5873 |  | 5883 |
|  | 5822 |  | 5832 |  | 5842 |  | 5852 |  | 5863 |  | 5873 |  | 5883 |
|  | 5822 |  | 5832 |  | 5842 |  | 5853 |  | 5863 |  | 5873 |  | 5883 |
|  | 5822 |  | 5832 |  | 5843 |  | 5853 |  | 5863 |  | 5873 |  | 5884 |
|  | 5822 |  | 5833 |  | 5843 |  | 5853 |  | 5863 |  | 5874 |  | 5884 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-PreChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5884 | PPD | 5894 | PPD | 5905 | PPD | 5915 | PPD | 5925 | PPD | 5935 | PPD | 5946 |
|  | 5884 |  | 5895 |  | 5905 |  | 5915 |  | 5925 |  | 5936 |  | 5946 |
|  | 5885 |  | 5895 |  | 5905 |  | 5915 |  | 5926 |  | 5936 |  | 5946 |
|  | 5885 |  | 5895 |  | 5905 |  | 5916 |  | 5926 |  | 5936 |  | 5946 |
|  | 5885 |  | 5895 |  | 5906 |  | 5916 |  | 5926 |  | 5936 |  | 5947 |
|  | 5885 |  | 5896 |  | 5906 |  | 5916 |  | 5926 |  | 5937 |  | 5947 |
|  | 5886 |  | 5896 |  | 5906 |  | 5916 |  | 5927 |  | 5937 |  | 5947 |
|  | 5886 |  | 5896 |  | 5906 |  | 5917 |  | 5927 |  | 5937 |  | 5947 |
|  | 5886 |  | 5896 |  | 5907 |  | 5917 |  | 5927 |  | 5937 |  | 5948 |
|  | 5886 |  | 5897 |  | 5907 |  | 5917 |  | 5927 |  | 5938 |  | 5948 |
|  | 5887 |  | 5897 |  | 5907 |  | 5917 |  | 5928 |  | 5938 |  | 5948 |
|  | 5887 |  | 5897 |  | 5907 |  | 5918 |  | 5928 |  | 5938 |  | 5948 |
|  | 5887 |  | 5897 |  | 5908 |  | 5918 |  | 5928 |  | 5938 |  | 5949 |
|  | 5887 |  | 5898 |  | 5908 |  | 5918 |  | 5928 |  | 5939 |  | 5949 |
|  | 5888 |  | 5898 |  | 5908 |  | 5918 |  | 5929 |  | 5939 |  | 5949 |
|  | 5888 |  | 5898 |  | 5908 |  | 5919 |  | 5929 |  | 5939 |  | 5949 |
|  | 5888 |  | 5898 |  | 5909 |  | 5919 |  | 5929 |  | 5939 |  | 5950 |
|  | 5888 |  | 5899 |  | 5909 |  | 5919 |  | 5929 |  | 5940 |  | 5950 |
|  | 5889 |  | 5899 |  | 5909 |  | 5919 |  | 5930 |  | 5940 |  | 5950 |
|  | 5889 |  | 5899 |  | 5909 |  | 5920 |  | 5930 |  | 5940 |  | 5950 |
|  | 5889 |  | 5899 |  | 5910 |  | 5920 |  | 5930 |  | 5940 |  | 5951 |
|  | 5889 |  | 5900 |  | 5910 |  | 5920 |  | 5930 |  | 5941 |  | 5951 |
|  | 5890 |  | 5900 |  | 5910 |  | 5920 |  | 5931 |  | 5941 |  | 5951 |
|  | 5890 |  | 5900 |  | 5910 |  | 5921 |  | 5931 |  | 5941 |  | 5951 |
|  | 5890 |  | 5900 |  | 5911 |  | 5921 |  | 5931 |  | 5941 |  | 5952 |
|  | 5890 |  | 5901 |  | 5911 |  | 5921 |  | 5931 |  | 5942 |  | 5952 |
|  | 5891 |  | 5901 |  | 5911 |  | 5921 |  | 5932 |  | 5942 |  | 5952 |
|  | 5891 |  | 5901 |  | 5911 |  | 5922 |  | 5932 |  | 5942 |  | 5952 |
|  | 5891 |  | 5901 |  | 5912 |  | 5922 |  | 5932 |  | 5942 |  | 5953 |
|  | 5891 |  | 5902 |  | 5912 |  | 5922 |  | 5932 |  | 5943 |  | 5953 |
|  | 5892 |  | 5902 |  | 5912 |  | 5922 |  | 5933 |  | 5943 |  | 5953 |
|  | 5892 |  | 5902 |  | 5912 |  | 5923 |  | 5933 |  | 5943 |  | 5953 |
|  | 5892 |  | 5902 |  | 5913 |  | 5923 |  | 5933 |  | 5943 |  | 5954 |
|  | 5892 |  | 5903 |  | 5913 |  | 5923 |  | 5933 |  | 5944 |  | 5954 |
|  | 5893 |  | 5903 |  | 5913 |  | 5923 |  | 5934 |  | 5944 |  | 5954 |
|  | 5893 |  | 5903 |  | 5913 |  | 5924 |  | 5934 |  | 5944 |  | 5954 |
|  | 5893 |  | 5903 |  | 5914 |  | 5924 |  | 5934 |  | 5944 |  | 5955 |
|  | 5893 |  | 5904 |  | 5914 |  | 5924 |  | 5934 |  | 5945 |  | 5955 |
|  | 5894 |  | 5904 |  | 5914 |  | 5924 |  | 5935 |  | 5945 |  | 5955 |
|  | 5894 |  | 5904 |  | 5914 |  | 5925 |  | 5935 |  | 5945 |  | 5955 |
|  | 5894 |  | 5904 |  | 5915 |  | 5925 |  | 5935 |  | 5945 |  | 5956 |



SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{gathered} \text { Trt. Bl. } \\ \text { No nb } \end{gathered}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1 | PPD | 42 | PPD | 83 | PPD | 124 | PPD | 165 | PPD | 206 | PPD | 247 |
|  | 2 |  | 43 |  | 84 |  | 125 |  | 166 |  | 207 |  | 248 |
|  | 3 |  | 44 |  | 85 |  | 126 |  | 167 |  | 208 |  | 249 |
|  | 4 |  | 45 |  | 86 |  | 127 |  | 168 |  | 209 |  | 250 |
|  | 5 |  | 46 |  | 87 |  | 128 |  | 169 |  | 210 |  | 251 |
|  | 6 |  | 47 |  | 88 |  | 129 |  | 170 |  | 211 |  | 252 |
|  | 7 |  | 48 |  | 89 |  | 130 |  | 171 |  | 212 |  | 253 |
|  | 8 |  | 49 |  | 90 |  | 131 |  | 172 |  | 213 |  | 254 |
|  | 9 |  | 50 |  | 91 |  | 132 |  | 173 |  | 214 |  | 255 |
|  | 10 |  | 51 |  | 92 |  | 133 |  | 174 |  | 215 |  | 256 |
|  | 11 |  | 52 |  | 93 |  | 134 |  | 175 |  | 216 |  | 257 |
|  | 12 |  | 53 |  | 94 |  | 135 |  | 176 |  | 217 |  | 258 |
|  | 13 |  | 54 |  | 95 |  | 136 |  | 177 |  | 218 |  | 259 |
|  | 14 |  | 55 |  | 96 |  | 137 |  | 178 |  | 219 |  | 260 |
|  | 15 |  | 56 |  | 97 |  | 138 |  | 179 |  | 220 |  | 261 |
|  | 16 |  | 57 |  | 98 |  | 139 |  | 180 |  | 221 |  | 262 |
|  | 17 |  | 58 |  | 99 |  | 140 |  | 181 |  | 222 |  | 263 |
|  | 18 |  | 59 |  | 100 |  | 141 |  | 182 |  | 223 |  | 264 |
|  | 19 |  | 60 |  | 101 |  | 142 |  | 183 |  | 224 |  | 265 |
|  | 20 |  | 61 |  | 102 |  | 143 |  | 184 |  | 225 |  | 266 |
|  | 21 |  | 62 |  | 103 |  | 144 |  | 185 |  | 226 |  | 267 |
|  | 22 |  | 63 |  | 104 |  | 145 |  | 186 |  | 227 |  | 268 |
|  | 23 |  | 64 |  | 105 |  | 146 |  | 187 |  | 228 |  | 269 |
|  | 24 |  | 65 |  | 106 |  | 147 |  | 188 |  | 229 |  | 270 |
|  | 25 |  | 66 |  | 107 |  | 148 |  | 189 |  | 230 |  | 271 |
|  | 26 |  | 67 |  | 108 |  | 149 |  | 190 |  | 231 |  | 272 |
|  | 27 |  | 68 |  | 109 |  | 150 |  | 191 |  | 232 |  | 273 |
|  | 28 |  | 69 |  | 110 |  | 151 |  | 192 |  | 233 |  | 274 |
|  | 29 |  | 70 |  | 111 |  | 152 |  | 193 |  | 234 |  | 275 |
|  | 30 |  | 71 |  | 112 |  | 153 |  | 194 |  | 235 |  | 276 |
|  | 31 |  | 72 |  | 113 |  | 154 |  | 195 |  | 236 |  | 277 |
|  | 32 |  | 73 |  | 114 |  | 155 |  | 196 |  | 237 |  | 278 |
|  | 33 |  | 74 |  | 115 |  | 156 |  | 197 |  | 238 |  | 279 |
|  | 34 |  | 75 |  | 116 |  | 157 |  | 198 |  | 239 |  | 280 |
|  | 35 |  | 76 |  | 117 |  | 158 |  | 199 |  | 240 |  | 281 |
|  | 36 |  | 77 |  | 118 |  | 159 |  | 200 |  | 241 |  | 282 |
|  | 37 |  | 78 |  | 119 |  | 160 |  | 201 |  | 242 |  | 283 |
|  | 38 |  | 79 |  | 120 |  | 161 |  | 202 |  | 243 |  | 284 |
|  | 39 |  | 80 |  | 121 |  | 162 |  | 203 |  | 244 |  | 285 |
|  | 40 |  | 81 |  | 122 |  | 163 |  | 204 |  | 245 |  | 286 |
|  | 41 |  | 82 |  | 123 |  | 164 |  | 205 |  | 246 |  | 287 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No n. } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 288 | PPD | 329 | PPD | 370 | PPD | 411 | PPD | 452 | PPD | 493 | PPD | 534 |
|  | 289 |  | 330 |  | 371 |  | 412 |  | 453 |  | 494 |  | 535 |
|  | 290 |  | 331 |  | 372 |  | 413 |  | 454 |  | 495 |  | 536 |
|  | 291 |  | 332 |  | 373 |  | 414 |  | 455 |  | 496 |  | 537 |
|  | 292 |  | 333 |  | 374 |  | 415 |  | 456 |  | 497 |  | 538 |
|  | 293 |  | 334 |  | 375 |  | 416 |  | 457 |  | 498 |  | 539 |
|  | 294 |  | 335 |  | 376 |  | 417 |  | 458 |  | 499 |  | 540 |
|  | 295 |  | 336 |  | 377 |  | 418 |  | 459 |  | 500 |  | 541 |
|  | 296 |  | 337 |  | 378 |  | 419 |  | 460 |  | 501 |  | 542 |
|  | 297 |  | 338 |  | 379 |  | 420 |  | 461 |  | 502 |  | 543 |
|  | 298 |  | 339 |  | 380 |  | 421 |  | 462 |  | 503 |  | 544 |
|  | 299 |  | 340 |  | 381 |  | 422 |  | 463 |  | 504 |  | 545 |
|  | 300 |  | 341 |  | 382 |  | 423 |  | 464 |  | 505 |  | 546 |
|  | 301 |  | 342 |  | 383 |  | 424 |  | 465 |  | 506 |  | 547 |
|  | 302 |  | 343 |  | 384 |  | 425 |  | 466 |  | 507 |  | 548 |
|  | 303 |  | 344 |  | 385 |  | 426 |  | 467 |  | 508 |  | 549 |
|  | 304 |  | 345 |  | 386 |  | 427 |  | 468 |  | 509 |  | 550 |
|  | 305 |  | 346 |  | 387 |  | 428 |  | 469 |  | 510 |  | 551 |
|  | 306 |  | 347 |  | 388 |  | 429 |  | 470 |  | 511 |  | 552 |
|  | 307 |  | 348 |  | 389 |  | 430 |  | 471 |  | 512 |  | 553 |
|  | 308 |  | 349 |  | 390 |  | 431 |  | 472 |  | 513 |  | 554 |
|  | 309 |  | 350 |  | 391 |  | 432 |  | 473 |  | 514 |  | 555 |
|  | 310 |  | 351 |  | 392 |  | 433 |  | 474 |  | 515 |  | 556 |
|  | 311 |  | 352 |  | 393 |  | 434 |  | 475 |  | 516 |  | 557 |
|  | 312 |  | 353 |  | 394 |  | 435 |  | 476 |  | 517 |  | 558 |
|  | 313 |  | 354 |  | 395 |  | 436 |  | 477 |  | 518 |  | 559 |
|  | 314 |  | 355 |  | 396 |  | 437 |  | 478 |  | 519 |  | 560 |
|  | 315 |  | 356 |  | 397 |  | 438 |  | 479 |  | 520 |  | 561 |
|  | 316 |  | 357 |  | 398 |  | 439 |  | 480 |  | 521 |  | 562 |
|  | 317 |  | 358 |  | 399 |  | 440 |  | 481 |  | 522 |  | 563 |
|  | 318 |  | 359 |  | 400 |  | 441 |  | 482 |  | 523 |  | 564 |
|  | 319 |  | 360 |  | 401 |  | 442 |  | 483 |  | 524 |  | 565 |
|  | 320 |  | 361 |  | 402 |  | 443 |  | 484 |  | 525 |  | 566 |
|  | 321 |  | 362 |  | 403 |  | 444 |  | 485 |  | 526 |  | 567 |
|  | 322 |  | 363 |  | 404 |  | 445 |  | 486 |  | 527 |  | 568 |
|  | 323 |  | 364 |  | 405 |  | 446 |  | 487 |  | 528 |  | 569 |
|  | 324 |  | 365 |  | 406 |  | 447 |  | 488 |  | 529 |  | 570 |
|  | 325 |  | 366 |  | 407 |  | 448 |  | 489 |  | 530 |  | 571 |
|  | 326 |  | 367 |  | 408 |  | 449 |  | 490 |  | 531 |  | 572 |
|  | 327 |  | 368 |  | 409 |  | 450 |  | 491 |  | 532 |  | 573 |
|  | 328 |  | 369 |  | 410 |  | 451 |  | 492 |  | 533 |  | 574 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| $\begin{array}{r} \text { Trt } \\ \mathrm{N} \mathbf{d} \end{array}$ | Bl nb | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 575 | PPD | 616 | PPD | 657 | PPD | 698 | PPD | 739 | PPD | 780 | PPD | 821 |
|  | 576 |  | 617 |  | 658 |  | 699 |  | 740 |  | 781 |  | 822 |
|  | 577 |  | 618 |  | 659 |  | 700 |  | 741 |  | 782 |  | 823 |
|  | 578 |  | 619 |  | 660 |  | 701 |  | 742 |  | 783 |  | 824 |
|  | 579 |  | 620 |  | 661 |  | 702 |  | 743 |  | 784 |  | 825 |
|  | 580 |  | 621 |  | 662 |  | 703 |  | 744 |  | 785 |  | 826 |
|  | 581 |  | 622 |  | 663 |  | 704 |  | 745 |  | 786 |  | 827 |
|  | 582 |  | 623 |  | 664 |  | 705 |  | 746 |  | 787 |  | 828 |
|  | 583 |  | 624 |  | 665 |  | 706 |  | 747 |  | 788 |  | 829 |
|  | 584 |  | 625 |  | 666 |  | 707 |  | 748 |  | 789 |  | 830 |
|  | 585 |  | 626 |  | 667 |  | 708 |  | 749 |  | 790 |  | 831 |
|  | 586 |  | 627 |  | 668 |  | 709 |  | 750 |  | 791 |  | 832 |
|  | 587 |  | 628 |  | 669 |  | 710 |  | 751 |  | 792 |  | 833 |
|  | 588 |  | 629 |  | 670 |  | 711 |  | 752 |  | 793 |  | 834 |
|  | 589 |  | 630 |  | 671 |  | 712 |  | 753 |  | 794 |  | 835 |
|  | 590 |  | 631 |  | 672 |  | 713 |  | 754 |  | 795 |  | 836 |
|  | 591 |  | 632 |  | 673 |  | 714 |  | 755 |  | 796 |  | 837 |
|  | 592 |  | 633 |  | 674 |  | 715 |  | 756 |  | 797 |  | 838 |
|  | 593 |  | 634 |  | 675 |  | 716 |  | 757 |  | 798 |  | 839 |
|  | 594 |  | 635 |  | 676 |  | 717 |  | 758 |  | 799 |  | 840 |
|  | 595 |  | 636 |  | 677 |  | 718 |  | 759 |  | 800 |  | 841 |
|  | 596 |  | 637 |  | 678 |  | 719 |  | 760 |  | 801 |  | 842 |
|  | 597 |  | 638 |  | 679 |  | 720 |  | 761 |  | 802 |  | 843 |
|  | 598 |  | 639 |  | 680 |  | 721 |  | 762 |  | 803 |  | 844 |
|  | 599 |  | 640 |  | 681 |  | 722 |  | 763 |  | 804 |  | 845 |
|  | 600 |  | 641 |  | 682 |  | 723 |  | 764 |  | 805 |  | 846 |
|  | 601 |  | 642 |  | 683 |  | 724 |  | 765 |  | 806 |  | 847 |
|  | 602 |  | 643 |  | 684 |  | 725 |  | 766 |  | 807 |  | 848 |
|  | 603 |  | 644 |  | 685 |  | 726 |  | 767 |  | 808 |  | 849 |
|  | 604 |  | 645 |  | 686 |  | 727 |  | 768 |  | 809 |  | 850 |
|  | 605 |  | 646 |  | 687 |  | 728 |  | 769 |  | 810 |  | 851 |
|  | 606 |  | 647 |  | 688 |  | 729 |  | 770 |  | 811 |  | 852 |
|  | 607 |  | 648 |  | 689 |  | 730 |  | 771 |  | 812 |  | 853 |
|  | 608 |  | 649 |  | 690 |  | 731 |  | 772 |  | 813 |  | 854 |
|  | 609 |  | 650 |  | 691 |  | 732 |  | 773 |  | 814 |  | 855 |
|  | 610 |  | 651 |  | 692 |  | 733 |  | 774 |  | 815 |  | 856 |
|  | 611 |  | 652 |  | 693 |  | 734 |  | 775 |  | 816 |  | 857 |
|  | 612 |  | 653 |  | 694 |  | 735 |  | 776 |  | 817 |  | 858 |
|  | 613 |  | 654 |  | 695 |  | 736 |  | 777 |  | 818 |  | 859 |
|  | 614 |  | 655 |  | 696 |  | 737 |  | 778 |  | 819 |  | 860 |
|  | 615 |  | 656 |  | 697 |  | 738 |  | 779 |  | 820 |  | 861 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  |  |  | Bl nb |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 862 | PPD | 903 | PPD | 944 | PPD | 985 | PPD | 1026 | PPD | 1067 | PPD | 1108 |
|  | 863 |  | 904 |  | 945 |  | 986 |  | 1027 |  | 1068 |  | 1109 |
|  | 864 |  | 905 |  | 946 |  | 987 |  | 1028 |  | 1069 |  | 1110 |
|  | 865 |  | 906 |  | 947 |  | 988 |  | 1029 |  | 1070 |  | 1111 |
|  | 866 |  | 907 |  | 948 |  | 989 |  | 1030 |  | 1071 |  | 1112 |
|  | 867 |  | 908 |  | 949 |  | 990 |  | 1031 |  | 1072 |  | 1113 |
|  | 868 |  | 909 |  | 950 |  | 991 |  | 1032 |  | 1073 |  | 1114 |
|  | 869 |  | 910 |  | 951 |  | 992 |  | 1033 |  | 1074 |  | 1115 |
|  | 870 |  | 911 |  | 952 |  | 993 |  | 1034 |  | 1075 |  | 1116 |
|  | 871 |  | 912 |  | 953 |  | 994 |  | 1035 |  | 1076 |  | 1117 |
|  | 872 |  | 913 |  | 954 |  | 995 |  | 1036 |  | 1077 |  | 1118 |
|  | 873 |  | 914 |  | 955 |  | 996 |  | 1037 |  | 1078 |  | 1119 |
|  | 874 |  | 915 |  | 956 |  | 997 |  | 1038 |  | 1079 |  | 1120 |
|  | 875 |  | 916 |  | 957 |  | 998 |  | 1039 |  | 1080 |  | 1121 |
|  | 876 |  | 917 |  | 958 |  | 999 |  | 1040 |  | 1081 |  | 1122 |
|  | 877 |  | 918 |  | 959 |  | 1000 |  | 1041 |  | 1082 |  | 1123 |
|  | 878 |  | 919 |  | 960 |  | 1001 |  | 1042 |  | 1083 |  | 1124 |
|  | 879 |  | 920 |  | 961 |  | 1002 |  | 1043 |  | 1084 |  | 1125 |
|  | 880 |  | 921 |  | 962 |  | 1003 |  | 1044 |  | 1085 |  | 1126 |
|  | 881 |  | 922 |  | 963 |  | 1004 |  | 1045 |  | 1086 |  | 1127 |
|  | 882 |  | 923 |  | 964 |  | 1005 |  | 1046 |  | 1087 |  | 1128 |
|  | 883 |  | 924 |  | 965 |  | 1006 |  | 1047 |  | 1088 |  | 1129 |
|  | 884 |  | 925 |  | 966 |  | 1007 |  | 1048 |  | 1089 |  | 1130 |
|  | 885 |  | 926 |  | 967 |  | 1008 |  | 1049 |  | 1090 |  | 1131 |
|  | 886 |  | 927 |  | 968 |  | 1009 |  | 1050 |  | 1091 |  | 1132 |
|  | 887 |  | 928 |  | 969 |  | 1010 |  | 1051 |  | 1092 |  | 1133 |
|  | 888 |  | 929 |  | 970 |  | 1011 |  | 1052 |  | 1093 |  | 1134 |
|  | 889 |  | 930 |  | 971 |  | 1012 |  | 1053 |  | 1094 |  | 1135 |
|  | 890 |  | 931 |  | 972 |  | 1013 |  | 1054 |  | 1095 |  | 1136 |
|  | 891 |  | 932 |  | 973 |  | 1014 |  | 1055 |  | 1096 |  | 1137 |
|  | 892 |  | 933 |  | 974 |  | 1015 |  | 1056 |  | 1097 |  | 1138 |
|  | 893 |  | 934 |  | 975 |  | 1016 |  | 1057 |  | 1098 |  | 1139 |
|  | 894 |  | 935 |  | 976 |  | 1017 |  | 1058 |  | 1099 |  | 1140 |
|  | 895 |  | 936 |  | 977 |  | 1018 |  | 1059 |  | 1100 |  | 1141 |
|  | 896 |  | 937 |  | 978 |  | 1019 |  | 1060 |  | 1101 |  | 1142 |
|  | 897 |  | 938 |  | 979 |  | 1020 |  | 1061 |  | 1102 |  | 1143 |
|  | 898 |  | 939 |  | 980 |  | 1021 |  | 1062 |  | 1103 |  | 1144 |
|  | 899 |  | 940 |  | 981 |  | 1022 |  | 1063 |  | 1104 |  | 1145 |
|  | 900 |  | 941 |  | 982 |  | 1023 |  | 1064 |  | 1105 |  | 1146 |
|  | 901 |  | 942 |  | 983 |  | 1024 |  | 1065 |  | 1106 |  | 1147 |
|  | 902 |  | 943 |  | 984 |  | 1025 |  | 1066 |  | 1107 |  | 1148 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1149 | PPD | 1190 | PPD | 1231 | PPD | 1272 | PPD | 1313 | PPD | 1354 | PPD | 1395 |
|  | 1150 |  | 1191 |  | 1232 |  | 1273 |  | 1314 |  | 1355 |  | 1396 |
|  | 1151 |  | 1192 |  | 1233 |  | 1274 |  | 1315 |  | 1356 |  | 1397 |
|  | 1152 |  | 1193 |  | 1234 |  | 1275 |  | 1316 |  | 1357 |  | 1398 |
|  | 1153 |  | 1194 |  | 1235 |  | 1276 |  | 1317 |  | 1358 |  | 1399 |
|  | 1154 |  | 1195 |  | 1236 |  | 1277 |  | 1318 |  | 1359 |  | 1400 |
|  | 1155 |  | 1196 |  | 1237 |  | 1278 |  | 1319 |  | 1360 |  | 1401 |
|  | 1156 |  | 1197 |  | 1238 |  | 1279 |  | 1320 |  | 1361 |  | 1402 |
|  | 1157 |  | 1198 |  | 1239 |  | 1280 |  | 1321 |  | 1362 |  | 1403 |
|  | 1158 |  | 1199 |  | 1240 |  | 1281 |  | 1322 |  | 1363 |  | 1404 |
|  | 1159 |  | 1200 |  | 1241 |  | 1282 |  | 1323 |  | 1364 |  | 1405 |
|  | 1160 |  | 1201 |  | 1242 |  | 1283 |  | 1324 |  | 1365 |  | 1406 |
|  | 1161 |  | 1202 |  | 1243 |  | 1284 |  | 1325 |  | 1366 |  | 1407 |
|  | 1162 |  | 1203 |  | 1244 |  | 1285 |  | 1326 |  | 1367 |  | 1408 |
|  | 1163 |  | 1204 |  | 1245 |  | 1286 |  | 1327 |  | 1368 |  | 1409 |
|  | 1164 |  | 1205 |  | 1246 |  | 1287 |  | 1328 |  | 1369 |  | 1410 |
|  | 1165 |  | 1206 |  | 1247 |  | 1288 |  | 1329 |  | 1370 |  | 1411 |
|  | 1166 |  | 1207 |  | 1248 |  | 1289 |  | 1330 |  | 1371 |  | 1412 |
|  | 1167 |  | 1208 |  | 1249 |  | 1290 |  | 1331 |  | 1372 |  | 1413 |
|  | 1168 |  | 1209 |  | 1250 |  | 1291 |  | 1332 |  | 1373 |  | 1414 |
|  | 1169 |  | 1210 |  | 1251 |  | 1292 |  | 1333 |  | 1374 |  | 1415 |
|  | 1170 |  | 1211 |  | 1252 |  | 1293 |  | 1334 |  | 1375 |  | 1416 |
|  | 1171 |  | 1212 |  | 1253 |  | 1294 |  | 1335 |  | 1376 |  | 1417 |
|  | 1172 |  | 1213 |  | 1254 |  | 1295 |  | 1336 |  | 1377 |  | 1418 |
|  | 1173 |  | 1214 |  | 1255 |  | 1296 |  | 1337 |  | 1378 |  | 1419 |
|  | 1174 |  | 1215 |  | 1256 |  | 1297 |  | 1338 |  | 1379 |  | 1420 |
|  | 1175 |  | 1216 |  | 1257 |  | 1298 |  | 1339 |  | 1380 |  | 1421 |
|  | 1176 |  | 1217 |  | 1258 |  | 1299 |  | 1340 |  | 1381 |  | 1422 |
|  | 1177 |  | 1218 |  | 1259 |  | 1300 |  | 1341 |  | 1382 |  | 1423 |
|  | 1178 |  | 1219 |  | 1260 |  | 1301 |  | 1342 |  | 1383 |  | 1424 |
|  | 1179 |  | 1220 |  | 1261 |  | 1302 |  | 1343 |  | 1384 |  | 1425 |
|  | 1180 |  | 1221 |  | 1262 |  | 1303 |  | 1344 |  | 1385 |  | 1426 |
|  | 1181 |  | 1222 |  | 1263 |  | 1304 |  | 1345 |  | 1386 |  | 1427 |
|  | 1182 |  | 1223 |  | 1264 |  | 1305 |  | 1346 |  | 1387 |  | 1428 |
|  | 1183 |  | 1224 |  | 1265 |  | 1306 |  | 1347 |  | 1388 |  | 1429 |
|  | 1184 |  | 1225 |  | 1266 |  | 1307 |  | 1348 |  | 1389 |  | 1430 |
|  | 1185 |  | 1226 |  | 1267 |  | 1308 |  | 1349 |  | 1390 |  | 1431 |
|  | 1186 |  | 1227 |  | 1268 |  | 1309 |  | 1350 |  | 1391 |  | 1432 |
|  | 1187 |  | 1228 |  | 1269 |  | 1310 |  | 1351 |  | 1392 |  | 1433 |
|  | 1188 |  | 1229 |  | 1270 |  | 1311 |  | 1352 |  | 1393 |  | 1434 |
|  | 1189 |  | 1230 |  | 1271 |  | 1312 |  | 1353 |  | 1394 |  | 1435 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  |  |  | Bl nb |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1436 | PPD | 1477 | PPD | 1518 | PPD | 1559 | PPD | 1600 | PPD | 1641 | PPD | 1682 |
|  | 1437 |  | 1478 |  | 1519 |  | 1560 |  | 1601 |  | 1642 |  | 1683 |
|  | 1438 |  | 1479 |  | 1520 |  | 1561 |  | 1602 |  | 1643 |  | 1684 |
|  | 1439 |  | 1480 |  | 1521 |  | 1562 |  | 1603 |  | 1644 |  | 1685 |
|  | 1440 |  | 1481 |  | 1522 |  | 1563 |  | 1604 |  | 1645 |  | 1686 |
|  | 1441 |  | 1482 |  | 1523 |  | 1564 |  | 1605 |  | 1646 |  | 1687 |
|  | 1442 |  | 1483 |  | 1524 |  | 1565 |  | 1606 |  | 1647 |  | 1688 |
|  | 1443 |  | 1484 |  | 1525 |  | 1566 |  | 1607 |  | 1648 |  | 1689 |
|  | 1444 |  | 1485 |  | 1526 |  | 1567 |  | 1608 |  | 1649 |  | 1690 |
|  | 1445 |  | 1486 |  | 1527 |  | 1568 |  | 1609 |  | 1650 |  | 1691 |
|  | 1446 |  | 1487 |  | 1528 |  | 1569 |  | 1610 |  | 1651 |  | 1692 |
|  | 1447 |  | 1488 |  | 1529 |  | 1570 |  | 1611 |  | 1652 |  | 1693 |
|  | 1448 |  | 1489 |  | 1530 |  | 1571 |  | 1612 |  | 1653 |  | 1694 |
|  | 1449 |  | 1490 |  | 1531 |  | 1572 |  | 1613 |  | 1654 |  | 1695 |
|  | 1450 |  | 1491 |  | 1532 |  | 1573 |  | 1614 |  | 1655 |  | 1696 |
|  | 1451 |  | 1492 |  | 1533 |  | 1574 |  | 1615 |  | 1656 |  | 1697 |
|  | 1452 |  | 1493 |  | 1534 |  | 1575 |  | 1616 |  | 1657 |  | 1698 |
|  | 1453 |  | 1494 |  | 1535 |  | 1576 |  | 1617 |  | 1658 |  | 1699 |
|  | 1454 |  | 1495 |  | 1536 |  | 1577 |  | 1618 |  | 1659 |  | 1700 |
|  | 1455 |  | 1496 |  | 1537 |  | 1578 |  | 1619 |  | 1660 |  | 1701 |
|  | 1456 |  | 1497 |  | 1538 |  | 1579 |  | 1620 |  | 1661 |  | 1702 |
|  | 1457 |  | 1498 |  | 1539 |  | 1580 |  | 1621 |  | 1662 |  | 1703 |
|  | 1458 |  | 1499 |  | 1540 |  | 1581 |  | 1622 |  | 1663 |  | 1704 |
|  | 1459 |  | 1500 |  | 1541 |  | 1582 |  | 1623 |  | 1664 |  | 1705 |
|  | 1460 |  | 1501 |  | 1542 |  | 1583 |  | 1624 |  | 1665 |  | 1706 |
|  | 1461 |  | 1502 |  | 1543 |  | 1584 |  | 1625 |  | 1666 |  | 1707 |
|  | 1462 |  | 1503 |  | 1544 |  | 1585 |  | 1626 |  | 1667 |  | 1708 |
|  | 1463 |  | 1504 |  | 1545 |  | 1586 |  | 1627 |  | 1668 |  | 1709 |
|  | 1464 |  | 1505 |  | 1546 |  | 1587 |  | 1628 |  | 1669 |  | 1710 |
|  | 1465 |  | 1506 |  | 1547 |  | 1588 |  | 1629 |  | 1670 |  | 1711 |
|  | 1466 |  | 1507 |  | 1548 |  | 1589 |  | 1630 |  | 1671 |  | 1712 |
|  | 1467 |  | 1508 |  | 1549 |  | 1590 |  | 1631 |  | 1672 |  | 1713 |
|  | 1468 |  | 1509 |  | 1550 |  | 1591 |  | 1632 |  | 1673 |  | 1714 |
|  | 1469 |  | 1510 |  | 1551 |  | 1592 |  | 1633 |  | 1674 |  | 1715 |
|  | 1470 |  | 1511 |  | 1552 |  | 1593 |  | 1634 |  | 1675 |  | 1716 |
|  | 1471 |  | 1512 |  | 1553 |  | 1594 |  | 1635 |  | 1676 |  | 1717 |
|  | 1472 |  | 1513 |  | 1554 |  | 1595 |  | 1636 |  | 1677 |  | 1718 |
|  | 1473 |  | 1514 |  | 1555 |  | 1596 |  | 1637 |  | 1678 |  | 1719 |
|  | 1474 |  | 1515 |  | 1556 |  | 1597 |  | 1638 |  | 1679 |  | 1720 |
|  | 1475 |  | 1516 |  | 1557 |  | 1598 |  | 1639 |  | 1680 |  | 1721 |
|  | 1476 |  | 1517 |  | 1558 |  | 1599 |  | 1640 |  | 1681 |  | 1722 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  | Bl nb |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1723 | PPD | 1764 | PPD | 1805 | PPD | 1846 | PPD | 1887 | PPD | 1928 | PPD | 1969 |
|  | 1724 |  | 1765 |  | 1806 |  | 1847 |  | 1888 |  | 1929 |  | 1970 |
|  | 1725 |  | 1766 |  | 1807 |  | 1848 |  | 1889 |  | 1930 |  | 1971 |
|  | 1726 |  | 1767 |  | 1808 |  | 1849 |  | 1890 |  | 1931 |  | 1972 |
|  | 1727 |  | 1768 |  | 1809 |  | 1850 |  | 1891 |  | 1932 |  | 1973 |
|  | 1728 |  | 1769 |  | 1810 |  | 1851 |  | 1892 |  | 1933 |  | 1974 |
|  | 1729 |  | 1770 |  | 1811 |  | 1852 |  | 1893 |  | 1934 |  | 1975 |
|  | 1730 |  | 1771 |  | 1812 |  | 1853 |  | 1894 |  | 1935 |  | 1976 |
|  | 1731 |  | 1772 |  | 1813 |  | 1854 |  | 1895 |  | 1936 |  | 1977 |
|  | 1732 |  | 1773 |  | 1814 |  | 1855 |  | 1896 |  | 1937 |  | 1978 |
|  | 1733 |  | 1774 |  | 1815 |  | 1856 |  | 1897 |  | 1938 |  | 1979 |
|  | 1734 |  | 1775 |  | 1816 |  | 1857 |  | 1898 |  | 1939 |  | 1980 |
|  | 1735 |  | 1776 |  | 1817 |  | 1858 |  | 1899 |  | 1940 |  | 1981 |
|  | 1736 |  | 1777 |  | 1818 |  | 1859 |  | 1900 |  | 1941 |  | 1982 |
|  | 1737 |  | 1778 |  | 1819 |  | 1860 |  | 1901 |  | 1942 |  | 1983 |
|  | 1738 |  | 1779 |  | 1820 |  | 1861 |  | 1902 |  | 1943 |  | 1984 |
|  | 1739 |  | 1780 |  | 1821 |  | 1862 |  | 1903 |  | 1944 |  | 1985 |
|  | 1740 |  | 1781 |  | 1822 |  | 1863 |  | 1904 |  | 1945 |  | 1986 |
|  | 1741 |  | 1782 |  | 1823 |  | 1864 |  | 1905 |  | 1946 |  | 1987 |
|  | 1742 |  | 1783 |  | 1824 |  | 1865 |  | 1906 |  | 1947 |  | 1988 |
|  | 1743 |  | 1784 |  | 1825 |  | 1866 |  | 1907 |  | 1948 |  | 1989 |
|  | 1744 |  | 1785 |  | 1826 |  | 1867 |  | 1908 |  | 1949 |  | 1990 |
|  | 1745 |  | 1786 |  | 1827 |  | 1868 |  | 1909 |  | 1950 |  | 1991 |
|  | 1746 |  | 1787 |  | 1828 |  | 1869 |  | 1910 |  | 1951 |  | 1992 |
|  | 1747 |  | 1788 |  | 1829 |  | 1870 |  | 1911 |  | 1952 |  | 1993 |
|  | 1748 |  | 1789 |  | 1830 |  | 1871 |  | 1912 |  | 1953 |  | 1994 |
|  | 1749 |  | 1790 |  | 1831 |  | 1872 |  | 1913 |  | 1954 |  | 1995 |
|  | 1750 |  | 1791 |  | 1832 |  | 1873 |  | 1914 |  | 1955 |  | 1996 |
|  | 1751 |  | 1792 |  | 1833 |  | 1874 |  | 1915 |  | 1956 |  | 1997 |
|  | 1752 |  | 1793 |  | 1834 |  | 1875 |  | 1916 |  | 1957 |  | 1998 |
|  | 1753 |  | 1794 |  | 1835 |  | 1876 |  | 1917 |  | 1958 |  | 1999 |
|  | 1754 |  | 1795 |  | 1836 |  | 1877 |  | 1918 |  | 1959 |  | 2000 |
|  | 1755 |  | 1796 |  | 1837 |  | 1878 |  | 1919 |  | 1960 |  | 2001 |
|  | 1756 |  | 1797 |  | 1838 |  | 1879 |  | 1920 |  | 1961 |  | 2002 |
|  | 1757 |  | 1798 |  | 1839 |  | 1880 |  | 1921 |  | 1962 |  | 2003 |
|  | 1758 |  | 1799 |  | 1840 |  | 1881 |  | 1922 |  | 1963 |  | 2004 |
|  | 1759 |  | 1800 |  | 1841 |  | 1882 |  | 1923 |  | 1964 |  | 2005 |
|  | 1760 |  | 1801 |  | 1842 |  | 1883 |  | 1924 |  | 1965 |  | 2006 |
|  | 1761 |  | 1802 |  | 1843 |  | 1884 |  | 1925 |  | 1966 |  | 2007 |
|  | 1762 |  | 1803 |  | 1844 |  | 1885 |  | 1926 |  | 1967 |  | 2008 |
|  | 1763 |  | 1804 |  | 1845 |  | 1886 |  | 1927 |  | 1968 |  | 2009 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| Trt. | Bl nb |  | $\mathrm{Bl} \mathrm{nb}^{\text {nb }}$ |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2010 | PPD | 2051 | PPD | 2092 | PPD | 2133 | PPD | 2174 | PPD | 2215 | PPD | 2256 |
|  | 2011 |  | 2052 |  | 2093 |  | 2134 |  | 2175 |  | 2216 |  | 2257 |
|  | 2012 |  | 2053 |  | 2094 |  | 2135 |  | 2176 |  | 2217 |  | 2258 |
|  | 2013 |  | 2054 |  | 2095 |  | 2136 |  | 2177 |  | 2218 |  | 2259 |
|  | 2014 |  | 2055 |  | 2096 |  | 2137 |  | 2178 |  | 2219 |  | 2260 |
|  | 2015 |  | 2056 |  | 2097 |  | 2138 |  | 2179 |  | 2220 |  | 2261 |
|  | 2016 |  | 2057 |  | 2098 |  | 2139 |  | 2180 |  | 2221 |  | 2262 |
|  | 2017 |  | 2058 |  | 2099 |  | 2140 |  | 2181 |  | 2222 |  | 2263 |
|  | 2018 |  | 2059 |  | 2100 |  | 2141 |  | 2182 |  | 2223 |  | 2264 |
|  | 2019 |  | 2060 |  | 2101 |  | 2142 |  | 2183 |  | 2224 |  | 2265 |
|  | 2020 |  | 2061 |  | 2102 |  | 2143 |  | 2184 |  | 2225 |  | 2266 |
|  | 2021 |  | 2062 |  | 2103 |  | 2144 |  | 2185 |  | 2226 |  | 2267 |
|  | 2022 |  | 2063 |  | 2104 |  | 2145 |  | 2186 |  | 2227 |  | 2268 |
|  | 2023 |  | 2064 |  | 2105 |  | 2146 |  | 2187 |  | 2228 |  | 2269 |
|  | 2024 |  | 2065 |  | 2106 |  | 2147 |  | 2188 |  | 2229 |  | 2270 |
|  | 2025 |  | 2066 |  | 2107 |  | 2148 |  | 2189 |  | 2230 |  | 2271 |
|  | 2026 |  | 2067 |  | 2108 |  | 2149 |  | 2190 |  | 2231 |  | 2272 |
|  | 2027 |  | 2068 |  | 2109 |  | 2150 |  | 2191 |  | 2232 |  | 2273 |
|  | 2028 |  | 2069 |  | 2110 |  | 2151 |  | 2192 |  | 2233 |  | 2274 |
|  | 2029 |  | 2070 |  | 2111 |  | 2152 |  | 2193 |  | 2234 |  | 2275 |
|  | 2030 |  | 2071 |  | 2112 |  | 2153 |  | 2194 |  | 2235 |  | 2276 |
|  | 2031 |  | 2072 |  | 2113 |  | 2154 |  | 2195 |  | 2236 |  | 2277 |
|  | 2032 |  | 2073 |  | 2114 |  | 2155 |  | 2196 |  | 2237 |  | 2278 |
|  | 2033 |  | 2074 |  | 2115 |  | 2156 |  | 2197 |  | 2238 |  | 2279 |
|  | 2034 |  | 2075 |  | 2116 |  | 2157 |  | 2198 |  | 2239 |  | 2280 |
|  | 2035 |  | 2076 |  | 2117 |  | 2158 |  | 2199 |  | 2240 |  | 2281 |
|  | 2036 |  | 2077 |  | 2118 |  | 2159 |  | 2200 |  | 2241 |  | 2282 |
|  | 2037 |  | 2078 |  | 2119 |  | 2160 |  | 2201 |  | 2242 |  | 2283 |
|  | 2038 |  | 2079 |  | 2120 |  | 2161 |  | 2202 |  | 2243 |  | 2284 |
|  | 2039 |  | 2080 |  | 2121 |  | 2162 |  | 2203 |  | 2244 |  | 2285 |
|  | 2040 |  | 2081 |  | 2122 |  | 2163 |  | 2204 |  | 2245 |  | 2286 |
|  | 2041 |  | 2082 |  | 2123 |  | 2164 |  | 2205 |  | 2246 |  | 2287 |
|  | 2042 |  | 2083 |  | 2124 |  | 2165 |  | 2206 |  | 2247 |  | 2288 |
|  | 2043 |  | 2084 |  | 2125 |  | 2166 |  | 2207 |  | 2248 |  | 2289 |
|  | 2044 |  | 2085 |  | 2126 |  | 2167 |  | 2208 |  | 2249 |  | 2290 |
|  | 2045 |  | 2086 |  | 2127 |  | 2168 |  | 2209 |  | 2250 |  | 2291 |
|  | 2046 |  | 2087 |  | 2128 |  | 2169 |  | 2210 |  | 2251 |  | 2292 |
|  | 2047 |  | 2088 |  | 2129 |  | 2170 |  | 2211 |  | 2252 |  | 2293 |
|  | 2048 |  | 2089 |  | 2130 |  | 2171 |  | 2212 |  | 2253 |  | 2294 |
|  | 2049 |  | 2090 |  | 2131 |  | 2172 |  | 2213 |  | 2254 |  | 2295 |
|  | 2050 |  | 2091 |  | 2132 |  | 2173 |  | 2214 |  | 2255 |  | 2296 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | Trt |  |  |  |  | Bl nb |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2297 | PPD | 2338 | PPD | 2379 | PPD | 2420 | PPD | 2461 | PPD | 2502 | PPD | 2543 |
|  | 2298 |  | 2339 |  | 2380 |  | 2421 |  | 2462 |  | 2503 |  | 2544 |
|  | 2299 |  | 2340 |  | 2381 |  | 2422 |  | 2463 |  | 2504 |  | 2545 |
|  | 2300 |  | 2341 |  | 2382 |  | 2423 |  | 2464 |  | 2505 |  | 2546 |
|  | 2301 |  | 2342 |  | 2383 |  | 2424 |  | 2465 |  | 2506 |  | 2547 |
|  | 2302 |  | 2343 |  | 2384 |  | 2425 |  | 2466 |  | 2507 |  | 2548 |
|  | 2303 |  | 2344 |  | 2385 |  | 2426 |  | 2467 |  | 2508 |  | 2549 |
|  | 2304 |  | 2345 |  | 2386 |  | 2427 |  | 2468 |  | 2509 |  | 2550 |
|  | 2305 |  | 2346 |  | 2387 |  | 2428 |  | 2469 |  | 2510 |  | 2551 |
|  | 2306 |  | 2347 |  | 2388 |  | 2429 |  | 2470 |  | 2511 |  | 2552 |
|  | 2307 |  | 2348 |  | 2389 |  | 2430 |  | 2471 |  | 2512 |  | 2553 |
|  | 2308 |  | 2349 |  | 2390 |  | 2431 |  | 2472 |  | 2513 |  | 2554 |
|  | 2309 |  | 2350 |  | 2391 |  | 2432 |  | 2473 |  | 2514 |  | 2555 |
|  | 2310 |  | 2351 |  | 2392 |  | 2433 |  | 2474 |  | 2515 |  | 2556 |
|  | 2311 |  | 2352 |  | 2393 |  | 2434 |  | 2475 |  | 2516 |  | 2557 |
|  | 2312 |  | 2353 |  | 2394 |  | 2435 |  | 2476 |  | 2517 |  | 2558 |
|  | 2313 |  | 2354 |  | 2395 |  | 2436 |  | 2477 |  | 2518 |  | 2559 |
|  | 2314 |  | 2355 |  | 2396 |  | 2437 |  | 2478 |  | 2519 |  | 2560 |
|  | 2315 |  | 2356 |  | 2397 |  | 2438 |  | 2479 |  | 2520 |  | 2561 |
|  | 2316 |  | 2357 |  | 2398 |  | 2439 |  | 2480 |  | 2521 |  | 2562 |
|  | 2317 |  | 2358 |  | 2399 |  | 2440 |  | 2481 |  | 2522 |  | 2563 |
|  | 2318 |  | 2359 |  | 2400 |  | 2441 |  | 2482 |  | 2523 |  | 2564 |
|  | 2319 |  | 2360 |  | 2401 |  | 2442 |  | 2483 |  | 2524 |  | 2565 |
|  | 2320 |  | 2361 |  | 2402 |  | 2443 |  | 2484 |  | 2525 |  | 2566 |
|  | 2321 |  | 2362 |  | 2403 |  | 2444 |  | 2485 |  | 2526 |  | 2567 |
|  | 2322 |  | 2363 |  | 2404 |  | 2445 |  | 2486 |  | 2527 |  | 2568 |
|  | 2323 |  | 2364 |  | 2405 |  | 2446 |  | 2487 |  | 2528 |  | 2569 |
|  | 2324 |  | 2365 |  | 2406 |  | 2447 |  | 2488 |  | 2529 |  | 2570 |
|  | 2325 |  | 2366 |  | 2407 |  | 2448 |  | 2489 |  | 2530 |  | 2571 |
|  | 2326 |  | 2367 |  | 2408 |  | 2449 |  | 2490 |  | 2531 |  | 2572 |
|  | 2327 |  | 2368 |  | 2409 |  | 2450 |  | 2491 |  | 2532 |  | 2573 |
|  | 2328 |  | 2369 |  | 2410 |  | 2451 |  | 2492 |  | 2533 |  | 2574 |
|  | 2329 |  | 2370 |  | 2411 |  | 2452 |  | 2493 |  | 2534 |  | 2575 |
|  | 2330 |  | 2371 |  | 2412 |  | 2453 |  | 2494 |  | 2535 |  | 2576 |
|  | 2331 |  | 2372 |  | 2413 |  | 2454 |  | 2495 |  | 2536 |  | 2577 |
|  | 2332 |  | 2373 |  | 2414 |  | 2455 |  | 2496 |  | 2537 |  | 2578 |
|  | 2333 |  | 2374 |  | 2415 |  | 2456 |  | 2497 |  | 2538 |  | 2579 |
|  | 2334 |  | 2375 |  | 2416 |  | 2457 |  | 2498 |  | 2539 |  | 2580 |
|  | 2335 |  | 2376 |  | 2417 |  | 2458 |  | 2499 |  | 2540 |  | 2581 |
|  | 2336 |  | 2377 |  | 2418 |  | 2459 |  | 2500 |  | 2541 |  | 2582 |
|  | 2337 |  | 2378 |  | 2419 |  | 2460 |  | 2501 |  | 2542 |  | 2583 |

Treatment number associated to material : Hz/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl. |  | Bl. |  |  |  | $\mathrm{Bl} \text {. }$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2584 | PPD | 2625 | PPD | 2666 | PPD | 2707 | PPD | 2748 | PPD | 2789 | PPD | 2830 |
|  | 2585 |  | 2626 |  | 2667 |  | 2708 |  | 2749 |  | 2790 |  | 2831 |
|  | 2586 |  | 2627 |  | 2668 |  | 2709 |  | 2750 |  | 2791 |  | 2832 |
|  | 2587 |  | 2628 |  | 2669 |  | 2710 |  | 2751 |  | 2792 |  | 2833 |
|  | 2588 |  | 2629 |  | 2670 |  | 2711 |  | 2752 |  | 2793 |  | 2834 |
|  | 2589 |  | 2630 |  | 2671 |  | 2712 |  | 2753 |  | 2794 |  | 2835 |
|  | 2590 |  | 2631 |  | 2672 |  | 2713 |  | 2754 |  | 2795 |  | 2836 |
|  | 2591 |  | 2632 |  | 2673 |  | 2714 |  | 2755 |  | 2796 |  | 2837 |
|  | 2592 |  | 2633 |  | 2674 |  | 2715 |  | 2756 |  | 2797 |  | 2838 |
|  | 2593 |  | 2634 |  | 2675 |  | 2716 |  | 2757 |  | 2798 |  | 2839 |
|  | 2594 |  | 2635 |  | 2676 |  | 2717 |  | 2758 |  | 2799 |  | 2840 |
|  | 2595 |  | 2636 |  | 2677 |  | 2718 |  | 2759 |  | 2800 |  | 2841 |
|  | 2596 |  | 2637 |  | 2678 |  | 2719 |  | 2760 |  | 2801 |  | 2842 |
|  | 2597 |  | 2638 |  | 2679 |  | 2720 |  | 2761 |  | 2802 |  | 2843 |
|  | 2598 |  | 2639 |  | 2680 |  | 2721 |  | 2762 |  | 2803 |  | 2844 |
|  | 2599 |  | 2640 |  | 2681 |  | 2722 |  | 2763 |  | 2804 |  | 2845 |
|  | 2600 |  | 2641 |  | 2682 |  | 2723 |  | 2764 |  | 2805 |  | 2846 |
|  | 2601 |  | 2642 |  | 2683 |  | 2724 |  | 2765 |  | 2806 |  | 2847 |
|  | 2602 |  | 2643 |  | 2684 |  | 2725 |  | 2766 |  | 2807 |  | 2848 |
|  | 2603 |  | 2644 |  | 2685 |  | 2726 |  | 2767 |  | 2808 |  | 2849 |
|  | 2604 |  | 2645 |  | 2686 |  | 2727 |  | 2768 |  | 2809 |  | 2850 |
|  | 2605 |  | 2646 |  | 2687 |  | 2728 |  | 2769 |  | 2810 |  | 2851 |
|  | 2606 |  | 2647 |  | 2688 |  | 2729 |  | 2770 |  | 2811 |  | 2852 |
|  | 2607 |  | 2648 |  | 2689 |  | 2730 |  | 2771 |  | 2812 |  | 2853 |
|  | 2608 |  | 2649 |  | 2690 |  | 2731 |  | 2772 |  | 2813 |  | 2854 |
|  | 2609 |  | 2650 |  | 2691 |  | 2732 |  | 2773 |  | 2814 |  | 2855 |
|  | 2610 |  | 2651 |  | 2692 |  | 2733 |  | 2774 |  | 2815 |  | 2856 |
|  | 2611 |  | 2652 |  | 2693 |  | 2734 |  | 2775 |  | 2816 |  | 2857 |
|  | 2612 |  | 2653 |  | 2694 |  | 2735 |  | 2776 |  | 2817 |  | 2858 |
|  | 2613 |  | 2654 |  | 2695 |  | 2736 |  | 2777 |  | 2818 |  | 2859 |
|  | 2614 |  | 2655 |  | 2696 |  | 2737 |  | 2778 |  | 2819 |  | 2860 |
|  | 2615 |  | 2656 |  | 2697 |  | 2738 |  | 2779 |  | 2820 |  | 2861 |
|  | 2616 |  | 2657 |  | 2698 |  | 2739 |  | 2780 |  | 2821 |  | 2862 |
|  | 2617 |  | 2658 |  | 2699 |  | 2740 |  | 2781 |  | 2822 |  | 2863 |
|  | 2618 |  | 2659 |  | 2700 |  | 2741 |  | 2782 |  | 2823 |  | 2864 |
|  | 2619 |  | 2660 |  | 2701 |  | 2742 |  | 2783 |  | 2824 |  | 2865 |
|  | 2620 |  | 2661 |  | 2702 |  | 2743 |  | 2784 |  | 2825 |  | 2866 |
|  | 2621 |  | 2662 |  | 2703 |  | 2744 |  | 2785 |  | 2826 |  | 2867 |
|  | 2622 |  | 2663 |  | 2704 |  | 2745 |  | 2786 |  | 2827 |  | 2868 |
|  | 2623 |  | 2664 |  | 2705 |  | 2746 |  | 2787 |  | 2828 |  | 2869 |
|  | 2624 |  | 2665 |  | 2706 |  | 2747 |  | 2788 |  | 2829 |  | 2870 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| Trt. |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2871 | PPD | 2912 | PPD | 2953 | PPD | 2994 | PPD | 3035 | PPD | 3076 | PPD | 3117 |
|  | 2872 |  | 2913 |  | 2954 |  | 2995 |  | 3036 |  | 3077 |  | 3118 |
|  | 2873 |  | 2914 |  | 2955 |  | 2996 |  | 3037 |  | 3078 |  | 3119 |
|  | 2874 |  | 2915 |  | 2956 |  | 2997 |  | 3038 |  | 3079 |  | 3120 |
|  | 2875 |  | 2916 |  | 2957 |  | 2998 |  | 3039 |  | 3080 |  | 3121 |
|  | 2876 |  | 2917 |  | 2958 |  | 2999 |  | 3040 |  | 3081 |  | 3122 |
|  | 2877 |  | 2918 |  | 2959 |  | 3000 |  | 3041 |  | 3082 |  | 3123 |
|  | 2878 |  | 2919 |  | 2960 |  | 3001 |  | 3042 |  | 3083 |  | 3124 |
|  | 2879 |  | 2920 |  | 2961 |  | 3002 |  | 3043 |  | 3084 |  | 3125 |
|  | 2880 |  | 2921 |  | 2962 |  | 3003 |  | 3044 |  | 3085 |  | 3126 |
|  | 2881 |  | 2922 |  | 2963 |  | 3004 |  | 3045 |  | 3086 |  | 3127 |
|  | 2882 |  | 2923 |  | 2964 |  | 3005 |  | 3046 |  | 3087 |  | 3128 |
|  | 2883 |  | 2924 |  | 2965 |  | 3006 |  | 3047 |  | 3088 |  | 3129 |
|  | 2884 |  | 2925 |  | 2966 |  | 3007 |  | 3048 |  | 3089 |  | 3130 |
|  | 2885 |  | 2926 |  | 2967 |  | 3008 |  | 3049 |  | 3090 |  | 3131 |
|  | 2886 |  | 2927 |  | 2968 |  | 3009 |  | 3050 |  | 3091 |  | 3132 |
|  | 2887 |  | 2928 |  | 2969 |  | 3010 |  | 3051 |  | 3092 |  | 3133 |
|  | 2888 |  | 2929 |  | 2970 |  | 3011 |  | 3052 |  | 3093 |  | 3134 |
|  | 2889 |  | 2930 |  | 2971 |  | 3012 |  | 3053 |  | 3094 |  | 3135 |
|  | 2890 |  | 2931 |  | 2972 |  | 3013 |  | 3054 |  | 3095 |  | 3136 |
|  | 2891 |  | 2932 |  | 2973 |  | 3014 |  | 3055 |  | 3096 |  | 3137 |
|  | 2892 |  | 2933 |  | 2974 |  | 3015 |  | 3056 |  | 3097 |  | 3138 |
|  | 2893 |  | 2934 |  | 2975 |  | 3016 |  | 3057 |  | 3098 |  | 3139 |
|  | 2894 |  | 2935 |  | 2976 |  | 3017 |  | 3058 |  | 3099 |  | 3140 |
|  | 2895 |  | 2936 |  | 2977 |  | 3018 |  | 3059 |  | 3100 |  | 3141 |
|  | 2896 |  | 2937 |  | 2978 |  | 3019 |  | 3060 |  | 3101 |  | 3142 |
|  | 2897 |  | 2938 |  | 2979 |  | 3020 |  | 3061 |  | 3102 |  | 3143 |
|  | 2898 |  | 2939 |  | 2980 |  | 3021 |  | 3062 |  | 3103 |  | 3144 |
|  | 2899 |  | 2940 |  | 2981 |  | 3022 |  | 3063 |  | 3104 |  | 3145 |
|  | 2900 |  | 2941 |  | 2982 |  | 3023 |  | 3064 |  | 3105 |  | 3146 |
|  | 2901 |  | 2942 |  | 2983 |  | 3024 |  | 3065 |  | 3106 |  | 3147 |
|  | 2902 |  | 2943 |  | 2984 |  | 3025 |  | 3066 |  | 3107 |  | 3148 |
|  | 2903 |  | 2944 |  | 2985 |  | 3026 |  | 3067 |  | 3108 |  | 3149 |
|  | 2904 |  | 2945 |  | 2986 |  | 3027 |  | 3068 |  | 3109 |  | 3150 |
|  | 2905 |  | 2946 |  | 2987 |  | 3028 |  | 3069 |  | 3110 |  | 3151 |
|  | 2906 |  | 2947 |  | 2988 |  | 3029 |  | 3070 |  | 3111 |  | 3152 |
|  | 2907 |  | 2948 |  | 2989 |  | 3030 |  | 3071 |  | 3112 |  | 3153 |
|  | 2908 |  | 2949 |  | 2990 |  | 3031 |  | 3072 |  | 3113 |  | 3154 |
|  | 2909 |  | 2950 |  | 2991 |  | 3032 |  | 3073 |  | 3114 |  | 3155 |
|  | 2910 |  | 2951 |  | 2992 |  | 3033 |  | 3074 |  | 3115 |  | 3156 |
|  | 2911 |  | 2952 |  | 2993 |  | 3034 |  | 3075 |  | 3116 |  | 3157 |

Treatment number associated to material : Hz/su-OnChemo

| Trt. |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | Trt | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3158 | PPD | 3199 | PPD | 3240 | PPD | 3281 | PPD | 3322 | PPD | 3363 | PPD | 3404 |
|  | 3159 |  | 3200 |  | 3241 |  | 3282 |  | 3323 |  | 3364 |  | 3405 |
|  | 3160 |  | 3201 |  | 3242 |  | 3283 |  | 3324 |  | 3365 |  | 3406 |
|  | 3161 |  | 3202 |  | 3243 |  | 3284 |  | 3325 |  | 3366 |  | 3407 |
|  | 3162 |  | 3203 |  | 3244 |  | 3285 |  | 3326 |  | 3367 |  | 3408 |
|  | 3163 |  | 3204 |  | 3245 |  | 3286 |  | 3327 |  | 3368 |  | 3409 |
|  | 3164 |  | 3205 |  | 3246 |  | 3287 |  | 3328 |  | 3369 |  | 3410 |
|  | 3165 |  | 3206 |  | 3247 |  | 3288 |  | 3329 |  | 3370 |  | 3411 |
|  | 3166 |  | 3207 |  | 3248 |  | 3289 |  | 3330 |  | 3371 |  | 3412 |
|  | 3167 |  | 3208 |  | 3249 |  | 3290 |  | 3331 |  | 3372 |  | 3413 |
|  | 3168 |  | 3209 |  | 3250 |  | 3291 |  | 3332 |  | 3373 |  | 3414 |
|  | 3169 |  | 3210 |  | 3251 |  | 3292 |  | 3333 |  | 3374 |  | 3415 |
|  | 3170 |  | 3211 |  | 3252 |  | 3293 |  | 3334 |  | 3375 |  | 3416 |
|  | 3171 |  | 3212 |  | 3253 |  | 3294 |  | 3335 |  | 3376 |  | 3417 |
|  | 3172 |  | 3213 |  | 3254 |  | 3295 |  | 3336 |  | 3377 |  | 3418 |
|  | 3173 |  | 3214 |  | 3255 |  | 3296 |  | 3337 |  | 3378 |  | 3419 |
|  | 3174 |  | 3215 |  | 3256 |  | 3297 |  | 3338 |  | 3379 |  | 3420 |
|  | 3175 |  | 3216 |  | 3257 |  | 3298 |  | 3339 |  | 3380 |  | 3421 |
|  | 3176 |  | 3217 |  | 3258 |  | 3299 |  | 3340 |  | 3381 |  | 3422 |
|  | 3177 |  | 3218 |  | 3259 |  | 3300 |  | 3341 |  | 3382 |  | 3423 |
|  | 3178 |  | 3219 |  | 3260 |  | 3301 |  | 3342 |  | 3383 |  | 3424 |
|  | 3179 |  | 3220 |  | 3261 |  | 3302 |  | 3343 |  | 3384 |  | 3425 |
|  | 3180 |  | 3221 |  | 3262 |  | 3303 |  | 3344 |  | 3385 |  | 3426 |
|  | 3181 |  | 3222 |  | 3263 |  | 3304 |  | 3345 |  | 3386 |  | 3427 |
|  | 3182 |  | 3223 |  | 3264 |  | 3305 |  | 3346 |  | 3387 |  | 3428 |
|  | 3183 |  | 3224 |  | 3265 |  | 3306 |  | 3347 |  | 3388 |  | 3429 |
|  | 3184 |  | 3225 |  | 3266 |  | 3307 |  | 3348 |  | 3389 |  | 3430 |
|  | 3185 |  | 3226 |  | 3267 |  | 3308 |  | 3349 |  | 3390 |  | 3431 |
|  | 3186 |  | 3227 |  | 3268 |  | 3309 |  | 3350 |  | 3391 |  | 3432 |
|  | 3187 |  | 3228 |  | 3269 |  | 3310 |  | 3351 |  | 3392 |  | 3433 |
|  | 3188 |  | 3229 |  | 3270 |  | 3311 |  | 3352 |  | 3393 |  | 3434 |
|  | 3189 |  | 3230 |  | 3271 |  | 3312 |  | 3353 |  | 3394 |  | 3435 |
|  | 3190 |  | 3231 |  | 3272 |  | 3313 |  | 3354 |  | 3395 |  | 3436 |
|  | 3191 |  | 3232 |  | 3273 |  | 3314 |  | 3355 |  | 3396 |  | 3437 |
|  | 3192 |  | 3233 |  | 3274 |  | 3315 |  | 3356 |  | 3397 |  | 3438 |
|  | 3193 |  | 3234 |  | 3275 |  | 3316 |  | 3357 |  | 3398 |  | 3439 |
|  | 3194 |  | 3235 |  | 3276 |  | 3317 |  | 3358 |  | 3399 |  | 3440 |
|  | 3195 |  | 3236 |  | 3277 |  | 3318 |  | 3359 |  | 3400 |  | 3441 |
|  | 3196 |  | 3237 |  | 3278 |  | 3319 |  | 3360 |  | 3401 |  | 3442 |
|  | 3197 |  | 3238 |  | 3279 |  | 3320 |  | 3361 |  | 3402 |  | 3443 |
|  | 3198 |  | 3239 |  | 3280 |  | 3321 |  | 3362 |  | 3403 |  | 3444 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  |  |  | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3445 | PPD | 3486 | PPD | 3527 | PPD | 3568 | PPD | 3609 | PPD | 3650 | PPD | 3691 |
|  | 3446 |  | 3487 |  | 3528 |  | 3569 |  | 3610 |  | 3651 |  | 3692 |
|  | 3447 |  | 3488 |  | 3529 |  | 3570 |  | 3611 |  | 3652 |  | 3693 |
|  | 3448 |  | 3489 |  | 3530 |  | 3571 |  | 3612 |  | 3653 |  | 3694 |
|  | 3449 |  | 3490 |  | 3531 |  | 3572 |  | 3613 |  | 3654 |  | 3695 |
|  | 3450 |  | 3491 |  | 3532 |  | 3573 |  | 3614 |  | 3655 |  | 3696 |
|  | 3451 |  | 3492 |  | 3533 |  | 3574 |  | 3615 |  | 3656 |  | 3697 |
|  | 3452 |  | 3493 |  | 3534 |  | 3575 |  | 3616 |  | 3657 |  | 3698 |
|  | 3453 |  | 3494 |  | 3535 |  | 3576 |  | 3617 |  | 3658 |  | 3699 |
|  | 3454 |  | 3495 |  | 3536 |  | 3577 |  | 3618 |  | 3659 |  | 3700 |
|  | 3455 |  | 3496 |  | 3537 |  | 3578 |  | 3619 |  | 3660 |  | 3701 |
|  | 3456 |  | 3497 |  | 3538 |  | 3579 |  | 3620 |  | 3661 |  | 3702 |
|  | 3457 |  | 3498 |  | 3539 |  | 3580 |  | 3621 |  | 3662 |  | 3703 |
|  | 3458 |  | 3499 |  | 3540 |  | 3581 |  | 3622 |  | 3663 |  | 3704 |
|  | 3459 |  | 3500 |  | 3541 |  | 3582 |  | 3623 |  | 3664 |  | 3705 |
|  | 3460 |  | 3501 |  | 3542 |  | 3583 |  | 3624 |  | 3665 |  | 3706 |
|  | 3461 |  | 3502 |  | 3543 |  | 3584 |  | 3625 |  | 3666 |  | 3707 |
|  | 3462 |  | 3503 |  | 3544 |  | 3585 |  | 3626 |  | 3667 |  | 3708 |
|  | 3463 |  | 3504 |  | 3545 |  | 3586 |  | 3627 |  | 3668 |  | 3709 |
|  | 3464 |  | 3505 |  | 3546 |  | 3587 |  | 3628 |  | 3669 |  | 3710 |
|  | 3465 |  | 3506 |  | 3547 |  | 3588 |  | 3629 |  | 3670 |  | 3711 |
|  | 3466 |  | 3507 |  | 3548 |  | 3589 |  | 3630 |  | 3671 |  | 3712 |
|  | 3467 |  | 3508 |  | 3549 |  | 3590 |  | 3631 |  | 3672 |  | 3713 |
|  | 3468 |  | 3509 |  | 3550 |  | 3591 |  | 3632 |  | 3673 |  | 3714 |
|  | 3469 |  | 3510 |  | 3551 |  | 3592 |  | 3633 |  | 3674 |  | 3715 |
|  | 3470 |  | 3511 |  | 3552 |  | 3593 |  | 3634 |  | 3675 |  | 3716 |
|  | 3471 |  | 3512 |  | 3553 |  | 3594 |  | 3635 |  | 3676 |  | 3717 |
|  | 3472 |  | 3513 |  | 3554 |  | 3595 |  | 3636 |  | 3677 |  | 3718 |
|  | 3473 |  | 3514 |  | 3555 |  | 3596 |  | 3637 |  | 3678 |  | 3719 |
|  | 3474 |  | 3515 |  | 3556 |  | 3597 |  | 3638 |  | 3679 |  | 3720 |
|  | 3475 |  | 3516 |  | 3557 |  | 3598 |  | 3639 |  | 3680 |  | 3721 |
|  | 3476 |  | 3517 |  | 3558 |  | 3599 |  | 3640 |  | 3681 |  | 3722 |
|  | 3477 |  | 3518 |  | 3559 |  | 3600 |  | 3641 |  | 3682 |  | 3723 |
|  | 3478 |  | 3519 |  | 3560 |  | 3601 |  | 3642 |  | 3683 |  | 3724 |
|  | 3479 |  | 3520 |  | 3561 |  | 3602 |  | 3643 |  | 3684 |  | 3725 |
|  | 3480 |  | 3521 |  | 3562 |  | 3603 |  | 3644 |  | 3685 |  | 3726 |
|  | 3481 |  | 3522 |  | 3563 |  | 3604 |  | 3645 |  | 3686 |  | 3727 |
|  | 3482 |  | 3523 |  | 3564 |  | 3605 |  | 3646 |  | 3687 |  | 3728 |
|  | 3483 |  | 3524 |  | 3565 |  | 3606 |  | 3647 |  | 3688 |  | 3729 |
|  | 3484 |  | 3525 |  | 3566 |  | 3607 |  | 3648 |  | 3689 |  | 3730 |
|  | 3485 |  | 3526 |  | 3567 |  | 3608 |  | 3649 |  | 3690 |  | 3731 |

Treatment number associated to material : Hz/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl. |  | Bl. |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3732 | PPD | 3773 | PPD | 3814 | PPD | 3855 | PPD | 3896 | PPD | 3937 | PPD | 3978 |
|  | 3733 |  | 3774 |  | 3815 |  | 3856 |  | 3897 |  | 3938 |  | 3979 |
|  | 3734 |  | 3775 |  | 3816 |  | 3857 |  | 3898 |  | 3939 |  | 3980 |
|  | 3735 |  | 3776 |  | 3817 |  | 3858 |  | 3899 |  | 3940 |  | 3981 |
|  | 3736 |  | 3777 |  | 3818 |  | 3859 |  | 3900 |  | 3941 |  | 3982 |
|  | 3737 |  | 3778 |  | 3819 |  | 3860 |  | 3901 |  | 3942 |  | 3983 |
|  | 3738 |  | 3779 |  | 3820 |  | 3861 |  | 3902 |  | 3943 |  | 3984 |
|  | 3739 |  | 3780 |  | 3821 |  | 3862 |  | 3903 |  | 3944 |  | 3985 |
|  | 3740 |  | 3781 |  | 3822 |  | 3863 |  | 3904 |  | 3945 |  | 3986 |
|  | 3741 |  | 3782 |  | 3823 |  | 3864 |  | 3905 |  | 3946 |  | 3987 |
|  | 3742 |  | 3783 |  | 3824 |  | 3865 |  | 3906 |  | 3947 |  | 3988 |
|  | 3743 |  | 3784 |  | 3825 |  | 3866 |  | 3907 |  | 3948 |  | 3989 |
|  | 3744 |  | 3785 |  | 3826 |  | 3867 |  | 3908 |  | 3949 |  | 3990 |
|  | 3745 |  | 3786 |  | 3827 |  | 3868 |  | 3909 |  | 3950 |  | 3991 |
|  | 3746 |  | 3787 |  | 3828 |  | 3869 |  | 3910 |  | 3951 |  | 3992 |
|  | 3747 |  | 3788 |  | 3829 |  | 3870 |  | 3911 |  | 3952 |  | 3993 |
|  | 3748 |  | 3789 |  | 3830 |  | 3871 |  | 3912 |  | 3953 |  | 3994 |
|  | 3749 |  | 3790 |  | 3831 |  | 3872 |  | 3913 |  | 3954 |  | 3995 |
|  | 3750 |  | 3791 |  | 3832 |  | 3873 |  | 3914 |  | 3955 |  | 3996 |
|  | 3751 |  | 3792 |  | 3833 |  | 3874 |  | 3915 |  | 3956 |  | 3997 |
|  | 3752 |  | 3793 |  | 3834 |  | 3875 |  | 3916 |  | 3957 |  | 3998 |
|  | 3753 |  | 3794 |  | 3835 |  | 3876 |  | 3917 |  | 3958 |  | 3999 |
|  | 3754 |  | 3795 |  | 3836 |  | 3877 |  | 3918 |  | 3959 |  | 4000 |
|  | 3755 |  | 3796 |  | 3837 |  | 3878 |  | 3919 |  | 3960 |  | 4001 |
|  | 3756 |  | 3797 |  | 3838 |  | 3879 |  | 3920 |  | 3961 |  | 4002 |
|  | 3757 |  | 3798 |  | 3839 |  | 3880 |  | 3921 |  | 3962 |  | 4003 |
|  | 3758 |  | 3799 |  | 3840 |  | 3881 |  | 3922 |  | 3963 |  | 4004 |
|  | 3759 |  | 3800 |  | 3841 |  | 3882 |  | 3923 |  | 3964 |  | 4005 |
|  | 3760 |  | 3801 |  | 3842 |  | 3883 |  | 3924 |  | 3965 |  | 4006 |
|  | 3761 |  | 3802 |  | 3843 |  | 3884 |  | 3925 |  | 3966 |  | 4007 |
|  | 3762 |  | 3803 |  | 3844 |  | 3885 |  | 3926 |  | 3967 |  | 4008 |
|  | 3763 |  | 3804 |  | 3845 |  | 3886 |  | 3927 |  | 3968 |  | 4009 |
|  | 3764 |  | 3805 |  | 3846 |  | 3887 |  | 3928 |  | 3969 |  | 4010 |
|  | 3765 |  | 3806 |  | 3847 |  | 3888 |  | 3929 |  | 3970 |  | 4011 |
|  | 3766 |  | 3807 |  | 3848 |  | 3889 |  | 3930 |  | 3971 |  | 4012 |
|  | 3767 |  | 3808 |  | 3849 |  | 3890 |  | 3931 |  | 3972 |  | 4013 |
|  | 3768 |  | 3809 |  | 3850 |  | 3891 |  | 3932 |  | 3973 |  | 4014 |
|  | 3769 |  | 3810 |  | 3851 |  | 3892 |  | 3933 |  | 3974 |  | 4015 |
|  | 3770 |  | 3811 |  | 3852 |  | 3893 |  | 3934 |  | 3975 |  | 4016 |
|  | 3771 |  | 3812 |  | 3853 |  | 3894 |  | 3935 |  | 3976 |  | 4017 |
|  | 3772 |  | 3813 |  | 3854 |  | 3895 |  | 3936 |  | 3977 |  | 4018 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | Bl nb |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4019 | PPD | 4060 | PPD | 4101 | PPD | 4142 | PPD | 4183 | PPD | 4224 | PPD | 4265 |
|  | 4020 |  | 4061 |  | 4102 |  | 4143 |  | 4184 |  | 4225 |  | 4266 |
|  | 4021 |  | 4062 |  | 4103 |  | 4144 |  | 4185 |  | 4226 |  | 4267 |
|  | 4022 |  | 4063 |  | 4104 |  | 4145 |  | 4186 |  | 4227 |  | 4268 |
|  | 4023 |  | 4064 |  | 4105 |  | 4146 |  | 4187 |  | 4228 |  | 4269 |
|  | 4024 |  | 4065 |  | 4106 |  | 4147 |  | 4188 |  | 4229 |  | 4270 |
|  | 4025 |  | 4066 |  | 4107 |  | 4148 |  | 4189 |  | 4230 |  | 4271 |
|  | 4026 |  | 4067 |  | 4108 |  | 4149 |  | 4190 |  | 4231 |  | 4272 |
|  | 4027 |  | 4068 |  | 4109 |  | 4150 |  | 4191 |  | 4232 |  | 4273 |
|  | 4028 |  | 4069 |  | 4110 |  | 4151 |  | 4192 |  | 4233 |  | 4274 |
|  | 4029 |  | 4070 |  | 4111 |  | 4152 |  | 4193 |  | 4234 |  | 4275 |
|  | 4030 |  | 4071 |  | 4112 |  | 4153 |  | 4194 |  | 4235 |  | 4276 |
|  | 4031 |  | 4072 |  | 4113 |  | 4154 |  | 4195 |  | 4236 |  | 4277 |
|  | 4032 |  | 4073 |  | 4114 |  | 4155 |  | 4196 |  | 4237 |  | 4278 |
|  | 4033 |  | 4074 |  | 4115 |  | 4156 |  | 4197 |  | 4238 |  | 4279 |
|  | 4034 |  | 4075 |  | 4116 |  | 4157 |  | 4198 |  | 4239 |  | 4280 |
|  | 4035 |  | 4076 |  | 4117 |  | 4158 |  | 4199 |  | 4240 |  | 4281 |
|  | 4036 |  | 4077 |  | 4118 |  | 4159 |  | 4200 |  | 4241 |  | 4282 |
|  | 4037 |  | 4078 |  | 4119 |  | 4160 |  | 4201 |  | 4242 |  | 4283 |
|  | 4038 |  | 4079 |  | 4120 |  | 4161 |  | 4202 |  | 4243 |  | 4284 |
|  | 4039 |  | 4080 |  | 4121 |  | 4162 |  | 4203 |  | 4244 |  | 4285 |
|  | 4040 |  | 4081 |  | 4122 |  | 4163 |  | 4204 |  | 4245 |  | 4286 |
|  | 4041 |  | 4082 |  | 4123 |  | 4164 |  | 4205 |  | 4246 |  | 4287 |
|  | 4042 |  | 4083 |  | 4124 |  | 4165 |  | 4206 |  | 4247 |  | 4288 |
|  | 4043 |  | 4084 |  | 4125 |  | 4166 |  | 4207 |  | 4248 |  | 4289 |
|  | 4044 |  | 4085 |  | 4126 |  | 4167 |  | 4208 |  | 4249 |  | 4290 |
|  | 4045 |  | 4086 |  | 4127 |  | 4168 |  | 4209 |  | 4250 |  | 4291 |
|  | 4046 |  | 4087 |  | 4128 |  | 4169 |  | 4210 |  | 4251 |  | 4292 |
|  | 4047 |  | 4088 |  | 4129 |  | 4170 |  | 4211 |  | 4252 |  | 4293 |
|  | 4048 |  | 4089 |  | 4130 |  | 4171 |  | 4212 |  | 4253 |  | 4294 |
|  | 4049 |  | 4090 |  | 4131 |  | 4172 |  | 4213 |  | 4254 |  | 4295 |
|  | 4050 |  | 4091 |  | 4132 |  | 4173 |  | 4214 |  | 4255 |  | 4296 |
|  | 4051 |  | 4092 |  | 4133 |  | 4174 |  | 4215 |  | 4256 |  | 4297 |
|  | 4052 |  | 4093 |  | 4134 |  | 4175 |  | 4216 |  | 4257 |  | 4298 |
|  | 4053 |  | 4094 |  | 4135 |  | 4176 |  | 4217 |  | 4258 |  | 4299 |
|  | 4054 |  | 4095 |  | 4136 |  | 4177 |  | 4218 |  | 4259 |  | 4300 |
|  | 4055 |  | 4096 |  | 4137 |  | 4178 |  | 4219 |  | 4260 |  | 4301 |
|  | 4056 |  | 4097 |  | 4138 |  | 4179 |  | 4220 |  | 4261 |  | 4302 |
|  | 4057 |  | 4098 |  | 4139 |  | 4180 |  | 4221 |  | 4262 |  | 4303 |
|  | 4058 |  | 4099 |  | 4140 |  | 4181 |  | 4222 |  | 4263 |  | 4304 |
|  | 4059 |  | 4100 |  | 4141 |  | 4182 |  | 4223 |  | 4264 |  | 4305 |

Treatment number associated to material : Hz/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl. |  | Bl. | Trt | Bl nb | Trt | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{n} . \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4306 | PPD | 4347 | PPD | 4388 | PPD | 4429 | PPD | 4470 | PPD | 4511 | PPD | 4552 |
|  | 4307 |  | 4348 |  | 4389 |  | 4430 |  | 4471 |  | 4512 |  | 4553 |
|  | 4308 |  | 4349 |  | 4390 |  | 4431 |  | 4472 |  | 4513 |  | 4554 |
|  | 4309 |  | 4350 |  | 4391 |  | 4432 |  | 4473 |  | 4514 |  | 4555 |
|  | 4310 |  | 4351 |  | 4392 |  | 4433 |  | 4474 |  | 4515 |  | 4556 |
|  | 4311 |  | 4352 |  | 4393 |  | 4434 |  | 4475 |  | 4516 |  | 4557 |
|  | 4312 |  | 4353 |  | 4394 |  | 4435 |  | 4476 |  | 4517 |  | 4558 |
|  | 4313 |  | 4354 |  | 4395 |  | 4436 |  | 4477 |  | 4518 |  | 4559 |
|  | 4314 |  | 4355 |  | 4396 |  | 4437 |  | 4478 |  | 4519 |  | 4560 |
|  | 4315 |  | 4356 |  | 4397 |  | 4438 |  | 4479 |  | 4520 |  | 4561 |
|  | 4316 |  | 4357 |  | 4398 |  | 4439 |  | 4480 |  | 4521 |  | 4562 |
|  | 4317 |  | 4358 |  | 4399 |  | 4440 |  | 4481 |  | 4522 |  | 4563 |
|  | 4318 |  | 4359 |  | 4400 |  | 4441 |  | 4482 |  | 4523 |  | 4564 |
|  | 4319 |  | 4360 |  | 4401 |  | 4442 |  | 4483 |  | 4524 |  | 4565 |
|  | 4320 |  | 4361 |  | 4402 |  | 4443 |  | 4484 |  | 4525 |  | 4566 |
|  | 4321 |  | 4362 |  | 4403 |  | 4444 |  | 4485 |  | 4526 |  | 4567 |
|  | 4322 |  | 4363 |  | 4404 |  | 4445 |  | 4486 |  | 4527 |  | 4568 |
|  | 4323 |  | 4364 |  | 4405 |  | 4446 |  | 4487 |  | 4528 |  | 4569 |
|  | 4324 |  | 4365 |  | 4406 |  | 4447 |  | 4488 |  | 4529 |  | 4570 |
|  | 4325 |  | 4366 |  | 4407 |  | 4448 |  | 4489 |  | 4530 |  | 4571 |
|  | 4326 |  | 4367 |  | 4408 |  | 4449 |  | 4490 |  | 4531 |  | 4572 |
|  | 4327 |  | 4368 |  | 4409 |  | 4450 |  | 4491 |  | 4532 |  | 4573 |
|  | 4328 |  | 4369 |  | 4410 |  | 4451 |  | 4492 |  | 4533 |  | 4574 |
|  | 4329 |  | 4370 |  | 4411 |  | 4452 |  | 4493 |  | 4534 |  | 4575 |
|  | 4330 |  | 4371 |  | 4412 |  | 4453 |  | 4494 |  | 4535 |  | 4576 |
|  | 4331 |  | 4372 |  | 4413 |  | 4454 |  | 4495 |  | 4536 |  | 4577 |
|  | 4332 |  | 4373 |  | 4414 |  | 4455 |  | 4496 |  | 4537 |  | 4578 |
|  | 4333 |  | 4374 |  | 4415 |  | 4456 |  | 4497 |  | 4538 |  | 4579 |
|  | 4334 |  | 4375 |  | 4416 |  | 4457 |  | 4498 |  | 4539 |  | 4580 |
|  | 4335 |  | 4376 |  | 4417 |  | 4458 |  | 4499 |  | 4540 |  | 4581 |
|  | 4336 |  | 4377 |  | 4418 |  | 4459 |  | 4500 |  | 4541 |  | 4582 |
|  | 4337 |  | 4378 |  | 4419 |  | 4460 |  | 4501 |  | 4542 |  | 4583 |
|  | 4338 |  | 4379 |  | 4420 |  | 4461 |  | 4502 |  | 4543 |  | 4584 |
|  | 4339 |  | 4380 |  | 4421 |  | 4462 |  | 4503 |  | 4544 |  | 4585 |
|  | 4340 |  | 4381 |  | 4422 |  | 4463 |  | 4504 |  | 4545 |  | 4586 |
|  | 4341 |  | 4382 |  | 4423 |  | 4464 |  | 4505 |  | 4546 |  | 4587 |
|  | 4342 |  | 4383 |  | 4424 |  | 4465 |  | 4506 |  | 4547 |  | 4588 |
|  | 4343 |  | 4384 |  | 4425 |  | 4466 |  | 4507 |  | 4548 |  | 4589 |
|  | 4344 |  | 4385 |  | 4426 |  | 4467 |  | 4508 |  | 4549 |  | 4590 |
|  | 4345 |  | 4386 |  | 4427 |  | 4468 |  | 4509 |  | 4550 |  | 4591 |
|  | 4346 |  | 4387 |  | 4428 |  | 4469 |  | 4510 |  | 4551 |  | 4592 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. | Trt | Bl nb | Trt | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4593 | PPD | 4634 | PPD | 4675 | PPD | 4716 | PPD | 4757 | PPD | 4798 | PPD | 4839 |
|  | 4594 |  | 4635 |  | 4676 |  | 4717 |  | 4758 |  | 4799 |  | 4840 |
|  | 4595 |  | 4636 |  | 4677 |  | 4718 |  | 4759 |  | 4800 |  | 4841 |
|  | 4596 |  | 4637 |  | 4678 |  | 4719 |  | 4760 |  | 4801 |  | 4842 |
|  | 4597 |  | 4638 |  | 4679 |  | 4720 |  | 4761 |  | 4802 |  | 4843 |
|  | 4598 |  | 4639 |  | 4680 |  | 4721 |  | 4762 |  | 4803 |  | 4844 |
|  | 4599 |  | 4640 |  | 4681 |  | 4722 |  | 4763 |  | 4804 |  | 4845 |
|  | 4600 |  | 4641 |  | 4682 |  | 4723 |  | 4764 |  | 4805 |  | 4846 |
|  | 4601 |  | 4642 |  | 4683 |  | 4724 |  | 4765 |  | 4806 |  | 4847 |
|  | 4602 |  | 4643 |  | 4684 |  | 4725 |  | 4766 |  | 4807 |  | 4848 |
|  | 4603 |  | 4644 |  | 4685 |  | 4726 |  | 4767 |  | 4808 |  | 4849 |
|  | 4604 |  | 4645 |  | 4686 |  | 4727 |  | 4768 |  | 4809 |  | 4850 |
|  | 4605 |  | 4646 |  | 4687 |  | 4728 |  | 4769 |  | 4810 |  | 4851 |
|  | 4606 |  | 4647 |  | 4688 |  | 4729 |  | 4770 |  | 4811 |  | 4852 |
|  | 4607 |  | 4648 |  | 4689 |  | 4730 |  | 4771 |  | 4812 |  | 4853 |
|  | 4608 |  | 4649 |  | 4690 |  | 4731 |  | 4772 |  | 4813 |  | 4854 |
|  | 4609 |  | 4650 |  | 4691 |  | 4732 |  | 4773 |  | 4814 |  | 4855 |
|  | 4610 |  | 4651 |  | 4692 |  | 4733 |  | 4774 |  | 4815 |  | 4856 |
|  | 4611 |  | 4652 |  | 4693 |  | 4734 |  | 4775 |  | 4816 |  | 4857 |
|  | 4612 |  | 4653 |  | 4694 |  | 4735 |  | 4776 |  | 4817 |  | 4858 |
|  | 4613 |  | 4654 |  | 4695 |  | 4736 |  | 4777 |  | 4818 |  | 4859 |
|  | 4614 |  | 4655 |  | 4696 |  | 4737 |  | 4778 |  | 4819 |  | 4860 |
|  | 4615 |  | 4656 |  | 4697 |  | 4738 |  | 4779 |  | 4820 |  | 4861 |
|  | 4616 |  | 4657 |  | 4698 |  | 4739 |  | 4780 |  | 4821 |  | 4862 |
|  | 4617 |  | 4658 |  | 4699 |  | 4740 |  | 4781 |  | 4822 |  | 4863 |
|  | 4618 |  | 4659 |  | 4700 |  | 4741 |  | 4782 |  | 4823 |  | 4864 |
|  | 4619 |  | 4660 |  | 4701 |  | 4742 |  | 4783 |  | 4824 |  | 4865 |
|  | 4620 |  | 4661 |  | 4702 |  | 4743 |  | 4784 |  | 4825 |  | 4866 |
|  | 4621 |  | 4662 |  | 4703 |  | 4744 |  | 4785 |  | 4826 |  | 4867 |
|  | 4622 |  | 4663 |  | 4704 |  | 4745 |  | 4786 |  | 4827 |  | 4868 |
|  | 4623 |  | 4664 |  | 4705 |  | 4746 |  | 4787 |  | 4828 |  | 4869 |
|  | 4624 |  | 4665 |  | 4706 |  | 4747 |  | 4788 |  | 4829 |  | 4870 |
|  | 4625 |  | 4666 |  | 4707 |  | 4748 |  | 4789 |  | 4830 |  | 4871 |
|  | 4626 |  | 4667 |  | 4708 |  | 4749 |  | 4790 |  | 4831 |  | 4872 |
|  | 4627 |  | 4668 |  | 4709 |  | 4750 |  | 4791 |  | 4832 |  | 4873 |
|  | 4628 |  | 4669 |  | 4710 |  | 4751 |  | 4792 |  | 4833 |  | 4874 |
|  | 4629 |  | 4670 |  | 4711 |  | 4752 |  | 4793 |  | 4834 |  | 4875 |
|  | 4630 |  | 4671 |  | 4712 |  | 4753 |  | 4794 |  | 4835 |  | 4876 |
|  | 4631 |  | 4672 |  | 4713 |  | 4754 |  | 4795 |  | 4836 |  | 4877 |
|  | 4632 |  | 4673 |  | 4714 |  | 4755 |  | 4796 |  | 4837 |  | 4878 |
|  | 4633 |  | 4674 |  | 4715 |  | 4756 |  | 4797 |  | 4838 |  | 4879 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : HZ/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  | Trt |  | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4880 | PPD | 4921 | PPD | 4962 | PPD | 5003 | PPD | 5044 | PPD | 5085 | PPD | 5126 |
|  | 4881 |  | 4922 |  | 4963 |  | 5004 |  | 5045 |  | 5086 |  | 5127 |
|  | 4882 |  | 4923 |  | 4964 |  | 5005 |  | 5046 |  | 5087 |  | 5128 |
|  | 4883 |  | 4924 |  | 4965 |  | 5006 |  | 5047 |  | 5088 |  | 5129 |
|  | 4884 |  | 4925 |  | 4966 |  | 5007 |  | 5048 |  | 5089 |  | 5130 |
|  | 4885 |  | 4926 |  | 4967 |  | 5008 |  | 5049 |  | 5090 |  | 5131 |
|  | 4886 |  | 4927 |  | 4968 |  | 5009 |  | 5050 |  | 5091 |  | 5132 |
|  | 4887 |  | 4928 |  | 4969 |  | 5010 |  | 5051 |  | 5092 |  | 5133 |
|  | 4888 |  | 4929 |  | 4970 |  | 5011 |  | 5052 |  | 5093 |  | 5134 |
|  | 4889 |  | 4930 |  | 4971 |  | 5012 |  | 5053 |  | 5094 |  | 5135 |
|  | 4890 |  | 4931 |  | 4972 |  | 5013 |  | 5054 |  | 5095 |  | 5136 |
|  | 4891 |  | 4932 |  | 4973 |  | 5014 |  | 5055 |  | 5096 |  | 5137 |
|  | 4892 |  | 4933 |  | 4974 |  | 5015 |  | 5056 |  | 5097 |  | 5138 |
|  | 4893 |  | 4934 |  | 4975 |  | 5016 |  | 5057 |  | 5098 |  | 5139 |
|  | 4894 |  | 4935 |  | 4976 |  | 5017 |  | 5058 |  | 5099 |  | 5140 |
|  | 4895 |  | 4936 |  | 4977 |  | 5018 |  | 5059 |  | 5100 |  | 5141 |
|  | 4896 |  | 4937 |  | 4978 |  | 5019 |  | 5060 |  | 5101 |  | 5142 |
|  | 4897 |  | 4938 |  | 4979 |  | 5020 |  | 5061 |  | 5102 |  | 5143 |
|  | 4898 |  | 4939 |  | 4980 |  | 5021 |  | 5062 |  | 5103 |  | 5144 |
|  | 4899 |  | 4940 |  | 4981 |  | 5022 |  | 5063 |  | 5104 |  | 5145 |
|  | 4900 |  | 4941 |  | 4982 |  | 5023 |  | 5064 |  | 5105 |  | 5146 |
|  | 4901 |  | 4942 |  | 4983 |  | 5024 |  | 5065 |  | 5106 |  | 5147 |
|  | 4902 |  | 4943 |  | 4984 |  | 5025 |  | 5066 |  | 5107 |  | 5148 |
|  | 4903 |  | 4944 |  | 4985 |  | 5026 |  | 5067 |  | 5108 |  | 5149 |
|  | 4904 |  | 4945 |  | 4986 |  | 5027 |  | 5068 |  | 5109 |  | 5150 |
|  | 4905 |  | 4946 |  | 4987 |  | 5028 |  | 5069 |  | 5110 |  | 5151 |
|  | 4906 |  | 4947 |  | 4988 |  | 5029 |  | 5070 |  | 5111 |  | 5152 |
|  | 4907 |  | 4948 |  | 4989 |  | 5030 |  | 5071 |  | 5112 |  | 5153 |
|  | 4908 |  | 4949 |  | 4990 |  | 5031 |  | 5072 |  | 5113 |  | 5154 |
|  | 4909 |  | 4950 |  | 4991 |  | 5032 |  | 5073 |  | 5114 |  | 5155 |
|  | 4910 |  | 4951 |  | 4992 |  | 5033 |  | 5074 |  | 5115 |  | 5156 |
|  | 4911 |  | 4952 |  | 4993 |  | 5034 |  | 5075 |  | 5116 |  | 5157 |
|  | 4912 |  | 4953 |  | 4994 |  | 5035 |  | 5076 |  | 5117 |  | 5158 |
|  | 4913 |  | 4954 |  | 4995 |  | 5036 |  | 5077 |  | 5118 |  | 5159 |
|  | 4914 |  | 4955 |  | 4996 |  | 5037 |  | 5078 |  | 5119 |  | 5160 |
|  | 4915 |  | 4956 |  | 4997 |  | 5038 |  | 5079 |  | 5120 |  | 5161 |
|  | 4916 |  | 4957 |  | 4998 |  | 5039 |  | 5080 |  | 5121 |  | 5162 |
|  | 4917 |  | 4958 |  | 4999 |  | 5040 |  | 5081 |  | 5122 |  | 5163 |
|  | 4918 |  | 4959 |  | 5000 |  | 5041 |  | 5082 |  | 5123 |  | 5164 |
|  | 4919 |  | 4960 |  | 5001 |  | 5042 |  | 5083 |  | 5124 |  | 5165 |
|  | 4920 |  | 4961 |  | 5002 |  | 5043 |  | 5084 |  | 5125 |  | 5166 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  | Trt | Bl nb | Trt | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5167 | PPD | 5208 | PPD | 5249 | PPD | 5290 | PPD | 5331 | PPD | 5372 | PPD | 5413 |
|  | 5168 |  | 5209 |  | 5250 |  | 5291 |  | 5332 |  | 5373 |  | 5414 |
|  | 5169 |  | 5210 |  | 5251 |  | 5292 |  | 5333 |  | 5374 |  | 5415 |
|  | 5170 |  | 5211 |  | 5252 |  | 5293 |  | 5334 |  | 5375 |  | 5416 |
|  | 5171 |  | 5212 |  | 5253 |  | 5294 |  | 5335 |  | 5376 |  | 5417 |
|  | 5172 |  | 5213 |  | 5254 |  | 5295 |  | 5336 |  | 5377 |  | 5418 |
|  | 5173 |  | 5214 |  | 5255 |  | 5296 |  | 5337 |  | 5378 |  | 5419 |
|  | 5174 |  | 5215 |  | 5256 |  | 5297 |  | 5338 |  | 5379 |  | 5420 |
|  | 5175 |  | 5216 |  | 5257 |  | 5298 |  | 5339 |  | 5380 |  | 5421 |
|  | 5176 |  | 5217 |  | 5258 |  | 5299 |  | 5340 |  | 5381 |  | 5422 |
|  | 5177 |  | 5218 |  | 5259 |  | 5300 |  | 5341 |  | 5382 |  | 5423 |
|  | 5178 |  | 5219 |  | 5260 |  | 5301 |  | 5342 |  | 5383 |  | 5424 |
|  | 5179 |  | 5220 |  | 5261 |  | 5302 |  | 5343 |  | 5384 |  | 5425 |
|  | 5180 |  | 5221 |  | 5262 |  | 5303 |  | 5344 |  | 5385 |  | 5426 |
|  | 5181 |  | 5222 |  | 5263 |  | 5304 |  | 5345 |  | 5386 |  | 5427 |
|  | 5182 |  | 5223 |  | 5264 |  | 5305 |  | 5346 |  | 5387 |  | 5428 |
|  | 5183 |  | 5224 |  | 5265 |  | 5306 |  | 5347 |  | 5388 |  | 5429 |
|  | 5184 |  | 5225 |  | 5266 |  | 5307 |  | 5348 |  | 5389 |  | 5430 |
|  | 5185 |  | 5226 |  | 5267 |  | 5308 |  | 5349 |  | 5390 |  | 5431 |
|  | 5186 |  | 5227 |  | 5268 |  | 5309 |  | 5350 |  | 5391 |  | 5432 |
|  | 5187 |  | 5228 |  | 5269 |  | 5310 |  | 5351 |  | 5392 |  | 5433 |
|  | 5188 |  | 5229 |  | 5270 |  | 5311 |  | 5352 |  | 5393 |  | 5434 |
|  | 5189 |  | 5230 |  | 5271 |  | 5312 |  | 5353 |  | 5394 |  | 5435 |
|  | 5190 |  | 5231 |  | 5272 |  | 5313 |  | 5354 |  | 5395 |  | 5436 |
|  | 5191 |  | 5232 |  | 5273 |  | 5314 |  | 5355 |  | 5396 |  | 5437 |
|  | 5192 |  | 5233 |  | 5274 |  | 5315 |  | 5356 |  | 5397 |  | 5438 |
|  | 5193 |  | 5234 |  | 5275 |  | 5316 |  | 5357 |  | 5398 |  | 5439 |
|  | 5194 |  | 5235 |  | 5276 |  | 5317 |  | 5358 |  | 5399 |  | 5440 |
|  | 5195 |  | 5236 |  | 5277 |  | 5318 |  | 5359 |  | 5400 |  | 5441 |
|  | 5196 |  | 5237 |  | 5278 |  | 5319 |  | 5360 |  | 5401 |  | 5442 |
|  | 5197 |  | 5238 |  | 5279 |  | 5320 |  | 5361 |  | 5402 |  | 5443 |
|  | 5198 |  | 5239 |  | 5280 |  | 5321 |  | 5362 |  | 5403 |  | 5444 |
|  | 5199 |  | 5240 |  | 5281 |  | 5322 |  | 5363 |  | 5404 |  | 5445 |
|  | 5200 |  | 5241 |  | 5282 |  | 5323 |  | 5364 |  | 5405 |  | 5446 |
|  | 5201 |  | 5242 |  | 5283 |  | 5324 |  | 5365 |  | 5406 |  | 5447 |
|  | 5202 |  | 5243 |  | 5284 |  | 5325 |  | 5366 |  | 5407 |  | 5448 |
|  | 5203 |  | 5244 |  | 5285 |  | 5326 |  | 5367 |  | 5408 |  | 5449 |
|  | 5204 |  | 5245 |  | 5286 |  | 5327 |  | 5368 |  | 5409 |  | 5450 |
|  | 5205 |  | 5246 |  | 5287 |  | 5328 |  | 5369 |  | 5410 |  | 5451 |
|  | 5206 |  | 5247 |  | 5288 |  | 5329 |  | 5370 |  | 5411 |  | 5452 |
|  | 5207 |  | 5248 |  | 5289 |  | 5330 |  | 5371 |  | 5412 |  | 5453 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| Trt. |  |  |  |  | Bl. |  | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5454 | PPD | 5495 | PPD | 5536 | PPD | 5577 | PPD | 5618 | PPD | 5659 | PPD | 5700 |
|  | 5455 |  | 5496 |  | 5537 |  | 5578 |  | 5619 |  | 5660 |  | 5701 |
|  | 5456 |  | 5497 |  | 5538 |  | 5579 |  | 5620 |  | 5661 |  | 5702 |
|  | 5457 |  | 5498 |  | 5539 |  | 5580 |  | 5621 |  | 5662 |  | 5703 |
|  | 5458 |  | 5499 |  | 5540 |  | 5581 |  | 5622 |  | 5663 |  | 5704 |
|  | 5459 |  | 5500 |  | 5541 |  | 5582 |  | 5623 |  | 5664 |  | 5705 |
|  | 5460 |  | 5501 |  | 5542 |  | 5583 |  | 5624 |  | 5665 |  | 5706 |
|  | 5461 |  | 5502 |  | 5543 |  | 5584 |  | 5625 |  | 5666 |  | 5707 |
|  | 5462 |  | 5503 |  | 5544 |  | 5585 |  | 5626 |  | 5667 |  | 5708 |
|  | 5463 |  | 5504 |  | 5545 |  | 5586 |  | 5627 |  | 5668 |  | 5709 |
|  | 5464 |  | 5505 |  | 5546 |  | 5587 |  | 5628 |  | 5669 |  | 5710 |
|  | 5465 |  | 5506 |  | 5547 |  | 5588 |  | 5629 |  | 5670 |  | 5711 |
|  | 5466 |  | 5507 |  | 5548 |  | 5589 |  | 5630 |  | 5671 |  | 5712 |
|  | 5467 |  | 5508 |  | 5549 |  | 5590 |  | 5631 |  | 5672 |  | 5713 |
|  | 5468 |  | 5509 |  | 5550 |  | 5591 |  | 5632 |  | 5673 |  | 5714 |
|  | 5469 |  | 5510 |  | 5551 |  | 5592 |  | 5633 |  | 5674 |  | 5715 |
|  | 5470 |  | 5511 |  | 5552 |  | 5593 |  | 5634 |  | 5675 |  | 5716 |
|  | 5471 |  | 5512 |  | 5553 |  | 5594 |  | 5635 |  | 5676 |  | 5717 |
|  | 5472 |  | 5513 |  | 5554 |  | 5595 |  | 5636 |  | 5677 |  | 5718 |
|  | 5473 |  | 5514 |  | 5555 |  | 5596 |  | 5637 |  | 5678 |  | 5719 |
|  | 5474 |  | 5515 |  | 5556 |  | 5597 |  | 5638 |  | 5679 |  | 5720 |
|  | 5475 |  | 5516 |  | 5557 |  | 5598 |  | 5639 |  | 5680 |  | 5721 |
|  | 5476 |  | 5517 |  | 5558 |  | 5599 |  | 5640 |  | 5681 |  | 5722 |
|  | 5477 |  | 5518 |  | 5559 |  | 5600 |  | 5641 |  | 5682 |  | 5723 |
|  | 5478 |  | 5519 |  | 5560 |  | 5601 |  | 5642 |  | 5683 |  | 5724 |
|  | 5479 |  | 5520 |  | 5561 |  | 5602 |  | 5643 |  | 5684 |  | 5725 |
|  | 5480 |  | 5521 |  | 5562 |  | 5603 |  | 5644 |  | 5685 |  | 5726 |
|  | 5481 |  | 5522 |  | 5563 |  | 5604 |  | 5645 |  | 5686 |  | 5727 |
|  | 5482 |  | 5523 |  | 5564 |  | 5605 |  | 5646 |  | 5687 |  | 5728 |
|  | 5483 |  | 5524 |  | 5565 |  | 5606 |  | 5647 |  | 5688 |  | 5729 |
|  | 5484 |  | 5525 |  | 5566 |  | 5607 |  | 5648 |  | 5689 |  | 5730 |
|  | 5485 |  | 5526 |  | 5567 |  | 5608 |  | 5649 |  | 5690 |  | 5731 |
|  | 5486 |  | 5527 |  | 5568 |  | 5609 |  | 5650 |  | 5691 |  | 5732 |
|  | 5487 |  | 5528 |  | 5569 |  | 5610 |  | 5651 |  | 5692 |  | 5733 |
|  | 5488 |  | 5529 |  | 5570 |  | 5611 |  | 5652 |  | 5693 |  | 5734 |
|  | 5489 |  | 5530 |  | 5571 |  | 5612 |  | 5653 |  | 5694 |  | 5735 |
|  | 5490 |  | 5531 |  | 5572 |  | 5613 |  | 5654 |  | 5695 |  | 5736 |
|  | 5491 |  | 5532 |  | 5573 |  | 5614 |  | 5655 |  | 5696 |  | 5737 |
|  | 5492 |  | 5533 |  | 5574 |  | 5615 |  | 5656 |  | 5697 |  | 5738 |
|  | 5493 |  | 5534 |  | 5575 |  | 5616 |  | 5657 |  | 5698 |  | 5739 |
|  | 5494 |  | 5535 |  | 5576 |  | 5617 |  | 5658 |  | 5699 |  | 5740 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Hz/su-OnChemo

| Trt. | Bl nb | Trt |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5741 | PPD | 5782 | PPD | 5823 | PPD | 5864 | PPD | 5905 | PPD | 5946 | PPD | 5987 |
|  | 5742 |  | 5783 |  | 5824 |  | 5865 |  | 5906 |  | 5947 |  | 5988 |
|  | 5743 |  | 5784 |  | 5825 |  | 5866 |  | 5907 |  | 5948 |  | 5989 |
|  | 5744 |  | 5785 |  | 5826 |  | 5867 |  | 5908 |  | 5949 |  | 5990 |
|  | 5745 |  | 5786 |  | 5827 |  | 5868 |  | 5909 |  | 5950 |  | 5991 |
|  | 5746 |  | 5787 |  | 5828 |  | 5869 |  | 5910 |  | 5951 |  | 5992 |
|  | 5747 |  | 5788 |  | 5829 |  | 5870 |  | 5911 |  | 5952 |  | 5993 |
|  | 5748 |  | 5789 |  | 5830 |  | 5871 |  | 5912 |  | 5953 |  | 5994 |
|  | 5749 |  | 5790 |  | 5831 |  | 5872 |  | 5913 |  | 5954 |  | 5995 |
|  | 5750 |  | 5791 |  | 5832 |  | 5873 |  | 5914 |  | 5955 |  | 5996 |
|  | 5751 |  | 5792 |  | 5833 |  | 5874 |  | 5915 |  | 5956 |  | 5997 |
|  | 5752 |  | 5793 |  | 5834 |  | 5875 |  | 5916 |  | 5957 |  | 5998 |
|  | 5753 |  | 5794 |  | 5835 |  | 5876 |  | 5917 |  | 5958 |  | 5999 |
|  | 5754 |  | 5795 |  | 5836 |  | 5877 |  | 5918 |  | 5959 |  | 6000 |
|  | 5755 |  | 5796 |  | 5837 |  | 5878 |  | 5919 |  | 5960 |  |  |
|  | 5756 |  | 5797 |  | 5838 |  | 5879 |  | 5920 |  | 5961 |  |  |
|  | 5757 |  | 5798 |  | 5839 |  | 5880 |  | 5921 |  | 5962 |  |  |
|  | 5758 |  | 5799 |  | 5840 |  | 5881 |  | 5922 |  | 5963 |  |  |
|  | 5759 |  | 5800 |  | 5841 |  | 5882 |  | 5923 |  | 5964 |  |  |
|  | 5760 |  | 5801 |  | 5842 |  | 5883 |  | 5924 |  | 5965 |  |  |
|  | 5761 |  | 5802 |  | 5843 |  | 5884 |  | 5925 |  | 5966 |  |  |
|  | 5762 |  | 5803 |  | 5844 |  | 5885 |  | 5926 |  | 5967 |  |  |
|  | 5763 |  | 5804 |  | 5845 |  | 5886 |  | 5927 |  | 5968 |  |  |
|  | 5764 |  | 5805 |  | 5846 |  | 5887 |  | 5928 |  | 5969 |  |  |
|  | 5765 |  | 5806 |  | 5847 |  | 5888 |  | 5929 |  | 5970 |  |  |
|  | 5766 |  | 5807 |  | 5848 |  | 5889 |  | 5930 |  | 5971 |  |  |
|  | 5767 |  | 5808 |  | 5849 |  | 5890 |  | 5931 |  | 5972 |  |  |
|  | 5768 |  | 5809 |  | 5850 |  | 5891 |  | 5932 |  | 5973 |  |  |
|  | 5769 |  | 5810 |  | 5851 |  | 5892 |  | 5933 |  | 5974 |  |  |
|  | 5770 |  | 5811 |  | 5852 |  | 5893 |  | 5934 |  | 5975 |  |  |
|  | 5771 |  | 5812 |  | 5853 |  | 5894 |  | 5935 |  | 5976 |  |  |
|  | 5772 |  | 5813 |  | 5854 |  | 5895 |  | 5936 |  | 5977 |  |  |
|  | 5773 |  | 5814 |  | 5855 |  | 5896 |  | 5937 |  | 5978 |  |  |
|  | 5774 |  | 5815 |  | 5856 |  | 5897 |  | 5938 |  | 5979 |  |  |
|  | 5775 |  | 5816 |  | 5857 |  | 5898 |  | 5939 |  | 5980 |  |  |
|  | 5776 |  | 5817 |  | 5858 |  | 5899 |  | 5940 |  | 5981 |  |  |
|  | 5777 |  | 5818 |  | 5859 |  | 5900 |  | 5941 |  | 5982 |  |  |
|  | 5778 |  | 5819 |  | 5860 |  | 5901 |  | 5942 |  | 5983 |  |  |
|  | 5779 |  | 5820 |  | 5861 |  | 5902 |  | 5943 |  | 5984 |  |  |
|  | 5780 |  | 5821 |  | 5862 |  | 5903 |  | 5944 |  | 5985 |  |  |
|  | 5781 |  | 5822 |  | 5863 |  | 5904 |  | 5945 |  | 5986 |  |  |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{array}{r} \operatorname{Tr} t \\ \mathrm{~N} \end{array}$ |  | Trt. Bl.No nb |  | $\begin{array}{r} \text { Trt. Bl. } \\ \text { No nb } \end{array}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{gathered} \text { Trt. Bl. } \\ \text { No nb } \end{gathered}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1 | PPD | 42 | PPD | 83 | PPD | 124 | PPD | 165 | PPD | 206 | PPD | 247 |
|  | 2 |  | 43 |  | 84 |  | 125 |  | 166 |  | 207 |  | 248 |
|  | 3 |  | 44 |  | 85 |  | 126 |  | 167 |  | 208 |  | 249 |
|  | 4 |  | 45 |  | 86 |  | 127 |  | 168 |  | 209 |  | 250 |
|  | 5 |  | 46 |  | 87 |  | 128 |  | 169 |  | 210 |  | 251 |
|  | 6 |  | 47 |  | 88 |  | 129 |  | 170 |  | 211 |  | 252 |
|  | 7 |  | 48 |  | 89 |  | 130 |  | 171 |  | 212 |  | 253 |
|  | 8 |  | 49 |  | 90 |  | 131 |  | 172 |  | 213 |  | 254 |
|  | 9 |  | 50 |  | 91 |  | 132 |  | 173 |  | 214 |  | 255 |
|  | 10 |  | 51 |  | 92 |  | 133 |  | 174 |  | 215 |  | 256 |
|  | 11 |  | 52 |  | 93 |  | 134 |  | 175 |  | 216 |  | 257 |
|  | 12 |  | 53 |  | 94 |  | 135 |  | 176 |  | 217 |  | 258 |
|  | 13 |  | 54 |  | 95 |  | 136 |  | 177 |  | 218 |  | 259 |
|  | 14 |  | 55 |  | 96 |  | 137 |  | 178 |  | 219 |  | 260 |
|  | 15 |  | 56 |  | 97 |  | 138 |  | 179 |  | 220 |  | 261 |
|  | 16 |  | 57 |  | 98 |  | 139 |  | 180 |  | 221 |  | 262 |
|  | 17 |  | 58 |  | 99 |  | 140 |  | 181 |  | 222 |  | 263 |
|  | 18 |  | 59 |  | 100 |  | 141 |  | 182 |  | 223 |  | 264 |
|  | 19 |  | 60 |  | 101 |  | 142 |  | 183 |  | 224 |  | 265 |
|  | 20 |  | 61 |  | 102 |  | 143 |  | 184 |  | 225 |  | 266 |
|  | 21 |  | 62 |  | 103 |  | 144 |  | 185 |  | 226 |  | 267 |
|  | 22 |  | 63 |  | 104 |  | 145 |  | 186 |  | 227 |  | 268 |
|  | 23 |  | 64 |  | 105 |  | 146 |  | 187 |  | 228 |  | 269 |
|  | 24 |  | 65 |  | 106 |  | 147 |  | 188 |  | 229 |  | 270 |
|  | 25 |  | 66 |  | 107 |  | 148 |  | 189 |  | 230 |  | 271 |
|  | 26 |  | 67 |  | 108 |  | 149 |  | 190 |  | 231 |  | 272 |
|  | 27 |  | 68 |  | 109 |  | 150 |  | 191 |  | 232 |  | 273 |
|  | 28 |  | 69 |  | 110 |  | 151 |  | 192 |  | 233 |  | 274 |
|  | 29 |  | 70 |  | 111 |  | 152 |  | 193 |  | 234 |  | 275 |
|  | 30 |  | 71 |  | 112 |  | 153 |  | 194 |  | 235 |  | 276 |
|  | 31 |  | 72 |  | 113 |  | 154 |  | 195 |  | 236 |  | 277 |
|  | 32 |  | 73 |  | 114 |  | 155 |  | 196 |  | 237 |  | 278 |
|  | 33 |  | 74 |  | 115 |  | 156 |  | 197 |  | 238 |  | 279 |
|  | 34 |  | 75 |  | 116 |  | 157 |  | 198 |  | 239 |  | 280 |
|  | 35 |  | 76 |  | 117 |  | 158 |  | 199 |  | 240 |  | 281 |
|  | 36 |  | 77 |  | 118 |  | 159 |  | 200 |  | 241 |  | 282 |
|  | 37 |  | 78 |  | 119 |  | 160 |  | 201 |  | 242 |  | 283 |
|  | 38 |  | 79 |  | 120 |  | 161 |  | 202 |  | 243 |  | 284 |
|  | 39 |  | 80 |  | 121 |  | 162 |  | 203 |  | 244 |  | 285 |
|  | 40 |  | 81 |  | 122 |  | 163 |  | 204 |  | 245 |  | 286 |
|  | 41 |  | 82 |  | 123 |  | 164 |  | 205 |  | 246 |  | 287 |

SD4\RDE\ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 288 | PPD | 329 | PPD | 370 | PPD | 411 | PPD | 452 | PPD | 493 | PPD | 534 |
|  | 289 |  | 330 |  | 371 |  | 412 |  | 453 |  | 494 |  | 535 |
|  | 290 |  | 331 |  | 372 |  | 413 |  | 454 |  | 495 |  | 536 |
|  | 291 |  | 332 |  | 373 |  | 414 |  | 455 |  | 496 |  | 537 |
|  | 292 |  | 333 |  | 374 |  | 415 |  | 456 |  | 497 |  | 538 |
|  | 293 |  | 334 |  | 375 |  | 416 |  | 457 |  | 498 |  | 539 |
|  | 294 |  | 335 |  | 376 |  | 417 |  | 458 |  | 499 |  | 540 |
|  | 295 |  | 336 |  | 377 |  | 418 |  | 459 |  | 500 |  | 541 |
|  | 296 |  | 337 |  | 378 |  | 419 |  | 460 |  | 501 |  | 542 |
|  | 297 |  | 338 |  | 379 |  | 420 |  | 461 |  | 502 |  | 543 |
|  | 298 |  | 339 |  | 380 |  | 421 |  | 462 |  | 503 |  | 544 |
|  | 299 |  | 340 |  | 381 |  | 422 |  | 463 |  | 504 |  | 545 |
|  | 300 |  | 341 |  | 382 |  | 423 |  | 464 |  | 505 |  | 546 |
|  | 301 |  | 342 |  | 383 |  | 424 |  | 465 |  | 506 |  | 547 |
|  | 302 |  | 343 |  | 384 |  | 425 |  | 466 |  | 507 |  | 548 |
|  | 303 |  | 344 |  | 385 |  | 426 |  | 467 |  | 508 |  | 549 |
|  | 304 |  | 345 |  | 386 |  | 427 |  | 468 |  | 509 |  | 550 |
|  | 305 |  | 346 |  | 387 |  | 428 |  | 469 |  | 510 |  | 551 |
|  | 306 |  | 347 |  | 388 |  | 429 |  | 470 |  | 511 |  | 552 |
|  | 307 |  | 348 |  | 389 |  | 430 |  | 471 |  | 512 |  | 553 |
|  | 308 |  | 349 |  | 390 |  | 431 |  | 472 |  | 513 |  | 554 |
|  | 309 |  | 350 |  | 391 |  | 432 |  | 473 |  | 514 |  | 555 |
|  | 310 |  | 351 |  | 392 |  | 433 |  | 474 |  | 515 |  | 556 |
|  | 311 |  | 352 |  | 393 |  | 434 |  | 475 |  | 516 |  | 557 |
|  | 312 |  | 353 |  | 394 |  | 435 |  | 476 |  | 517 |  | 558 |
|  | 313 |  | 354 |  | 395 |  | 436 |  | 477 |  | 518 |  | 559 |
|  | 314 |  | 355 |  | 396 |  | 437 |  | 478 |  | 519 |  | 560 |
|  | 315 |  | 356 |  | 397 |  | 438 |  | 479 |  | 520 |  | 561 |
|  | 316 |  | 357 |  | 398 |  | 439 |  | 480 |  | 521 |  | 562 |
|  | 317 |  | 358 |  | 399 |  | 440 |  | 481 |  | 522 |  | 563 |
|  | 318 |  | 359 |  | 400 |  | 441 |  | 482 |  | 523 |  | 564 |
|  | 319 |  | 360 |  | 401 |  | 442 |  | 483 |  | 524 |  | 565 |
|  | 320 |  | 361 |  | 402 |  | 443 |  | 484 |  | 525 |  | 566 |
|  | 321 |  | 362 |  | 403 |  | 444 |  | 485 |  | 526 |  | 567 |
|  | 322 |  | 363 |  | 404 |  | 445 |  | 486 |  | 527 |  | 568 |
|  | 323 |  | 364 |  | 405 |  | 446 |  | 487 |  | 528 |  | 569 |
|  | 324 |  | 365 |  | 406 |  | 447 |  | 488 |  | 529 |  | 570 |
|  | 325 |  | 366 |  | 407 |  | 448 |  | 489 |  | 530 |  | 571 |
|  | 326 |  | 367 |  | 408 |  | 449 |  | 490 |  | 531 |  | 572 |
|  | 327 |  | 368 |  | 409 |  | 450 |  | 491 |  | 532 |  | 573 |
|  | 328 |  | 369 |  | 410 |  | 451 |  | 492 |  | 533 |  | 574 |

SD4 $\backslash$ RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | Trt. Bl.No nb |  | Trt. Bl.No nb |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 575 | PPD | 616 | PPD | 657 | PPD | 698 | PPD | 739 | PPD | 780 | PPD | 821 |
|  | 576 |  | 617 |  | 658 |  | 699 |  | 740 |  | 781 |  | 822 |
|  | 577 |  | 618 |  | 659 |  | 700 |  | 741 |  | 782 |  | 823 |
|  | 578 |  | 619 |  | 660 |  | 701 |  | 742 |  | 783 |  | 824 |
|  | 579 |  | 620 |  | 661 |  | 702 |  | 743 |  | 784 |  | 825 |
|  | 580 |  | 621 |  | 662 |  | 703 |  | 744 |  | 785 |  | 826 |
|  | 581 |  | 622 |  | 663 |  | 704 |  | 745 |  | 786 |  | 827 |
|  | 582 |  | 623 |  | 664 |  | 705 |  | 746 |  | 787 |  | 828 |
|  | 583 |  | 624 |  | 665 |  | 706 |  | 747 |  | 788 |  | 829 |
|  | 584 |  | 625 |  | 666 |  | 707 |  | 748 |  | 789 |  | 830 |
|  | 585 |  | 626 |  | 667 |  | 708 |  | 749 |  | 790 |  | 831 |
|  | 586 |  | 627 |  | 668 |  | 709 |  | 750 |  | 791 |  | 832 |
|  | 587 |  | 628 |  | 669 |  | 710 |  | 751 |  | 792 |  | 833 |
|  | 588 |  | 629 |  | 670 |  | 711 |  | 752 |  | 793 |  | 834 |
|  | 589 |  | 630 |  | 671 |  | 712 |  | 753 |  | 794 |  | 835 |
|  | 590 |  | 631 |  | 672 |  | 713 |  | 754 |  | 795 |  | 836 |
|  | 591 |  | 632 |  | 673 |  | 714 |  | 755 |  | 796 |  | 837 |
|  | 592 |  | 633 |  | 674 |  | 715 |  | 756 |  | 797 |  | 838 |
|  | 593 |  | 634 |  | 675 |  | 716 |  | 757 |  | 798 |  | 839 |
|  | 594 |  | 635 |  | 676 |  | 717 |  | 758 |  | 799 |  | 840 |
|  | 595 |  | 636 |  | 677 |  | 718 |  | 759 |  | 800 |  | 841 |
|  | 596 |  | 637 |  | 678 |  | 719 |  | 760 |  | 801 |  | 842 |
|  | 597 |  | 638 |  | 679 |  | 720 |  | 761 |  | 802 |  | 843 |
|  | 598 |  | 639 |  | 680 |  | 721 |  | 762 |  | 803 |  | 844 |
|  | 599 |  | 640 |  | 681 |  | 722 |  | 763 |  | 804 |  | 845 |
|  | 600 |  | 641 |  | 682 |  | 723 |  | 764 |  | 805 |  | 846 |
|  | 601 |  | 642 |  | 683 |  | 724 |  | 765 |  | 806 |  | 847 |
|  | 602 |  | 643 |  | 684 |  | 725 |  | 766 |  | 807 |  | 848 |
|  | 603 |  | 644 |  | 685 |  | 726 |  | 767 |  | 808 |  | 849 |
|  | 604 |  | 645 |  | 686 |  | 727 |  | 768 |  | 809 |  | 850 |
|  | 605 |  | 646 |  | 687 |  | 728 |  | 769 |  | 810 |  | 851 |
|  | 606 |  | 647 |  | 688 |  | 729 |  | 770 |  | 811 |  | 852 |
|  | 607 |  | 648 |  | 689 |  | 730 |  | 771 |  | 812 |  | 853 |
|  | 608 |  | 649 |  | 690 |  | 731 |  | 772 |  | 813 |  | 854 |
|  | 609 |  | 650 |  | 691 |  | 732 |  | 773 |  | 814 |  | 855 |
|  | 610 |  | 651 |  | 692 |  | 733 |  | 774 |  | 815 |  | 856 |
|  | 611 |  | 652 |  | 693 |  | 734 |  | 775 |  | 816 |  | 857 |
|  | 612 |  | 653 |  | 694 |  | 735 |  | 776 |  | 817 |  | 858 |
|  | 613 |  | 654 |  | 695 |  | 736 |  | 777 |  | 818 |  | 859 |
|  | 614 |  | 655 |  | 696 |  | 737 |  | 778 |  | 819 |  | 860 |
|  | 615 |  | 656 |  | 697 |  | 738 |  | 779 |  | 820 |  | 861 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 862 | PPD | 903 | PPD | 944 | PPD | 985 | PPD | 1026 | PPD | 1067 | PPD | 1108 |
|  | 863 |  | 904 |  | 945 |  | 986 |  | 1027 |  | 1068 |  | 1109 |
|  | 864 |  | 905 |  | 946 |  | 987 |  | 1028 |  | 1069 |  | 1110 |
|  | 865 |  | 906 |  | 947 |  | 988 |  | 1029 |  | 1070 |  | 1111 |
|  | 866 |  | 907 |  | 948 |  | 989 |  | 1030 |  | 1071 |  | 1112 |
|  | 867 |  | 908 |  | 949 |  | 990 |  | 1031 |  | 1072 |  | 1113 |
|  | 868 |  | 909 |  | 950 |  | 991 |  | 1032 |  | 1073 |  | 1114 |
|  | 869 |  | 910 |  | 951 |  | 992 |  | 1033 |  | 1074 |  | 1115 |
|  | 870 |  | 911 |  | 952 |  | 993 |  | 1034 |  | 1075 |  | 1116 |
|  | 871 |  | 912 |  | 953 |  | 994 |  | 1035 |  | 1076 |  | 1117 |
|  | 872 |  | 913 |  | 954 |  | 995 |  | 1036 |  | 1077 |  | 1118 |
|  | 873 |  | 914 |  | 955 |  | 996 |  | 1037 |  | 1078 |  | 1119 |
|  | 874 |  | 915 |  | 956 |  | 997 |  | 1038 |  | 1079 |  | 1120 |
|  | 875 |  | 916 |  | 957 |  | 998 |  | 1039 |  | 1080 |  | 1121 |
|  | 876 |  | 917 |  | 958 |  | 999 |  | 1040 |  | 1081 |  | 1122 |
|  | 877 |  | 918 |  | 959 |  | 1000 |  | 1041 |  | 1082 |  | 1123 |
|  | 878 |  | 919 |  | 960 |  | 1001 |  | 1042 |  | 1083 |  | 1124 |
|  | 879 |  | 920 |  | 961 |  | 1002 |  | 1043 |  | 1084 |  | 1125 |
|  | 880 |  | 921 |  | 962 |  | 1003 |  | 1044 |  | 1085 |  | 1126 |
|  | 881 |  | 922 |  | 963 |  | 1004 |  | 1045 |  | 1086 |  | 1127 |
|  | 882 |  | 923 |  | 964 |  | 1005 |  | 1046 |  | 1087 |  | 1128 |
|  | 883 |  | 924 |  | 965 |  | 1006 |  | 1047 |  | 1088 |  | 1129 |
|  | 884 |  | 925 |  | 966 |  | 1007 |  | 1048 |  | 1089 |  | 1130 |
|  | 885 |  | 926 |  | 967 |  | 1008 |  | 1049 |  | 1090 |  | 1131 |
|  | 886 |  | 927 |  | 968 |  | 1009 |  | 1050 |  | 1091 |  | 1132 |
|  | 887 |  | 928 |  | 969 |  | 1010 |  | 1051 |  | 1092 |  | 1133 |
|  | 888 |  | 929 |  | 970 |  | 1011 |  | 1052 |  | 1093 |  | 1134 |
|  | 889 |  | 930 |  | 971 |  | 1012 |  | 1053 |  | 1094 |  | 1135 |
|  | 890 |  | 931 |  | 972 |  | 1013 |  | 1054 |  | 1095 |  | 1136 |
|  | 891 |  | 932 |  | 973 |  | 1014 |  | 1055 |  | 1096 |  | 1137 |
|  | 892 |  | 933 |  | 974 |  | 1015 |  | 1056 |  | 1097 |  | 1138 |
|  | 893 |  | 934 |  | 975 |  | 1016 |  | 1057 |  | 1098 |  | 1139 |
|  | 894 |  | 935 |  | 976 |  | 1017 |  | 1058 |  | 1099 |  | 1140 |
|  | 895 |  | 936 |  | 977 |  | 1018 |  | 1059 |  | 1100 |  | 1141 |
|  | 896 |  | 937 |  | 978 |  | 1019 |  | 1060 |  | 1101 |  | 1142 |
|  | 897 |  | 938 |  | 979 |  | 1020 |  | 1061 |  | 1102 |  | 1143 |
|  | 898 |  | 939 |  | 980 |  | 1021 |  | 1062 |  | 1103 |  | 1144 |
|  | 899 |  | 940 |  | 981 |  | 1022 |  | 1063 |  | 1104 |  | 1145 |
|  | 900 |  | 941 |  | 982 |  | 1023 |  | 1064 |  | 1105 |  | 1146 |
|  | 901 |  | 942 |  | 983 |  | 1024 |  | 1065 |  | 1106 |  | 1147 |
|  | 902 |  | 943 |  | 984 |  | 1025 |  | 1066 |  | 1107 |  | 1148 |

Treatment number associated to material : Placeb-OnChemo

| Trt. |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1149 | PPD | 1190 | PPD | 1231 | PPD | 1272 | PPD | 1313 | PPD | 1354 | PPD | 1395 |
|  | 1150 |  | 1191 |  | 1232 |  | 1273 |  | 1314 |  | 1355 |  | 1396 |
|  | 1151 |  | 1192 |  | 1233 |  | 1274 |  | 1315 |  | 1356 |  | 1397 |
|  | 1152 |  | 1193 |  | 1234 |  | 1275 |  | 1316 |  | 1357 |  | 1398 |
|  | 1153 |  | 1194 |  | 1235 |  | 1276 |  | 1317 |  | 1358 |  | 1399 |
|  | 1154 |  | 1195 |  | 1236 |  | 1277 |  | 1318 |  | 1359 |  | 1400 |
|  | 1155 |  | 1196 |  | 1237 |  | 1278 |  | 1319 |  | 1360 |  | 1401 |
|  | 1156 |  | 1197 |  | 1238 |  | 1279 |  | 1320 |  | 1361 |  | 1402 |
|  | 1157 |  | 1198 |  | 1239 |  | 1280 |  | 1321 |  | 1362 |  | 1403 |
|  | 1158 |  | 1199 |  | 1240 |  | 1281 |  | 1322 |  | 1363 |  | 1404 |
|  | 1159 |  | 1200 |  | 1241 |  | 1282 |  | 1323 |  | 1364 |  | 1405 |
|  | 1160 |  | 1201 |  | 1242 |  | 1283 |  | 1324 |  | 1365 |  | 1406 |
|  | 1161 |  | 1202 |  | 1243 |  | 1284 |  | 1325 |  | 1366 |  | 1407 |
|  | 1162 |  | 1203 |  | 1244 |  | 1285 |  | 1326 |  | 1367 |  | 1408 |
|  | 1163 |  | 1204 |  | 1245 |  | 1286 |  | 1327 |  | 1368 |  | 1409 |
|  | 1164 |  | 1205 |  | 1246 |  | 1287 |  | 1328 |  | 1369 |  | 1410 |
|  | 1165 |  | 1206 |  | 1247 |  | 1288 |  | 1329 |  | 1370 |  | 1411 |
|  | 1166 |  | 1207 |  | 1248 |  | 1289 |  | 1330 |  | 1371 |  | 1412 |
|  | 1167 |  | 1208 |  | 1249 |  | 1290 |  | 1331 |  | 1372 |  | 1413 |
|  | 1168 |  | 1209 |  | 1250 |  | 1291 |  | 1332 |  | 1373 |  | 1414 |
|  | 1169 |  | 1210 |  | 1251 |  | 1292 |  | 1333 |  | 1374 |  | 1415 |
|  | 1170 |  | 1211 |  | 1252 |  | 1293 |  | 1334 |  | 1375 |  | 1416 |
|  | 1171 |  | 1212 |  | 1253 |  | 1294 |  | 1335 |  | 1376 |  | 1417 |
|  | 1172 |  | 1213 |  | 1254 |  | 1295 |  | 1336 |  | 1377 |  | 1418 |
|  | 1173 |  | 1214 |  | 1255 |  | 1296 |  | 1337 |  | 1378 |  | 1419 |
|  | 1174 |  | 1215 |  | 1256 |  | 1297 |  | 1338 |  | 1379 |  | 1420 |
|  | 1175 |  | 1216 |  | 1257 |  | 1298 |  | 1339 |  | 1380 |  | 1421 |
|  | 1176 |  | 1217 |  | 1258 |  | 1299 |  | 1340 |  | 1381 |  | 1422 |
|  | 1177 |  | 1218 |  | 1259 |  | 1300 |  | 1341 |  | 1382 |  | 1423 |
|  | 1178 |  | 1219 |  | 1260 |  | 1301 |  | 1342 |  | 1383 |  | 1424 |
|  | 1179 |  | 1220 |  | 1261 |  | 1302 |  | 1343 |  | 1384 |  | 1425 |
|  | 1180 |  | 1221 |  | 1262 |  | 1303 |  | 1344 |  | 1385 |  | 1426 |
|  | 1181 |  | 1222 |  | 1263 |  | 1304 |  | 1345 |  | 1386 |  | 1427 |
|  | 1182 |  | 1223 |  | 1264 |  | 1305 |  | 1346 |  | 1387 |  | 1428 |
|  | 1183 |  | 1224 |  | 1265 |  | 1306 |  | 1347 |  | 1388 |  | 1429 |
|  | 1184 |  | 1225 |  | 1266 |  | 1307 |  | 1348 |  | 1389 |  | 1430 |
|  | 1185 |  | 1226 |  | 1267 |  | 1308 |  | 1349 |  | 1390 |  | 1431 |
|  | 1186 |  | 1227 |  | 1268 |  | 1309 |  | 1350 |  | 1391 |  | 1432 |
|  | 1187 |  | 1228 |  | 1269 |  | 1310 |  | 1351 |  | 1392 |  | 1433 |
|  | 1188 |  | 1229 |  | 1270 |  | 1311 |  | 1352 |  | 1393 |  | 1434 |
|  | 1189 |  | 1230 |  | 1271 |  | 1312 |  | 1353 |  | 1394 |  | 1435 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo


SD4 4 RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ |  |  | Bl nb |  | Bl nb |  | Bl. |  |  |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 1723 | PPD | 1764 | PPD | 1805 | PPD | 1846 | PPD | 1887 | PPD | 1928 | PPD | 1969 |
|  | 1724 |  | 1765 |  | 1806 |  | 1847 |  | 1888 |  | 1929 |  | 1970 |
|  | 1725 |  | 1766 |  | 1807 |  | 1848 |  | 1889 |  | 1930 |  | 1971 |
|  | 1726 |  | 1767 |  | 1808 |  | 1849 |  | 1890 |  | 1931 |  | 1972 |
|  | 1727 |  | 1768 |  | 1809 |  | 1850 |  | 1891 |  | 1932 |  | 1973 |
|  | 1728 |  | 1769 |  | 1810 |  | 1851 |  | 1892 |  | 1933 |  | 1974 |
|  | 1729 |  | 1770 |  | 1811 |  | 1852 |  | 1893 |  | 1934 |  | 1975 |
|  | 1730 |  | 1771 |  | 1812 |  | 1853 |  | 1894 |  | 1935 |  | 1976 |
|  | 1731 |  | 1772 |  | 1813 |  | 1854 |  | 1895 |  | 1936 |  | 1977 |
|  | 1732 |  | 1773 |  | 1814 |  | 1855 |  | 1896 |  | 1937 |  | 1978 |
|  | 1733 |  | 1774 |  | 1815 |  | 1856 |  | 1897 |  | 1938 |  | 1979 |
|  | 1734 |  | 1775 |  | 1816 |  | 1857 |  | 1898 |  | 1939 |  | 1980 |
|  | 1735 |  | 1776 |  | 1817 |  | 1858 |  | 1899 |  | 1940 |  | 1981 |
|  | 1736 |  | 1777 |  | 1818 |  | 1859 |  | 1900 |  | 1941 |  | 1982 |
|  | 1737 |  | 1778 |  | 1819 |  | 1860 |  | 1901 |  | 1942 |  | 1983 |
|  | 1738 |  | 1779 |  | 1820 |  | 1861 |  | 1902 |  | 1943 |  | 1984 |
|  | 1739 |  | 1780 |  | 1821 |  | 1862 |  | 1903 |  | 1944 |  | 1985 |
|  | 1740 |  | 1781 |  | 1822 |  | 1863 |  | 1904 |  | 1945 |  | 1986 |
|  | 1741 |  | 1782 |  | 1823 |  | 1864 |  | 1905 |  | 1946 |  | 1987 |
|  | 1742 |  | 1783 |  | 1824 |  | 1865 |  | 1906 |  | 1947 |  | 1988 |
|  | 1743 |  | 1784 |  | 1825 |  | 1866 |  | 1907 |  | 1948 |  | 1989 |
|  | 1744 |  | 1785 |  | 1826 |  | 1867 |  | 1908 |  | 1949 |  | 1990 |
|  | 1745 |  | 1786 |  | 1827 |  | 1868 |  | 1909 |  | 1950 |  | 1991 |
|  | 1746 |  | 1787 |  | 1828 |  | 1869 |  | 1910 |  | 1951 |  | 1992 |
|  | 1747 |  | 1788 |  | 1829 |  | 1870 |  | 1911 |  | 1952 |  | 1993 |
|  | 1748 |  | 1789 |  | 1830 |  | 1871 |  | 1912 |  | 1953 |  | 1994 |
|  | 1749 |  | 1790 |  | 1831 |  | 1872 |  | 1913 |  | 1954 |  | 1995 |
|  | 1750 |  | 1791 |  | 1832 |  | 1873 |  | 1914 |  | 1955 |  | 1996 |
|  | 1751 |  | 1792 |  | 1833 |  | 1874 |  | 1915 |  | 1956 |  | 1997 |
|  | 1752 |  | 1793 |  | 1834 |  | 1875 |  | 1916 |  | 1957 |  | 1998 |
|  | 1753 |  | 1794 |  | 1835 |  | 1876 |  | 1917 |  | 1958 |  | 1999 |
|  | 1754 |  | 1795 |  | 1836 |  | 1877 |  | 1918 |  | 1959 |  | 2000 |
|  | 1755 |  | 1796 |  | 1837 |  | 1878 |  | 1919 |  | 1960 |  | 2001 |
|  | 1756 |  | 1797 |  | 1838 |  | 1879 |  | 1920 |  | 1961 |  | 2002 |
|  | 1757 |  | 1798 |  | 1839 |  | 1880 |  | 1921 |  | 1962 |  | 2003 |
|  | 1758 |  | 1799 |  | 1840 |  | 1881 |  | 1922 |  | 1963 |  | 2004 |
|  | 1759 |  | 1800 |  | 1841 |  | 1882 |  | 1923 |  | 1964 |  | 2005 |
|  | 1760 |  | 1801 |  | 1842 |  | 1883 |  | 1924 |  | 1965 |  | 2006 |
|  | 1761 |  | 1802 |  | 1843 |  | 1884 |  | 1925 |  | 1966 |  | 2007 |
|  | 1762 |  | 1803 |  | 1844 |  | 1885 |  | 1926 |  | 1967 |  | 2008 |
|  | 1763 |  | 1804 |  | 1845 |  | 1886 |  | 1927 |  | 1968 |  | 2009 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{array}{ll} \mathrm{Bl} . \\ \mathrm{nb} \end{array}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2010 | PPD | 2051 | PPD | 2092 | PPD | 2133 | PPD | 2174 | PPD | 2215 | PPD | 2256 |
| PPD | 2011 | PPD | 2052 |  | 2093 |  | 2134 |  | 2175 |  | 2216 |  | 2257 |
|  | 2012 |  | 2053 |  | 2094 |  | 2135 |  | 2176 |  | 2217 |  | 2258 |
|  | 2013 |  | 2054 |  | 2095 |  | 2136 |  | 2177 |  | 2218 |  | 2259 |
|  | 2014 |  | 2055 |  | 2096 |  | 2137 |  | 2178 |  | 2219 |  | 2260 |
|  | 2015 |  | 2056 |  | 2097 |  | 2138 |  | 2179 |  | 2220 |  | 2261 |
|  | 2016 |  | 2057 |  | 2098 |  | 2139 |  | 2180 |  | 2221 |  | 2262 |
|  | 2017 |  | 2058 |  | 2099 |  | 2140 |  | 2181 |  | 2222 |  | 2263 |
|  | 2018 |  | 2059 |  | 2100 |  | 2141 |  | 2182 |  | 2223 |  | 2264 |
|  | 2019 |  | 2060 |  | 2101 |  | 2142 |  | 2183 |  | 2224 |  | 2265 |
|  | 2020 |  | 2061 |  | 2102 |  | 2143 |  | 2184 |  | 2225 |  | 2266 |
|  | 2021 |  | 2062 |  | 2103 |  | 2144 |  | 2185 |  | 2226 |  | 2267 |
|  | 2022 |  | 2063 |  | 2104 |  | 2145 |  | 2186 |  | 2227 |  | 2268 |
|  | 2023 |  | 2064 |  | 2105 |  | 2146 |  | 2187 |  | 2228 |  | 2269 |
|  | 2024 |  | 2065 |  | 2106 |  | 2147 |  | 2188 |  | 2229 |  | 2270 |
|  | 2025 |  | 2066 |  | 2107 |  | 2148 |  | 2189 |  | 2230 |  | 2271 |
|  | 2026 |  | 2067 |  | 2108 |  | 2149 |  | 2190 |  | 2231 |  | 2272 |
|  | 2027 |  | 2068 |  | 2109 |  | 2150 |  | 2191 |  | 2232 |  | 2273 |
|  | 2028 |  | 2069 |  | 2110 |  | 2151 |  | 2192 |  | 2233 |  | 2274 |
|  | 2029 |  | 2070 |  | 2111 |  | 2152 |  | 2193 |  | 2234 |  | 2275 |
|  | 2030 |  | 2071 |  | 2112 |  | 2153 |  | 2194 |  | 2235 |  | 2276 |
|  | 2031 |  | 2072 |  | 2113 |  | 2154 |  | 2195 |  | 2236 |  | 2277 |
|  | 2032 |  | 2073 |  | 2114 |  | 2155 |  | 2196 |  | 2237 |  | 2278 |
|  | 2033 |  | 2074 |  | 2115 |  | 2156 |  | 2197 |  | 2238 |  | 2279 |
|  | 2034 |  | 2075 |  | 2116 |  | 2157 |  | 2198 |  | 2239 |  | 2280 |
|  | 2035 |  | 2076 |  | 2117 |  | 2158 |  | 2199 |  | 2240 |  | 2281 |
|  | 2036 |  | 2077 |  | 2118 |  | 2159 |  | 2200 |  | 2241 |  | 2282 |
|  | 2037 |  | 2078 |  | 2119 |  | 2160 |  | 2201 |  | 2242 |  | 2283 |
|  | 2038 |  | 2079 |  | 2120 |  | 2161 |  | 2202 |  | 2243 |  | 2284 |
|  | 2039 |  | 2080 |  | 2121 |  | 2162 |  | 2203 |  | 2244 |  | 2285 |
|  | 2040 |  | 2081 |  | 2122 |  | 2163 |  | 2204 |  | 2245 |  | 2286 |
|  | 2041 |  | 2082 |  | 2123 |  | 2164 |  | 2205 |  | 2246 |  | 2287 |
|  | 2042 |  | 2083 |  | 2124 |  | 2165 |  | 2206 |  | 2247 |  | 2288 |
|  | 2043 |  | 2084 |  | 2125 |  | 2166 |  | 2207 |  | 2248 |  | 2289 |
|  | 2044 |  | 2085 |  | 2126 |  | 2167 |  | 2208 |  | 2249 |  | 2290 |
|  | 2045 |  | 2086 |  | 2127 |  | 2168 |  | 2209 |  | 2250 |  | 2291 |
|  | 2046 |  | 2087 |  | 2128 |  | 2169 |  | 2210 |  | 2251 |  | 2292 |
|  | 2047 |  | 2088 |  | 2129 |  | 2170 |  | 2211 |  | 2252 |  | 2293 |
|  | 2048 |  | 2089 |  | 2130 |  | 2171 |  | 2212 |  | 2253 |  | 2294 |
|  | 2049 |  | 2090 |  | 2131 |  | 2172 |  | 2213 |  | 2254 |  | 2295 |
|  | 2050 |  | 2091 |  | 2132 |  | 2173 |  | 2214 |  | 2255 |  | 2296 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt |  |  | Bl nb |  | Bl nb |  | Bl. |  | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2297 | PPD | 2338 | PPD | 2379 | PPD | 2420 | PPD | 2461 | PPD | 2502 | PPD | 2543 |
|  | 2298 |  | 2339 |  | 2380 |  | 2421 |  | 2462 |  | 2503 |  | 2544 |
|  | 2299 |  | 2340 |  | 2381 |  | 2422 |  | 2463 |  | 2504 |  | 2545 |
|  | 2300 |  | 2341 |  | 2382 |  | 2423 |  | 2464 |  | 2505 |  | 2546 |
|  | 2301 |  | 2342 |  | 2383 |  | 2424 |  | 2465 |  | 2506 |  | 2547 |
|  | 2302 |  | 2343 |  | 2384 |  | 2425 |  | 2466 |  | 2507 |  | 2548 |
|  | 2303 |  | 2344 |  | 2385 |  | 2426 |  | 2467 |  | 2508 |  | 2549 |
|  | 2304 |  | 2345 |  | 2386 |  | 2427 |  | 2468 |  | 2509 |  | 2550 |
|  | 2305 |  | 2346 |  | 2387 |  | 2428 |  | 2469 |  | 2510 |  | 2551 |
|  | 2306 |  | 2347 |  | 2388 |  | 2429 |  | 2470 |  | 2511 |  | 2552 |
|  | 2307 |  | 2348 |  | 2389 |  | 2430 |  | 2471 |  | 2512 |  | 2553 |
|  | 2308 |  | 2349 |  | 2390 |  | 2431 |  | 2472 |  | 2513 |  | 2554 |
|  | 2309 |  | 2350 |  | 2391 |  | 2432 |  | 2473 |  | 2514 |  | 2555 |
|  | 2310 |  | 2351 |  | 2392 |  | 2433 |  | 2474 |  | 2515 |  | 2556 |
|  | 2311 |  | 2352 |  | 2393 |  | 2434 |  | 2475 |  | 2516 |  | 2557 |
|  | 2312 |  | 2353 |  | 2394 |  | 2435 |  | 2476 |  | 2517 |  | 2558 |
|  | 2313 |  | 2354 |  | 2395 |  | 2436 |  | 2477 |  | 2518 |  | 2559 |
|  | 2314 |  | 2355 |  | 2396 |  | 2437 |  | 2478 |  | 2519 |  | 2560 |
|  | 2315 |  | 2356 |  | 2397 |  | 2438 |  | 2479 |  | 2520 |  | 2561 |
|  | 2316 |  | 2357 |  | 2398 |  | 2439 |  | 2480 |  | 2521 |  | 2562 |
|  | 2317 |  | 2358 |  | 2399 |  | 2440 |  | 2481 |  | 2522 |  | 2563 |
|  | 2318 |  | 2359 |  | 2400 |  | 2441 |  | 2482 |  | 2523 |  | 2564 |
|  | 2319 |  | 2360 |  | 2401 |  | 2442 |  | 2483 |  | 2524 |  | 2565 |
|  | 2320 |  | 2361 |  | 2402 |  | 2443 |  | 2484 |  | 2525 |  | 2566 |
|  | 2321 |  | 2362 |  | 2403 |  | 2444 |  | 2485 |  | 2526 |  | 2567 |
|  | 2322 |  | 2363 |  | 2404 |  | 2445 |  | 2486 |  | 2527 |  | 2568 |
|  | 2323 |  | 2364 |  | 2405 |  | 2446 |  | 2487 |  | 2528 |  | 2569 |
|  | 2324 |  | 2365 |  | 2406 |  | 2447 |  | 2488 |  | 2529 |  | 2570 |
|  | 2325 |  | 2366 |  | 2407 |  | 2448 |  | 2489 |  | 2530 |  | 2571 |
|  | 2326 |  | 2367 |  | 2408 |  | 2449 |  | 2490 |  | 2531 |  | 2572 |
|  | 2327 |  | 2368 |  | 2409 |  | 2450 |  | 2491 |  | 2532 |  | 2573 |
|  | 2328 |  | 2369 |  | 2410 |  | 2451 |  | 2492 |  | 2533 |  | 2574 |
|  | 2329 |  | 2370 |  | 2411 |  | 2452 |  | 2493 |  | 2534 |  | 2575 |
|  | 2330 |  | 2371 |  | 2412 |  | 2453 |  | 2494 |  | 2535 |  | 2576 |
|  | 2331 |  | 2372 |  | 2413 |  | 2454 |  | 2495 |  | 2536 |  | 2577 |
|  | 2332 |  | 2373 |  | 2414 |  | 2455 |  | 2496 |  | 2537 |  | 2578 |
|  | 2333 |  | 2374 |  | 2415 |  | 2456 |  | 2497 |  | 2538 |  | 2579 |
|  | 2334 |  | 2375 |  | 2416 |  | 2457 |  | 2498 |  | 2539 |  | 2580 |
|  | 2335 |  | 2376 |  | 2417 |  | 2458 |  | 2499 |  | 2540 |  | 2581 |
|  | 2336 |  | 2377 |  | 2418 |  | 2459 |  | 2500 |  | 2541 |  | 2582 |
|  | 2337 |  | 2378 |  | 2419 |  | 2460 |  | 2501 |  | 2542 |  | 2583 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| Trt. |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | Bl. | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2584 | PPD | 2625 | PPD | 2666 | PPD | 2707 | PPD | 2748 | PPD | 2789 | PPD | 2830 |
|  | 2585 |  | 2626 |  | 2667 |  | 2708 |  | 2749 |  | 2790 |  | 2831 |
|  | 2586 |  | 2627 |  | 2668 |  | 2709 |  | 2750 |  | 2791 |  | 2832 |
|  | 2587 |  | 2628 |  | 2669 |  | 2710 |  | 2751 |  | 2792 |  | 2833 |
|  | 2588 |  | 2629 |  | 2670 |  | 2711 |  | 2752 |  | 2793 |  | 2834 |
|  | 2589 |  | 2630 |  | 2671 |  | 2712 |  | 2753 |  | 2794 |  | 2835 |
|  | 2590 |  | 2631 |  | 2672 |  | 2713 |  | 2754 |  | 2795 |  | 2836 |
|  | 2591 |  | 2632 |  | 2673 |  | 2714 |  | 2755 |  | 2796 |  | 2837 |
|  | 2592 |  | 2633 |  | 2674 |  | 2715 |  | 2756 |  | 2797 |  | 2838 |
|  | 2593 |  | 2634 |  | 2675 |  | 2716 |  | 2757 |  | 2798 |  | 2839 |
|  | 2594 |  | 2635 |  | 2676 |  | 2717 |  | 2758 |  | 2799 |  | 2840 |
|  | 2595 |  | 2636 |  | 2677 |  | 2718 |  | 2759 |  | 2800 |  | 2841 |
|  | 2596 |  | 2637 |  | 2678 |  | 2719 |  | 2760 |  | 2801 |  | 2842 |
|  | 2597 |  | 2638 |  | 2679 |  | 2720 |  | 2761 |  | 2802 |  | 2843 |
|  | 2598 |  | 2639 |  | 2680 |  | 2721 |  | 2762 |  | 2803 |  | 2844 |
|  | 2599 |  | 2640 |  | 2681 |  | 2722 |  | 2763 |  | 2804 |  | 2845 |
|  | 2600 |  | 2641 |  | 2682 |  | 2723 |  | 2764 |  | 2805 |  | 2846 |
|  | 2601 |  | 2642 |  | 2683 |  | 2724 |  | 2765 |  | 2806 |  | 2847 |
|  | 2602 |  | 2643 |  | 2684 |  | 2725 |  | 2766 |  | 2807 |  | 2848 |
|  | 2603 |  | 2644 |  | 2685 |  | 2726 |  | 2767 |  | 2808 |  | 2849 |
|  | 2604 |  | 2645 |  | 2686 |  | 2727 |  | 2768 |  | 2809 |  | 2850 |
|  | 2605 |  | 2646 |  | 2687 |  | 2728 |  | 2769 |  | 2810 |  | 2851 |
|  | 2606 |  | 2647 |  | 2688 |  | 2729 |  | 2770 |  | 2811 |  | 2852 |
|  | 2607 |  | 2648 |  | 2689 |  | 2730 |  | 2771 |  | 2812 |  | 2853 |
|  | 2608 |  | 2649 |  | 2690 |  | 2731 |  | 2772 |  | 2813 |  | 2854 |
|  | 2609 |  | 2650 |  | 2691 |  | 2732 |  | 2773 |  | 2814 |  | 2855 |
|  | 2610 |  | 2651 |  | 2692 |  | 2733 |  | 2774 |  | 2815 |  | 2856 |
|  | 2611 |  | 2652 |  | 2693 |  | 2734 |  | 2775 |  | 2816 |  | 2857 |
|  | 2612 |  | 2653 |  | 2694 |  | 2735 |  | 2776 |  | 2817 |  | 2858 |
|  | 2613 |  | 2654 |  | 2695 |  | 2736 |  | 2777 |  | 2818 |  | 2859 |
|  | 2614 |  | 2655 |  | 2696 |  | 2737 |  | 2778 |  | 2819 |  | 2860 |
|  | 2615 |  | 2656 |  | 2697 |  | 2738 |  | 2779 |  | 2820 |  | 2861 |
|  | 2616 |  | 2657 |  | 2698 |  | 2739 |  | 2780 |  | 2821 |  | 2862 |
|  | 2617 |  | 2658 |  | 2699 |  | 2740 |  | 2781 |  | 2822 |  | 2863 |
|  | 2618 |  | 2659 |  | 2700 |  | 2741 |  | 2782 |  | 2823 |  | 2864 |
|  | 2619 |  | 2660 |  | 2701 |  | 2742 |  | 2783 |  | 2824 |  | 2865 |
|  | 2620 |  | 2661 |  | 2702 |  | 2743 |  | 2784 |  | 2825 |  | 2866 |
|  | 2621 |  | 2662 |  | 2703 |  | 2744 |  | 2785 |  | 2826 |  | 2867 |
|  | 2622 |  | 2663 |  | 2704 |  | 2745 |  | 2786 |  | 2827 |  | 2868 |
|  | 2623 |  | 2664 |  | 2705 |  | 2746 |  | 2787 |  | 2828 |  | 2869 |
|  | 2624 |  | 2665 |  | 2706 |  | 2747 |  | 2788 |  | 2829 |  | 2870 |

Treatment number associated to material : Placeb-OnChemo

| Trt. |  |  | $\mathrm{Bl} \mathrm{nb}^{\text {nb }}$ |  |  |  | $\mathrm{Bl} \text {. }$ |  | $\mathrm{Bl} \text {. }$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 2871 | PPD | 2912 | PPD | 2953 | PPD | 2994 | PPD | 3035 | PPD | 3076 | PPD | 3117 |
|  | 2872 |  | 2913 |  | 2954 |  | 2995 |  | 3036 |  | 3077 |  | 3118 |
|  | 2873 |  | 2914 |  | 2955 |  | 2996 |  | 3037 |  | 3078 |  | 3119 |
|  | 2874 |  | 2915 |  | 2956 |  | 2997 |  | 3038 |  | 3079 |  | 3120 |
|  | 2875 |  | 2916 |  | 2957 |  | 2998 |  | 3039 |  | 3080 |  | 3121 |
|  | 2876 |  | 2917 |  | 2958 |  | 2999 |  | 3040 |  | 3081 |  | 3122 |
|  | 2877 |  | 2918 |  | 2959 |  | 3000 |  | 3041 |  | 3082 |  | 3123 |
|  | 2878 |  | 2919 |  | 2960 |  | 3001 |  | 3042 |  | 3083 |  | 3124 |
|  | 2879 |  | 2920 |  | 2961 |  | 3002 |  | 3043 |  | 3084 |  | 3125 |
|  | 2880 |  | 2921 |  | 2962 |  | 3003 |  | 3044 |  | 3085 |  | 3126 |
|  | 2881 |  | 2922 |  | 2963 |  | 3004 |  | 3045 |  | 3086 |  | 3127 |
|  | 2882 |  | 2923 |  | 2964 |  | 3005 |  | 3046 |  | 3087 |  | 3128 |
|  | 2883 |  | 2924 |  | 2965 |  | 3006 |  | 3047 |  | 3088 |  | 3129 |
|  | 2884 |  | 2925 |  | 2966 |  | 3007 |  | 3048 |  | 3089 |  | 3130 |
|  | 2885 |  | 2926 |  | 2967 |  | 3008 |  | 3049 |  | 3090 |  | 3131 |
|  | 2886 |  | 2927 |  | 2968 |  | 3009 |  | 3050 |  | 3091 |  | 3132 |
|  | 2887 |  | 2928 |  | 2969 |  | 3010 |  | 3051 |  | 3092 |  | 3133 |
|  | 2888 |  | 2929 |  | 2970 |  | 3011 |  | 3052 |  | 3093 |  | 3134 |
|  | 2889 |  | 2930 |  | 2971 |  | 3012 |  | 3053 |  | 3094 |  | 3135 |
|  | 2890 |  | 2931 |  | 2972 |  | 3013 |  | 3054 |  | 3095 |  | 3136 |
|  | 2891 |  | 2932 |  | 2973 |  | 3014 |  | 3055 |  | 3096 |  | 3137 |
|  | 2892 |  | 2933 |  | 2974 |  | 3015 |  | 3056 |  | 3097 |  | 3138 |
|  | 2893 |  | 2934 |  | 2975 |  | 3016 |  | 3057 |  | 3098 |  | 3139 |
|  | 2894 |  | 2935 |  | 2976 |  | 3017 |  | 3058 |  | 3099 |  | 3140 |
|  | 2895 |  | 2936 |  | 2977 |  | 3018 |  | 3059 |  | 3100 |  | 3141 |
|  | 2896 |  | 2937 |  | 2978 |  | 3019 |  | 3060 |  | 3101 |  | 3142 |
|  | 2897 |  | 2938 |  | 2979 |  | 3020 |  | 3061 |  | 3102 |  | 3143 |
|  | 2898 |  | 2939 |  | 2980 |  | 3021 |  | 3062 |  | 3103 |  | 3144 |
|  | 2899 |  | 2940 |  | 2981 |  | 3022 |  | 3063 |  | 3104 |  | 3145 |
|  | 2900 |  | 2941 |  | 2982 |  | 3023 |  | 3064 |  | 3105 |  | 3146 |
|  | 2901 |  | 2942 |  | 2983 |  | 3024 |  | 3065 |  | 3106 |  | 3147 |
|  | 2902 |  | 2943 |  | 2984 |  | 3025 |  | 3066 |  | 3107 |  | 3148 |
|  | 2903 |  | 2944 |  | 2985 |  | 3026 |  | 3067 |  | 3108 |  | 3149 |
|  | 2904 |  | 2945 |  | 2986 |  | 3027 |  | 3068 |  | 3109 |  | 3150 |
|  | 2905 |  | 2946 |  | 2987 |  | 3028 |  | 3069 |  | 3110 |  | 3151 |
|  | 2906 |  | 2947 |  | 2988 |  | 3029 |  | 3070 |  | 3111 |  | 3152 |
|  | 2907 |  | 2948 |  | 2989 |  | 3030 |  | 3071 |  | 3112 |  | 3153 |
|  | 2908 |  | 2949 |  | 2990 |  | 3031 |  | 3072 |  | 3113 |  | 3154 |
|  | 2909 |  | 2950 |  | 2991 |  | 3032 |  | 3073 |  | 3114 |  | 3155 |
|  | 2910 |  | 2951 |  | 2992 |  | 3033 |  | 3074 |  | 3115 |  | 3156 |
|  | 2911 |  | 2952 |  | 2993 |  | 3034 |  | 3075 |  | 3116 |  | 3157 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | Trt. Bl. No nb |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3158 | PPD | 3199 | PPD | 3240 | PPD | 3281 | PPD | 3322 | PPD | 3363 | PPD | 3404 |
|  | 3159 |  | 3200 |  | 3241 |  | 3282 |  | 3323 |  | 3364 |  | 3405 |
|  | 3160 |  | 3201 |  | 3242 |  | 3283 |  | 3324 |  | 3365 |  | 3406 |
|  | 3161 |  | 3202 |  | 3243 |  | 3284 |  | 3325 |  | 3366 |  | 3407 |
|  | 3162 |  | 3203 |  | 3244 |  | 3285 |  | 3326 |  | 3367 |  | 3408 |
|  | 3163 |  | 3204 |  | 3245 |  | 3286 |  | 3327 |  | 3368 |  | 3409 |
|  | 3164 |  | 3205 |  | 3246 |  | 3287 |  | 3328 |  | 3369 |  | 3410 |
|  | 3165 |  | 3206 |  | 3247 |  | 3288 |  | 3329 |  | 3370 |  | 3411 |
|  | 3166 |  | 3207 |  | 3248 |  | 3289 |  | 3330 |  | 3371 |  | 3412 |
|  | 3167 |  | 3208 |  | 3249 |  | 3290 |  | 3331 |  | 3372 |  | 3413 |
|  | 3168 |  | 3209 |  | 3250 |  | 3291 |  | 3332 |  | 3373 |  | 3414 |
|  | 3169 |  | 3210 |  | 3251 |  | 3292 |  | 3333 |  | 3374 |  | 3415 |
|  | 3170 |  | 3211 |  | 3252 |  | 3293 |  | 3334 |  | 3375 |  | 3416 |
|  | 3171 |  | 3212 |  | 3253 |  | 3294 |  | 3335 |  | 3376 |  | 3417 |
|  | 3172 |  | 3213 |  | 3254 |  | 3295 |  | 3336 |  | 3377 |  | 3418 |
|  | 3173 |  | 3214 |  | 3255 |  | 3296 |  | 3337 |  | 3378 |  | 3419 |
|  | 3174 |  | 3215 |  | 3256 |  | 3297 |  | 3338 |  | 3379 |  | 3420 |
|  | 3175 |  | 3216 |  | 3257 |  | 3298 |  | 3339 |  | 3380 |  | 3421 |
|  | 3176 |  | 3217 |  | 3258 |  | 3299 |  | 3340 |  | 3381 |  | 3422 |
|  | 3177 |  | 3218 |  | 3259 |  | 3300 |  | 3341 |  | 3382 |  | 3423 |
|  | 3178 |  | 3219 |  | 3260 |  | 3301 |  | 3342 |  | 3383 |  | 3424 |
|  | 3179 |  | 3220 |  | 3261 |  | 3302 |  | 3343 |  | 3384 |  | 3425 |
|  | 3180 |  | 3221 |  | 3262 |  | 3303 |  | 3344 |  | 3385 |  | 3426 |
|  | 3181 |  | 3222 |  | 3263 |  | 3304 |  | 3345 |  | 3386 |  | 3427 |
|  | 3182 |  | 3223 |  | 3264 |  | 3305 |  | 3346 |  | 3387 |  | 3428 |
|  | 3183 |  | 3224 |  | 3265 |  | 3306 |  | 3347 |  | 3388 |  | 3429 |
|  | 3184 |  | 3225 |  | 3266 |  | 3307 |  | 3348 |  | 3389 |  | 3430 |
|  | 3185 |  | 3226 |  | 3267 |  | 3308 |  | 3349 |  | 3390 |  | 3431 |
|  | 3186 |  | 3227 |  | 3268 |  | 3309 |  | 3350 |  | 3391 |  | 3432 |
|  | 3187 |  | 3228 |  | 3269 |  | 3310 |  | 3351 |  | 3392 |  | 3433 |
|  | 3188 |  | 3229 |  | 3270 |  | 3311 |  | 3352 |  | 3393 |  | 3434 |
|  | 3189 |  | 3230 |  | 3271 |  | 3312 |  | 3353 |  | 3394 |  | 3435 |
|  | 3190 |  | 3231 |  | 3272 |  | 3313 |  | 3354 |  | 3395 |  | 3436 |
|  | 3191 |  | 3232 |  | 3273 |  | 3314 |  | 3355 |  | 3396 |  | 3437 |
|  | 3192 |  | 3233 |  | 3274 |  | 3315 |  | 3356 |  | 3397 |  | 3438 |
|  | 3193 |  | 3234 |  | 3275 |  | 3316 |  | 3357 |  | 3398 |  | 3439 |
|  | 3194 |  | 3235 |  | 3276 |  | 3317 |  | 3358 |  | 3399 |  | 3440 |
|  | 3195 |  | 3236 |  | 3277 |  | 3318 |  | 3359 |  | 3400 |  | 3441 |
|  | 3196 |  | 3237 |  | 3278 |  | 3319 |  | 3360 |  | 3401 |  | 3442 |
|  | 3197 |  | 3238 |  | 3279 |  | 3320 |  | 3361 |  | 3402 |  | 3443 |
|  | 3198 |  | 3239 |  | 3280 |  | 3321 |  | 3362 |  | 3403 |  | 3444 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text { n. } \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3445 | PPD | 3486 | PPD | 3527 | PPD | 3568 | PPD | 3609 | PPD | 3650 | PPD | 3691 |
|  | 3446 |  | 3487 |  | 3528 |  | 3569 |  | 3610 |  | 3651 |  | 3692 |
|  | 3447 |  | 3488 |  | 3529 |  | 3570 |  | 3611 |  | 3652 |  | 3693 |
|  | 3448 |  | 3489 |  | 3530 |  | 3571 |  | 3612 |  | 3653 |  | 3694 |
|  | 3449 |  | 3490 |  | 3531 |  | 3572 |  | 3613 |  | 3654 |  | 3695 |
|  | 3450 |  | 3491 |  | 3532 |  | 3573 |  | 3614 |  | 3655 |  | 3696 |
|  | 3451 |  | 3492 |  | 3533 |  | 3574 |  | 3615 |  | 3656 |  | 3697 |
|  | 3452 |  | 3493 |  | 3534 |  | 3575 |  | 3616 |  | 3657 |  | 3698 |
|  | 3453 |  | 3494 |  | 3535 |  | 3576 |  | 3617 |  | 3658 |  | 3699 |
|  | 3454 |  | 3495 |  | 3536 |  | 3577 |  | 3618 |  | 3659 |  | 3700 |
|  | 3455 |  | 3496 |  | 3537 |  | 3578 |  | 3619 |  | 3660 |  | 3701 |
|  | 3456 |  | 3497 |  | 3538 |  | 3579 |  | 3620 |  | 3661 |  | 3702 |
|  | 3457 |  | 3498 |  | 3539 |  | 3580 |  | 3621 |  | 3662 |  | 3703 |
|  | 3458 |  | 3499 |  | 3540 |  | 3581 |  | 3622 |  | 3663 |  | 3704 |
|  | 3459 |  | 3500 |  | 3541 |  | 3582 |  | 3623 |  | 3664 |  | 3705 |
|  | 3460 |  | 3501 |  | 3542 |  | 3583 |  | 3624 |  | 3665 |  | 3706 |
|  | 3461 |  | 3502 |  | 3543 |  | 3584 |  | 3625 |  | 3666 |  | 3707 |
|  | 3462 |  | 3503 |  | 3544 |  | 3585 |  | 3626 |  | 3667 |  | 3708 |
|  | 3463 |  | 3504 |  | 3545 |  | 3586 |  | 3627 |  | 3668 |  | 3709 |
|  | 3464 |  | 3505 |  | 3546 |  | 3587 |  | 3628 |  | 3669 |  | 3710 |
|  | 3465 |  | 3506 |  | 3547 |  | 3588 |  | 3629 |  | 3670 |  | 3711 |
|  | 3466 |  | 3507 |  | 3548 |  | 3589 |  | 3630 |  | 3671 |  | 3712 |
|  | 3467 |  | 3508 |  | 3549 |  | 3590 |  | 3631 |  | 3672 |  | 3713 |
|  | 3468 |  | 3509 |  | 3550 |  | 3591 |  | 3632 |  | 3673 |  | 3714 |
|  | 3469 |  | 3510 |  | 3551 |  | 3592 |  | 3633 |  | 3674 |  | 3715 |
|  | 3470 |  | 3511 |  | 3552 |  | 3593 |  | 3634 |  | 3675 |  | 3716 |
|  | 3471 |  | 3512 |  | 3553 |  | 3594 |  | 3635 |  | 3676 |  | 3717 |
|  | 3472 |  | 3513 |  | 3554 |  | 3595 |  | 3636 |  | 3677 |  | 3718 |
|  | 3473 |  | 3514 |  | 3555 |  | 3596 |  | 3637 |  | 3678 |  | 3719 |
|  | 3474 |  | 3515 |  | 3556 |  | 3597 |  | 3638 |  | 3679 |  | 3720 |
|  | 3475 |  | 3516 |  | 3557 |  | 3598 |  | 3639 |  | 3680 |  | 3721 |
|  | 3476 |  | 3517 |  | 3558 |  | 3599 |  | 3640 |  | 3681 |  | 3722 |
|  | 3477 |  | 3518 |  | 3559 |  | 3600 |  | 3641 |  | 3682 |  | 3723 |
|  | 3478 |  | 3519 |  | 3560 |  | 3601 |  | 3642 |  | 3683 |  | 3724 |
|  | 3479 |  | 3520 |  | 3561 |  | 3602 |  | 3643 |  | 3684 |  | 3725 |
|  | 3480 |  | 3521 |  | 3562 |  | 3603 |  | 3644 |  | 3685 |  | 3726 |
|  | 3481 |  | 3522 |  | 3563 |  | 3604 |  | 3645 |  | 3686 |  | 3727 |
|  | 3482 |  | 3523 |  | 3564 |  | 3605 |  | 3646 |  | 3687 |  | 3728 |
|  | 3483 |  | 3524 |  | 3565 |  | 3606 |  | 3647 |  | 3688 |  | 3729 |
|  | 3484 |  | 3525 |  | 3566 |  | 3607 |  | 3648 |  | 3689 |  | 3730 |
|  | 3485 |  | 3526 |  | 3567 |  | 3608 |  | 3649 |  | 3690 |  | 3731 |

SD4 4 RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 3732 | PPD | 3773 | PPD | 3814 | PPD | 3855 | PPD | 3896 | PPD | 3937 | PPD | 3978 |
|  | 3733 |  | 3774 |  | 3815 |  | 3856 |  | 3897 |  | 3938 |  | 3979 |
|  | 3734 |  | 3775 |  | 3816 |  | 3857 |  | 3898 |  | 3939 |  | 3980 |
|  | 3735 |  | 3776 |  | 3817 |  | 3858 |  | 3899 |  | 3940 |  | 3981 |
|  | 3736 |  | 3777 |  | 3818 |  | 3859 |  | 3900 |  | 3941 |  | 3982 |
|  | 3737 |  | 3778 |  | 3819 |  | 3860 |  | 3901 |  | 3942 |  | 3983 |
|  | 3738 |  | 3779 |  | 3820 |  | 3861 |  | 3902 |  | 3943 |  | 3984 |
|  | 3739 |  | 3780 |  | 3821 |  | 3862 |  | 3903 |  | 3944 |  | 3985 |
|  | 3740 |  | 3781 |  | 3822 |  | 3863 |  | 3904 |  | 3945 |  | 3986 |
|  | 3741 |  | 3782 |  | 3823 |  | 3864 |  | 3905 |  | 3946 |  | 3987 |
|  | 3742 |  | 3783 |  | 3824 |  | 3865 |  | 3906 |  | 3947 |  | 3988 |
|  | 3743 |  | 3784 |  | 3825 |  | 3866 |  | 3907 |  | 3948 |  | 3989 |
|  | 3744 |  | 3785 |  | 3826 |  | 3867 |  | 3908 |  | 3949 |  | 3990 |
|  | 3745 |  | 3786 |  | 3827 |  | 3868 |  | 3909 |  | 3950 |  | 3991 |
|  | 3746 |  | 3787 |  | 3828 |  | 3869 |  | 3910 |  | 3951 |  | 3992 |
|  | 3747 |  | 3788 |  | 3829 |  | 3870 |  | 3911 |  | 3952 |  | 3993 |
|  | 3748 |  | 3789 |  | 3830 |  | 3871 |  | 3912 |  | 3953 |  | 3994 |
|  | 3749 |  | 3790 |  | 3831 |  | 3872 |  | 3913 |  | 3954 |  | 3995 |
|  | 3750 |  | 3791 |  | 3832 |  | 3873 |  | 3914 |  | 3955 |  | 3996 |
|  | 3751 |  | 3792 |  | 3833 |  | 3874 |  | 3915 |  | 3956 |  | 3997 |
|  | 3752 |  | 3793 |  | 3834 |  | 3875 |  | 3916 |  | 3957 |  | 3998 |
|  | 3753 |  | 3794 |  | 3835 |  | 3876 |  | 3917 |  | 3958 |  | 3999 |
|  | 3754 |  | 3795 |  | 3836 |  | 3877 |  | 3918 |  | 3959 |  | 4000 |
|  | 3755 |  | 3796 |  | 3837 |  | 3878 |  | 3919 |  | 3960 |  | 4001 |
|  | 3756 |  | 3797 |  | 3838 |  | 3879 |  | 3920 |  | 3961 |  | 4002 |
|  | 3757 |  | 3798 |  | 3839 |  | 3880 |  | 3921 |  | 3962 |  | 4003 |
|  | 3758 |  | 3799 |  | 3840 |  | 3881 |  | 3922 |  | 3963 |  | 4004 |
|  | 3759 |  | 3800 |  | 3841 |  | 3882 |  | 3923 |  | 3964 |  | 4005 |
|  | 3760 |  | 3801 |  | 3842 |  | 3883 |  | 3924 |  | 3965 |  | 4006 |
|  | 3761 |  | 3802 |  | 3843 |  | 3884 |  | 3925 |  | 3966 |  | 4007 |
|  | 3762 |  | 3803 |  | 3844 |  | 3885 |  | 3926 |  | 3967 |  | 4008 |
|  | 3763 |  | 3804 |  | 3845 |  | 3886 |  | 3927 |  | 3968 |  | 4009 |
|  | 3764 |  | 3805 |  | 3846 |  | 3887 |  | 3928 |  | 3969 |  | 4010 |
|  | 3765 |  | 3806 |  | 3847 |  | 3888 |  | 3929 |  | 3970 |  | 4011 |
|  | 3766 |  | 3807 |  | 3848 |  | 3889 |  | 3930 |  | 3971 |  | 4012 |
|  | 3767 |  | 3808 |  | 3849 |  | 3890 |  | 3931 |  | 3972 |  | 4013 |
|  | 3768 |  | 3809 |  | 3850 |  | 3891 |  | 3932 |  | 3973 |  | 4014 |
|  | 3769 |  | 3810 |  | 3851 |  | 3892 |  | 3933 |  | 3974 |  | 4015 |
|  | 3770 |  | 3811 |  | 3852 |  | 3893 |  | 3934 |  | 3975 |  | 4016 |
|  | 3771 |  | 3812 |  | 3853 |  | 3894 |  | 3935 |  | 3976 |  | 4017 |
|  | 3772 |  | 3813 |  | 3854 |  | 3895 |  | 3936 |  | 3977 |  | 4018 |

Treatment number associated to material : Placeb-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl. |  | Bl. |  |  |  | $\mathrm{Bl} \text {. }$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4019 | PPD | 4060 | PPD | 4101 | PPD | 4142 | PPD | 4183 | PPD | 4224 | PPD | 4265 |
|  | 4020 |  | 4061 |  | 4102 |  | 4143 |  | 4184 |  | 4225 |  | 4266 |
|  | 4021 |  | 4062 |  | 4103 |  | 4144 |  | 4185 |  | 4226 |  | 4267 |
|  | 4022 |  | 4063 |  | 4104 |  | 4145 |  | 4186 |  | 4227 |  | 4268 |
|  | 4023 |  | 4064 |  | 4105 |  | 4146 |  | 4187 |  | 4228 |  | 4269 |
|  | 4024 |  | 4065 |  | 4106 |  | 4147 |  | 4188 |  | 4229 |  | 4270 |
|  | 4025 |  | 4066 |  | 4107 |  | 4148 |  | 4189 |  | 4230 |  | 4271 |
|  | 4026 |  | 4067 |  | 4108 |  | 4149 |  | 4190 |  | 4231 |  | 4272 |
|  | 4027 |  | 4068 |  | 4109 |  | 4150 |  | 4191 |  | 4232 |  | 4273 |
|  | 4028 |  | 4069 |  | 4110 |  | 4151 |  | 4192 |  | 4233 |  | 4274 |
|  | 4029 |  | 4070 |  | 4111 |  | 4152 |  | 4193 |  | 4234 |  | 4275 |
|  | 4030 |  | 4071 |  | 4112 |  | 4153 |  | 4194 |  | 4235 |  | 4276 |
|  | 4031 |  | 4072 |  | 4113 |  | 4154 |  | 4195 |  | 4236 |  | 4277 |
|  | 4032 |  | 4073 |  | 4114 |  | 4155 |  | 4196 |  | 4237 |  | 4278 |
|  | 4033 |  | 4074 |  | 4115 |  | 4156 |  | 4197 |  | 4238 |  | 4279 |
|  | 4034 |  | 4075 |  | 4116 |  | 4157 |  | 4198 |  | 4239 |  | 4280 |
|  | 4035 |  | 4076 |  | 4117 |  | 4158 |  | 4199 |  | 4240 |  | 4281 |
|  | 4036 |  | 4077 |  | 4118 |  | 4159 |  | 4200 |  | 4241 |  | 4282 |
|  | 4037 |  | 4078 |  | 4119 |  | 4160 |  | 4201 |  | 4242 |  | 4283 |
|  | 4038 |  | 4079 |  | 4120 |  | 4161 |  | 4202 |  | 4243 |  | 4284 |
|  | 4039 |  | 4080 |  | 4121 |  | 4162 |  | 4203 |  | 4244 |  | 4285 |
|  | 4040 |  | 4081 |  | 4122 |  | 4163 |  | 4204 |  | 4245 |  | 4286 |
|  | 4041 |  | 4082 |  | 4123 |  | 4164 |  | 4205 |  | 4246 |  | 4287 |
|  | 4042 |  | 4083 |  | 4124 |  | 4165 |  | 4206 |  | 4247 |  | 4288 |
|  | 4043 |  | 4084 |  | 4125 |  | 4166 |  | 4207 |  | 4248 |  | 4289 |
|  | 4044 |  | 4085 |  | 4126 |  | 4167 |  | 4208 |  | 4249 |  | 4290 |
|  | 4045 |  | 4086 |  | 4127 |  | 4168 |  | 4209 |  | 4250 |  | 4291 |
|  | 4046 |  | 4087 |  | 4128 |  | 4169 |  | 4210 |  | 4251 |  | 4292 |
|  | 4047 |  | 4088 |  | 4129 |  | 4170 |  | 4211 |  | 4252 |  | 4293 |
|  | 4048 |  | 4089 |  | 4130 |  | 4171 |  | 4212 |  | 4253 |  | 4294 |
|  | 4049 |  | 4090 |  | 4131 |  | 4172 |  | 4213 |  | 4254 |  | 4295 |
|  | 4050 |  | 4091 |  | 4132 |  | 4173 |  | 4214 |  | 4255 |  | 4296 |
|  | 4051 |  | 4092 |  | 4133 |  | 4174 |  | 4215 |  | 4256 |  | 4297 |
|  | 4052 |  | 4093 |  | 4134 |  | 4175 |  | 4216 |  | 4257 |  | 4298 |
|  | 4053 |  | 4094 |  | 4135 |  | 4176 |  | 4217 |  | 4258 |  | 4299 |
|  | 4054 |  | 4095 |  | 4136 |  | 4177 |  | 4218 |  | 4259 |  | 4300 |
|  | 4055 |  | 4096 |  | 4137 |  | 4178 |  | 4219 |  | 4260 |  | 4301 |
|  | 4056 |  | 4097 |  | 4138 |  | 4179 |  | 4220 |  | 4261 |  | 4302 |
|  | 4057 |  | 4098 |  | 4139 |  | 4180 |  | 4221 |  | 4262 |  | 4303 |
|  | 4058 |  | 4099 |  | 4140 |  | 4181 |  | 4222 |  | 4263 |  | 4304 |
|  | 4059 |  | 4100 |  | 4141 |  | 4182 |  | 4223 |  | 4264 |  | 4305 |

Treatment number associated to material : Placeb-OnChemo

| $\begin{array}{r} \operatorname{Trt} \\ \mathrm{N} \end{array}$ |  | Trt |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} . \end{aligned}$ | $\begin{aligned} & \text { Trt. } \\ & \text { No nl. } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4306 | PPD | 4347 | PPD | 4388 | PPD | 4429 | PPD | 4470 | PPD | 4511 | PPD | 4552 |
|  | 4307 |  | 4348 |  | 4389 |  | 4430 |  | 4471 |  | 4512 |  | 4553 |
|  | 4308 |  | 4349 |  | 4390 |  | 4431 |  | 4472 |  | 4513 |  | 4554 |
|  | 4309 |  | 4350 |  | 4391 |  | 4432 |  | 4473 |  | 4514 |  | 4555 |
|  | 4310 |  | 4351 |  | 4392 |  | 4433 |  | 4474 |  | 4515 |  | 4556 |
|  | 4311 |  | 4352 |  | 4393 |  | 4434 |  | 4475 |  | 4516 |  | 4557 |
|  | 4312 |  | 4353 |  | 4394 |  | 4435 |  | 4476 |  | 4517 |  | 4558 |
|  | 4313 |  | 4354 |  | 4395 |  | 4436 |  | 4477 |  | 4518 |  | 4559 |
|  | 4314 |  | 4355 |  | 4396 |  | 4437 |  | 4478 |  | 4519 |  | 4560 |
|  | 4315 |  | 4356 |  | 4397 |  | 4438 |  | 4479 |  | 4520 |  | 4561 |
|  | 4316 |  | 4357 |  | 4398 |  | 4439 |  | 4480 |  | 4521 |  | 4562 |
|  | 4317 |  | 4358 |  | 4399 |  | 4440 |  | 4481 |  | 4522 |  | 4563 |
|  | 4318 |  | 4359 |  | 4400 |  | 4441 |  | 4482 |  | 4523 |  | 4564 |
|  | 4319 |  | 4360 |  | 4401 |  | 4442 |  | 4483 |  | 4524 |  | 4565 |
|  | 4320 |  | 4361 |  | 4402 |  | 4443 |  | 4484 |  | 4525 |  | 4566 |
|  | 4321 |  | 4362 |  | 4403 |  | 4444 |  | 4485 |  | 4526 |  | 4567 |
|  | 4322 |  | 4363 |  | 4404 |  | 4445 |  | 4486 |  | 4527 |  | 4568 |
|  | 4323 |  | 4364 |  | 4405 |  | 4446 |  | 4487 |  | 4528 |  | 4569 |
|  | 4324 |  | 4365 |  | 4406 |  | 4447 |  | 4488 |  | 4529 |  | 4570 |
|  | 4325 |  | 4366 |  | 4407 |  | 4448 |  | 4489 |  | 4530 |  | 4571 |
|  | 4326 |  | 4367 |  | 4408 |  | 4449 |  | 4490 |  | 4531 |  | 4572 |
|  | 4327 |  | 4368 |  | 4409 |  | 4450 |  | 4491 |  | 4532 |  | 4573 |
|  | 4328 |  | 4369 |  | 4410 |  | 4451 |  | 4492 |  | 4533 |  | 4574 |
|  | 4329 |  | 4370 |  | 4411 |  | 4452 |  | 4493 |  | 4534 |  | 4575 |
|  | 4330 |  | 4371 |  | 4412 |  | 4453 |  | 4494 |  | 4535 |  | 4576 |
|  | 4331 |  | 4372 |  | 4413 |  | 4454 |  | 4495 |  | 4536 |  | 4577 |
|  | 4332 |  | 4373 |  | 4414 |  | 4455 |  | 4496 |  | 4537 |  | 4578 |
|  | 4333 |  | 4374 |  | 4415 |  | 4456 |  | 4497 |  | 4538 |  | 4579 |
|  | 4334 |  | 4375 |  | 4416 |  | 4457 |  | 4498 |  | 4539 |  | 4580 |
|  | 4335 |  | 4376 |  | 4417 |  | 4458 |  | 4499 |  | 4540 |  | 4581 |
|  | 4336 |  | 4377 |  | 4418 |  | 4459 |  | 4500 |  | 4541 |  | 4582 |
|  | 4337 |  | 4378 |  | 4419 |  | 4460 |  | 4501 |  | 4542 |  | 4583 |
|  | 4338 |  | 4379 |  | 4420 |  | 4461 |  | 4502 |  | 4543 |  | 4584 |
|  | 4339 |  | 4380 |  | 4421 |  | 4462 |  | 4503 |  | 4544 |  | 4585 |
|  | 4340 |  | 4381 |  | 4422 |  | 4463 |  | 4504 |  | 4545 |  | 4586 |
|  | 4341 |  | 4382 |  | 4423 |  | 4464 |  | 4505 |  | 4546 |  | 4587 |
|  | 4342 |  | 4383 |  | 4424 |  | 4465 |  | 4506 |  | 4547 |  | 4588 |
|  | 4343 |  | 4384 |  | 4425 |  | 4466 |  | 4507 |  | 4548 |  | 4589 |
|  | 4344 |  | 4385 |  | 4426 |  | 4467 |  | 4508 |  | 4549 |  | 4590 |
|  | 4345 |  | 4386 |  | 4427 |  | 4468 |  | 4509 |  | 4550 |  | 4591 |
|  | 4346 |  | 4387 |  | 4428 |  | 4469 |  | 4510 |  | 4551 |  | 4592 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{array}{r} \operatorname{Trt} \\ \mathrm{N} \end{array}$ |  | Trt |  | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} \text {. } \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. } \mathrm{Bl} . \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4593 | PPD | 4634 | PPD | 4675 | PPD | 4716 | PPD | 4757 | PPD | 4798 | PPD | 4839 |
|  | 4594 |  | 4635 |  | 4676 |  | 4717 |  | 4758 |  | 4799 |  | 4840 |
|  | 4595 |  | 4636 |  | 4677 |  | 4718 |  | 4759 |  | 4800 |  | 4841 |
|  | 4596 |  | 4637 |  | 4678 |  | 4719 |  | 4760 |  | 4801 |  | 4842 |
|  | 4597 |  | 4638 |  | 4679 |  | 4720 |  | 4761 |  | 4802 |  | 4843 |
|  | 4598 |  | 4639 |  | 4680 |  | 4721 |  | 4762 |  | 4803 |  | 4844 |
|  | 4599 |  | 4640 |  | 4681 |  | 4722 |  | 4763 |  | 4804 |  | 4845 |
|  | 4600 |  | 4641 |  | 4682 |  | 4723 |  | 4764 |  | 4805 |  | 4846 |
|  | 4601 |  | 4642 |  | 4683 |  | 4724 |  | 4765 |  | 4806 |  | 4847 |
|  | 4602 |  | 4643 |  | 4684 |  | 4725 |  | 4766 |  | 4807 |  | 4848 |
|  | 4603 |  | 4644 |  | 4685 |  | 4726 |  | 4767 |  | 4808 |  | 4849 |
|  | 4604 |  | 4645 |  | 4686 |  | 4727 |  | 4768 |  | 4809 |  | 4850 |
|  | 4605 |  | 4646 |  | 4687 |  | 4728 |  | 4769 |  | 4810 |  | 4851 |
|  | 4606 |  | 4647 |  | 4688 |  | 4729 |  | 4770 |  | 4811 |  | 4852 |
|  | 4607 |  | 4648 |  | 4689 |  | 4730 |  | 4771 |  | 4812 |  | 4853 |
|  | 4608 |  | 4649 |  | 4690 |  | 4731 |  | 4772 |  | 4813 |  | 4854 |
|  | 4609 |  | 4650 |  | 4691 |  | 4732 |  | 4773 |  | 4814 |  | 4855 |
|  | 4610 |  | 4651 |  | 4692 |  | 4733 |  | 4774 |  | 4815 |  | 4856 |
|  | 4611 |  | 4652 |  | 4693 |  | 4734 |  | 4775 |  | 4816 |  | 4857 |
|  | 4612 |  | 4653 |  | 4694 |  | 4735 |  | 4776 |  | 4817 |  | 4858 |
|  | 4613 |  | 4654 |  | 4695 |  | 4736 |  | 4777 |  | 4818 |  | 4859 |
|  | 4614 |  | 4655 |  | 4696 |  | 4737 |  | 4778 |  | 4819 |  | 4860 |
|  | 4615 |  | 4656 |  | 4697 |  | 4738 |  | 4779 |  | 4820 |  | 4861 |
|  | 4616 |  | 4657 |  | 4698 |  | 4739 |  | 4780 |  | 4821 |  | 4862 |
|  | 4617 |  | 4658 |  | 4699 |  | 4740 |  | 4781 |  | 4822 |  | 4863 |
|  | 4618 |  | 4659 |  | 4700 |  | 4741 |  | 4782 |  | 4823 |  | 4864 |
|  | 4619 |  | 4660 |  | 4701 |  | 4742 |  | 4783 |  | 4824 |  | 4865 |
|  | 4620 |  | 4661 |  | 4702 |  | 4743 |  | 4784 |  | 4825 |  | 4866 |
|  | 4621 |  | 4662 |  | 4703 |  | 4744 |  | 4785 |  | 4826 |  | 4867 |
|  | 4622 |  | 4663 |  | 4704 |  | 4745 |  | 4786 |  | 4827 |  | 4868 |
|  | 4623 |  | 4664 |  | 4705 |  | 4746 |  | 4787 |  | 4828 |  | 4869 |
|  | 4624 |  | 4665 |  | 4706 |  | 4747 |  | 4788 |  | 4829 |  | 4870 |
|  | 4625 |  | 4666 |  | 4707 |  | 4748 |  | 4789 |  | 4830 |  | 4871 |
|  | 4626 |  | 4667 |  | 4708 |  | 4749 |  | 4790 |  | 4831 |  | 4872 |
|  | 4627 |  | 4668 |  | 4709 |  | 4750 |  | 4791 |  | 4832 |  | 4873 |
|  | 4628 |  | 4669 |  | 4710 |  | 4751 |  | 4792 |  | 4833 |  | 4874 |
|  | 4629 |  | 4670 |  | 4711 |  | 4752 |  | 4793 |  | 4834 |  | 4875 |
|  | 4630 |  | 4671 |  | 4712 |  | 4753 |  | 4794 |  | 4835 |  | 4876 |
|  | 4631 |  | 4672 |  | 4713 |  | 4754 |  | 4795 |  | 4836 |  | 4877 |
|  | 4632 |  | 4673 |  | 4714 |  | 4755 |  | 4796 |  | 4837 |  | 4878 |
|  | 4633 |  | 4674 |  | 4715 |  | 4756 |  | 4797 |  | 4838 |  | 4879 |

SD4 4 RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ | $\mathrm{Bl}_{\mathrm{Bl}}^{\mathrm{nb}}$. |  |  | Trt |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ | Trt | $\begin{aligned} & \mathrm{Bl} \text {. } \\ & \mathrm{nb} \end{aligned}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 4880 | PPD | 4921 | PPD | 4962 | PPD | 5003 | PPD | 5044 | PPD | 5085 | PPD | 5126 |
|  | 4881 |  | 4922 |  | 4963 |  | 5004 |  | 5045 |  | 5086 |  | 5127 |
|  | 4882 |  | 4923 |  | 4964 |  | 5005 |  | 5046 |  | 5087 |  | 5128 |
|  | 4883 |  | 4924 |  | 4965 |  | 5006 |  | 5047 |  | 5088 |  | 5129 |
|  | 4884 |  | 4925 |  | 4966 |  | 5007 |  | 5048 |  | 5089 |  | 5130 |
|  | 4885 |  | 4926 |  | 4967 |  | 5008 |  | 5049 |  | 5090 |  | 5131 |
|  | 4886 |  | 4927 |  | 4968 |  | 5009 |  | 5050 |  | 5091 |  | 5132 |
|  | 4887 |  | 4928 |  | 4969 |  | 5010 |  | 5051 |  | 5092 |  | 5133 |
|  | 4888 |  | 4929 |  | 4970 |  | 5011 |  | 5052 |  | 5093 |  | 5134 |
|  | 4889 |  | 4930 |  | 4971 |  | 5012 |  | 5053 |  | 5094 |  | 5135 |
|  | 4890 |  | 4931 |  | 4972 |  | 5013 |  | 5054 |  | 5095 |  | 5136 |
|  | 4891 |  | 4932 |  | 4973 |  | 5014 |  | 5055 |  | 5096 |  | 5137 |
|  | 4892 |  | 4933 |  | 4974 |  | 5015 |  | 5056 |  | 5097 |  | 5138 |
|  | 4893 |  | 4934 |  | 4975 |  | 5016 |  | 5057 |  | 5098 |  | 5139 |
|  | 4894 |  | 4935 |  | 4976 |  | 5017 |  | 5058 |  | 5099 |  | 5140 |
|  | 4895 |  | 4936 |  | 4977 |  | 5018 |  | 5059 |  | 5100 |  | 5141 |
|  | 4896 |  | 4937 |  | 4978 |  | 5019 |  | 5060 |  | 5101 |  | 5142 |
|  | 4897 |  | 4938 |  | 4979 |  | 5020 |  | 5061 |  | 5102 |  | 5143 |
|  | 4898 |  | 4939 |  | 4980 |  | 5021 |  | 5062 |  | 5103 |  | 5144 |
|  | 4899 |  | 4940 |  | 4981 |  | 5022 |  | 5063 |  | 5104 |  | 5145 |
|  | 4900 |  | 4941 |  | 4982 |  | 5023 |  | 5064 |  | 5105 |  | 5146 |
|  | 4901 |  | 4942 |  | 4983 |  | 5024 |  | 5065 |  | 5106 |  | 5147 |
|  | 4902 |  | 4943 |  | 4984 |  | 5025 |  | 5066 |  | 5107 |  | 5148 |
|  | 4903 |  | 4944 |  | 4985 |  | 5026 |  | 5067 |  | 5108 |  | 5149 |
|  | 4904 |  | 4945 |  | 4986 |  | 5027 |  | 5068 |  | 5109 |  | 5150 |
|  | 4905 |  | 4946 |  | 4987 |  | 5028 |  | 5069 |  | 5110 |  | 5151 |
|  | 4906 |  | 4947 |  | 4988 |  | 5029 |  | 5070 |  | 5111 |  | 5152 |
|  | 4907 |  | 4948 |  | 4989 |  | 5030 |  | 5071 |  | 5112 |  | 5153 |
|  | 4908 |  | 4949 |  | 4990 |  | 5031 |  | 5072 |  | 5113 |  | 5154 |
|  | 4909 |  | 4950 |  | 4991 |  | 5032 |  | 5073 |  | 5114 |  | 5155 |
|  | 4910 |  | 4951 |  | 4992 |  | 5033 |  | 5074 |  | 5115 |  | 5156 |
|  | 4911 |  | 4952 |  | 4993 |  | 5034 |  | 5075 |  | 5116 |  | 5157 |
|  | 4912 |  | 4953 |  | 4994 |  | 5035 |  | 5076 |  | 5117 |  | 5158 |
|  | 4913 |  | 4954 |  | 4995 |  | 5036 |  | 5077 |  | 5118 |  | 5159 |
|  | 4914 |  | 4955 |  | 4996 |  | 5037 |  | 5078 |  | 5119 |  | 5160 |
|  | 4915 |  | 4956 |  | 4997 |  | 5038 |  | 5079 |  | 5120 |  | 5161 |
|  | 4916 |  | 4957 |  | 4998 |  | 5039 |  | 5080 |  | 5121 |  | 5162 |
|  | 4917 |  | 4958 |  | 4999 |  | 5040 |  | 5081 |  | 5122 |  | 5163 |
|  | 4918 |  | 4959 |  | 5000 |  | 5041 |  | 5082 |  | 5123 |  | 5164 |
|  | 4919 |  | 4960 |  | 5001 |  | 5042 |  | 5083 |  | 5124 |  | 5165 |
|  | 4920 |  | 4961 |  | 5002 |  | 5043 |  | 5084 |  | 5125 |  | 5166 |

Treatment number associated to material : Placeb-OnChemo

| $\begin{array}{r} \text { Trt. } \\ \text { No } \end{array}$ | ${ }_{\text {Bl }}^{\text {nl. }}$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5167 | PPD | 5208 | PPD | 5249 | PPD | 5290 | PPD | 5331 | PPD | 5372 | PPD | 5413 |
|  | 5168 |  | 5209 |  | 5250 |  | 5291 |  | 5332 |  | 5373 |  | 5414 |
|  | 5169 |  | 5210 |  | 5251 |  | 5292 |  | 5333 |  | 5374 |  | 5415 |
|  | 5170 |  | 5211 |  | 5252 |  | 5293 |  | 5334 |  | 5375 |  | 5416 |
|  | 5171 |  | 5212 |  | 5253 |  | 5294 |  | 5335 |  | 5376 |  | 5417 |
|  | 5172 |  | 5213 |  | 5254 |  | 5295 |  | 5336 |  | 5377 |  | 5418 |
|  | 5173 |  | 5214 |  | 5255 |  | 5296 |  | 5337 |  | 5378 |  | 5419 |
|  | 5174 |  | 5215 |  | 5256 |  | 5297 |  | 5338 |  | 5379 |  | 5420 |
|  | 5175 |  | 5216 |  | 5257 |  | 5298 |  | 5339 |  | 5380 |  | 5421 |
|  | 5176 |  | 5217 |  | 5258 |  | 5299 |  | 5340 |  | 5381 |  | 5422 |
|  | 5177 |  | 5218 |  | 5259 |  | 5300 |  | 5341 |  | 5382 |  | 5423 |
|  | 5178 |  | 5219 |  | 5260 |  | 5301 |  | 5342 |  | 5383 |  | 5424 |
|  | 5179 |  | 5220 |  | 5261 |  | 5302 |  | 5343 |  | 5384 |  | 5425 |
|  | 5180 |  | 5221 |  | 5262 |  | 5303 |  | 5344 |  | 5385 |  | 5426 |
|  | 5181 |  | 5222 |  | 5263 |  | 5304 |  | 5345 |  | 5386 |  | 5427 |
|  | 5182 |  | 5223 |  | 5264 |  | 5305 |  | 5346 |  | 5387 |  | 5428 |
|  | 5183 |  | 5224 |  | 5265 |  | 5306 |  | 5347 |  | 5388 |  | 5429 |
|  | 5184 |  | 5225 |  | 5266 |  | 5307 |  | 5348 |  | 5389 |  | 5430 |
|  | 5185 |  | 5226 |  | 5267 |  | 5308 |  | 5349 |  | 5390 |  | 5431 |
|  | 5186 |  | 5227 |  | 5268 |  | 5309 |  | 5350 |  | 5391 |  | 5432 |
|  | 5187 |  | 5228 |  | 5269 |  | 5310 |  | 5351 |  | 5392 |  | 5433 |
|  | 5188 |  | 5229 |  | 5270 |  | 5311 |  | 5352 |  | 5393 |  | 5434 |
|  | 5189 |  | 5230 |  | 5271 |  | 5312 |  | 5353 |  | 5394 |  | 5435 |
|  | 5190 |  | 5231 |  | 5272 |  | 5313 |  | 5354 |  | 5395 |  | 5436 |
|  | 5191 |  | 5232 |  | 5273 |  | 5314 |  | 5355 |  | 5396 |  | 5437 |
|  | 5192 |  | 5233 |  | 5274 |  | 5315 |  | 5356 |  | 5397 |  | 5438 |
|  | 5193 |  | 5234 |  | 5275 |  | 5316 |  | 5357 |  | 5398 |  | 5439 |
|  | 5194 |  | 5235 |  | 5276 |  | 5317 |  | 5358 |  | 5399 |  | 5440 |
|  | 5195 |  | 5236 |  | 5277 |  | 5318 |  | 5359 |  | 5400 |  | 5441 |
|  | 5196 |  | 5237 |  | 5278 |  | 5319 |  | 5360 |  | 5401 |  | 5442 |
|  | 5197 |  | 5238 |  | 5279 |  | 5320 |  | 5361 |  | 5402 |  | 5443 |
|  | 5198 |  | 5239 |  | 5280 |  | 5321 |  | 5362 |  | 5403 |  | 5444 |
|  | 5199 |  | 5240 |  | 5281 |  | 5322 |  | 5363 |  | 5404 |  | 5445 |
|  | 5200 |  | 5241 |  | 5282 |  | 5323 |  | 5364 |  | 5405 |  | 5446 |
|  | 5201 |  | 5242 |  | 5283 |  | 5324 |  | 5365 |  | 5406 |  | 5447 |
|  | 5202 |  | 5243 |  | 5284 |  | 5325 |  | 5366 |  | 5407 |  | 5448 |
|  | 5203 |  | 5244 |  | 5285 |  | 5326 |  | 5367 |  | 5408 |  | 5449 |
|  | 5204 |  | 5245 |  | 5286 |  | 5327 |  | 5368 |  | 5409 |  | 5450 |
|  | 5205 |  | 5246 |  | 5287 |  | 5328 |  | 5369 |  | 5410 |  | 5451 |
|  | 5206 |  | 5247 |  | 5288 |  | 5329 |  | 5370 |  | 5411 |  | 5452 |
|  | 5207 |  | 5248 |  | 5289 |  | 5330 |  | 5371 |  | 5412 |  | 5453 |

SD4 \RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ |  |  |  |  |  |  | $\begin{aligned} & \mathrm{Bl} . \\ & \mathrm{nb} \end{aligned}$ |  | $\begin{aligned} & \mathrm{Bl} \text { n. } \end{aligned}$ |  | $\mathrm{Bl} \text {. }$ | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5454 | PPD | 5495 | PPD | 5536 | PPD | 5577 | PPD | 5618 | PPD | 5659 | PPD | 5700 |
|  | 5455 |  | 5496 |  | 5537 |  | 5578 |  | 5619 |  | 5660 |  | 5701 |
|  | 5456 |  | 5497 |  | 5538 |  | 5579 |  | 5620 |  | 5661 |  | 5702 |
|  | 5457 |  | 5498 |  | 5539 |  | 5580 |  | 5621 |  | 5662 |  | 5703 |
|  | 5458 |  | 5499 |  | 5540 |  | 5581 |  | 5622 |  | 5663 |  | 5704 |
|  | 5459 |  | 5500 |  | 5541 |  | 5582 |  | 5623 |  | 5664 |  | 5705 |
|  | 5460 |  | 5501 |  | 5542 |  | 5583 |  | 5624 |  | 5665 |  | 5706 |
|  | 5461 |  | 5502 |  | 5543 |  | 5584 |  | 5625 |  | 5666 |  | 5707 |
|  | 5462 |  | 5503 |  | 5544 |  | 5585 |  | 5626 |  | 5667 |  | 5708 |
|  | 5463 |  | 5504 |  | 5545 |  | 5586 |  | 5627 |  | 5668 |  | 5709 |
|  | 5464 |  | 5505 |  | 5546 |  | 5587 |  | 5628 |  | 5669 |  | 5710 |
|  | 5465 |  | 5506 |  | 5547 |  | 5588 |  | 5629 |  | 5670 |  | 5711 |
|  | 5466 |  | 5507 |  | 5548 |  | 5589 |  | 5630 |  | 5671 |  | 5712 |
|  | 5467 |  | 5508 |  | 5549 |  | 5590 |  | 5631 |  | 5672 |  | 5713 |
|  | 5468 |  | 5509 |  | 5550 |  | 5591 |  | 5632 |  | 5673 |  | 5714 |
|  | 5469 |  | 5510 |  | 5551 |  | 5592 |  | 5633 |  | 5674 |  | 5715 |
|  | 5470 |  | 5511 |  | 5552 |  | 5593 |  | 5634 |  | 5675 |  | 5716 |
|  | 5471 |  | 5512 |  | 5553 |  | 5594 |  | 5635 |  | 5676 |  | 5717 |
|  | 5472 |  | 5513 |  | 5554 |  | 5595 |  | 5636 |  | 5677 |  | 5718 |
|  | 5473 |  | 5514 |  | 5555 |  | 5596 |  | 5637 |  | 5678 |  | 5719 |
|  | 5474 |  | 5515 |  | 5556 |  | 5597 |  | 5638 |  | 5679 |  | 5720 |
|  | 5475 |  | 5516 |  | 5557 |  | 5598 |  | 5639 |  | 5680 |  | 5721 |
|  | 5476 |  | 5517 |  | 5558 |  | 5599 |  | 5640 |  | 5681 |  | 5722 |
|  | 5477 |  | 5518 |  | 5559 |  | 5600 |  | 5641 |  | 5682 |  | 5723 |
|  | 5478 |  | 5519 |  | 5560 |  | 5601 |  | 5642 |  | 5683 |  | 5724 |
|  | 5479 |  | 5520 |  | 5561 |  | 5602 |  | 5643 |  | 5684 |  | 5725 |
|  | 5480 |  | 5521 |  | 5562 |  | 5603 |  | 5644 |  | 5685 |  | 5726 |
|  | 5481 |  | 5522 |  | 5563 |  | 5604 |  | 5645 |  | 5686 |  | 5727 |
|  | 5482 |  | 5523 |  | 5564 |  | 5605 |  | 5646 |  | 5687 |  | 5728 |
|  | 5483 |  | 5524 |  | 5565 |  | 5606 |  | 5647 |  | 5688 |  | 5729 |
|  | 5484 |  | 5525 |  | 5566 |  | 5607 |  | 5648 |  | 5689 |  | 5730 |
|  | 5485 |  | 5526 |  | 5567 |  | 5608 |  | 5649 |  | 5690 |  | 5731 |
|  | 5486 |  | 5527 |  | 5568 |  | 5609 |  | 5650 |  | 5691 |  | 5732 |
|  | 5487 |  | 5528 |  | 5569 |  | 5610 |  | 5651 |  | 5692 |  | 5733 |
|  | 5488 |  | 5529 |  | 5570 |  | 5611 |  | 5652 |  | 5693 |  | 5734 |
|  | 5489 |  | 5530 |  | 5571 |  | 5612 |  | 5653 |  | 5694 |  | 5735 |
|  | 5490 |  | 5531 |  | 5572 |  | 5613 |  | 5654 |  | 5695 |  | 5736 |
|  | 5491 |  | 5532 |  | 5573 |  | 5614 |  | 5655 |  | 5696 |  | 5737 |
|  | 5492 |  | 5533 |  | 5574 |  | 5615 |  | 5656 |  | 5697 |  | 5738 |
|  | 5493 |  | 5534 |  | 5575 |  | 5616 |  | 5657 |  | 5698 |  | 5739 |
|  | 5494 |  | 5535 |  | 5576 |  | 5617 |  | 5658 |  | 5699 |  | 5740 |

SD4 4 RDE $\backslash$ ENABLE
ZOSTER-028 (A.10FEB2017)

Treatment number associated to material : Placeb-OnChemo

| $\begin{aligned} & \text { Trt. } \\ & \text { No } \end{aligned}$ | Bl . | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. } \mathrm{Bl} . \\ & \text { No no } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No nb } \end{aligned}$ |  | $\begin{aligned} & \text { Trt. Bl. } \\ & \text { No no } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| PPD | 5741 | PPD | 5782 | PPD | 5823 | PPD | 5864 | PPD | 5905 | PPD | 5946 | PPD | 5987 |
|  | 5742 | PPD | 5783 |  | 5824 |  | 5865 |  | 5906 |  | 5947 |  | 5988 |
|  | 5743 |  | 5784 |  | 5825 |  | 5866 |  | 5907 |  | 5948 |  | 5989 |
|  | 5744 |  | 5785 |  | 5826 |  | 5867 |  | 5908 |  | 5949 |  | 5990 |
|  | 5745 |  | 5786 |  | 5827 |  | 5868 |  | 5909 |  | 5950 |  | 5991 |
|  | 5746 |  | 5787 |  | 5828 |  | 5869 |  | 5910 |  | 5951 |  | 5992 |
|  | 5747 |  | 5788 |  | 5829 |  | 5870 |  | 5911 |  | 5952 |  | 5993 |
|  | 5748 |  | 5789 |  | 5830 |  | 5871 |  | 5912 |  | 5953 |  | 5994 |
|  | 5749 |  | 5790 |  | 5831 |  | 5872 |  | 5913 |  | 5954 |  | 5995 |
|  | 5750 |  | 5791 |  | 5832 |  | 5873 |  | 5914 |  | 5955 |  | 5996 |
|  | 5751 |  | 5792 |  | 5833 |  | 5874 |  | 5915 |  | 5956 |  | 5997 |
|  | 5752 |  | 5793 |  | 5834 |  | 5875 |  | 5916 |  | 5957 |  | 5998 |
|  | 5753 |  | 5794 |  | 5835 |  | 5876 |  | 5917 |  | 5958 |  | 5999 |
|  | 5754 |  | 5795 |  | 5836 |  | 5877 |  | 5918 |  | 5959 |  | 6000 |
|  | 5755 |  | 5796 |  | 5837 |  | 5878 |  | 5919 |  | 5960 |  |  |
|  | 5756 |  | 5797 |  | 5838 |  | 5879 |  | 5920 |  | 5961 |  |  |
|  | 5757 |  | 5798 |  | 5839 |  | 5880 |  | 5921 |  | 5962 |  |  |
|  | 5758 |  | 5799 |  | 5840 |  | 5881 |  | 5922 |  | 5963 |  |  |
|  | 5759 |  | 5800 |  | 5841 |  | 5882 |  | 5923 |  | 5964 |  |  |
|  | 5760 |  | 5801 |  | 5842 |  | 5883 |  | 5924 |  | 5965 |  |  |
|  | 5761 |  | 5802 |  | 5843 |  | 5884 |  | 5925 |  | 5966 |  |  |
|  | 5762 |  | 5803 |  | 5844 |  | 5885 |  | 5926 |  | 5967 |  |  |
|  | 5763 |  | 5804 |  | 5845 |  | 5886 |  | 5927 |  | 5968 |  |  |
|  | 5764 |  | 5805 |  | 5846 |  | 5887 |  | 5928 |  | 5969 |  |  |
|  | 5765 |  | 5806 |  | 5847 |  | 5888 |  | 5929 |  | 5970 |  |  |
|  | 5766 |  | 5807 |  | 5848 |  | 5889 |  | 5930 |  | 5971 |  |  |
|  | 5767 |  | 5808 |  | 5849 |  | 5890 |  | 5931 |  | 5972 |  |  |
|  | 5768 |  | 5809 |  | 5850 |  | 5891 |  | 5932 |  | 5973 |  |  |
|  | 5769 |  | 5810 |  | 5851 |  | 5892 |  | 5933 |  | 5974 |  |  |
|  | 5770 |  | 5811 |  | 5852 |  | 5893 |  | 5934 |  | 5975 |  |  |
|  | 5771 |  | 5812 |  | 5853 |  | 5894 |  | 5935 |  | 5976 |  |  |
|  | 5772 |  | 5813 |  | 5854 |  | 5895 |  | 5936 |  | 5977 |  |  |
|  | 5773 |  | 5814 |  | 5855 |  | 5896 |  | 5937 |  | 5978 |  |  |
|  | 5774 |  | 5815 |  | 5856 |  | 5897 |  | 5938 |  | 5979 |  |  |
|  | 5775 |  | 5816 |  | 5857 |  | 5898 |  | 5939 |  | 5980 |  |  |
|  | 5776 |  | 5817 |  | 5858 |  | 5899 |  | 5940 |  | 5981 |  |  |
|  | 5777 |  | 5818 |  | 5859 |  | 5900 |  | 5941 |  | 5982 |  |  |
|  | 5778 |  | 5819 |  | 5860 |  | 5901 |  | 5942 |  | 5983 |  |  |
|  | 5779 |  | 5820 |  | 5861 |  | 5902 |  | 5943 |  | 5984 |  |  |
|  | 5780 |  | 5821 |  | 5862 |  | 5903 |  | 5944 |  | 5985 |  |  |
|  | 5781 |  | 5822 |  | 5863 |  | 5904 |  | 5945 |  | 5986 |  |  |

## Audit Certificates

## AUDIT CERTIFICATE

## Study Number: 116427

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.

Clinical studies are conducted by or on behalf of GlaxoSmithKline in accordance with Standard Operating Procedures, which conform to the requirements of international GCP guidelines (ICH Harmonised Tripartite Guidelines E6 for Good Clinical Practice, FDA 21CFR parts 50, 56 and 312).

During the conduct and reporting of this study, the following independent audits were performed by or on behalf of GlaxoSmithKline.

| Study Number | Type | Conducted by | Centre number | Country | Audit Date |
| :--- | :--- | :--- | :--- | :--- | :--- |
| 116427 | Investigator Site | GSK-CDQA-Korea | PPD | South Korea | 06-08 November 2013 |
| 116427 | Investigator Site | GSK-CDQA-UK |  |  | Spain |
| 116427 | Investigator Site | GSK-CDQA-UK |  |  | United Kingdom |

Clinical Development Quality Assurance hereby confirm that the audits detailed above were carried out in accordance with appropriate regulatory requirements and guidelines in order to assess compliance with the study protocol, ICH GCP, FDA 21CFR parts 314.50 and 601.2, appropriate standard operating procedures and policies.

## Name: <br> $\qquad$

Date: February 20,2017
Role: Manager
Clinical Development Quality Assurance GlaxoSmithKline Research and Development

## Documentation of statistical methods

Not applicable

## Documentation of inter-laboratory standardization methods and quality assurance procedures

Not Applicable

## Publications based on the study

Not Applicable

## Important publications referenced in the report

Cunningham AL, Lal H, Kovac M, et al., Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older. N Engl J Med. 2016; 375(11): 1019-32 DOI: 10.1056/NEJMoa1603800

Lal H, Cunningham AL, Godeaux O, et al., Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults. N Engl J Med. 2015; 372(22): 2087-96 DOI: 10.1056/NEJMoa1501184.

## CRF leCRFs for deaths, other SAEs and withdrawals due to adverse events

Page(s) removed - Out of Scope of phase 1 of Policy 0070 - CRF/eCRFs

## Study Administrative Table

| Clinical Trial Activity | Performed by | Responsibilities and scope of activities | Site address |
| :---: | :---: | :---: | :---: |
| Sponsor | GlaxoSmithKline Biologicals, SA ${ }^{1}$ | ICH E6(R1) - Guideline for Good Clinical Practice definition of "Sponsor": <br> - 1.53 Sponsor: An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial. <br> GSK Biologicals SA was responsible for coordinating activities for manufacturing of the Herpes Zoster/subunit (HZ/su) vaccine, initiating and conducting the study, including clinical trial supply management, monitoring, randomization, data management and statistical analyses. | GlaxoSmithKline Biologicals, SA, Rue de l'Institut 89, 1330 Rixensart (Belgium) |
| Monitoring | Central Study Monitor (Study Delivery Lead) | - co-ordinates operational aspects of running the study from preparation of study supplies and data capture tools, to study tracking <br> - has regular contacts with local monitors in order to review the study progress and any issue raised by the local monitor. In this way compliance with the protocol and GCP/ICH guidelines is ensured during preparation, active and cleaning phases of the study <br> - is responsible for maintaining and archiving a comprehensive study file. If required, transitioning of a study from one monitor to another is documented in the study file <br> - is responsible for reviewing and signing off of the clinical study report | GlaxoSmithKline Biologicals, SA, Rue de l'Institut 89, 1330 Rixensart (Belgium) |

${ }^{1}$ In this document, GlaxoSmithKline Biologicals SA is also referred to as GSK Biologicals SA

| Clinical Trial Activity | Performed by | Responsibilities and scope of activities | Site address |
| :---: | :---: | :---: | :---: |
| Monitoring | Local Monitor | Prior to study start: <br> is responsible for the evaluation of the study site and ensures that the staff and facilities are trained and appropriate for running of the study according to protocol and GCP guidelines <br> - is involved in the preparation of study package for submission to Ethics Committee and/or Independent Review Board (EC/IRBs) and appropriate authorities <br> At study initiation: <br> - conducts study specific training <br> While trial is ongoing: <br> - discusses all aspects of the trial with the study staff <br> - verifies source documents and Case Report Forms (CRFs) <br> - conducts a $100 \%$ review of all Informed Consent documentation <br> - checks accountability of investigational product and its storage conditions <br> - checks the collection and storage of biological samples and transport to central laboratory <br> - reviews each SAE report <br> All monitoring visits are documented via a monitoring report, which will be reviewed by the monitor's manager. These reports allow the identification and escalation of protocol violation, re-education of site staff and communication of significant issues (SAEs, quality, efficacy and GCP compliance) to the central organisation. In this way the Local Monitors oversee the progress of the clinical trial and ensure that it is conducted, recorded and reported in accordance with the protocol and current GCP/ICH guidelines. <br> The Local Monitor works in close partnership with the Local Medical Advisor and the Central Study Monitor. | Canada <br> GSK <br> 7333 Mississauga Road North, Mississauga, Ontario, L5N 6L4, Canada <br> Czech Republic <br> GSK <br> Hvězdova 1734/2c <br> 14000 Praha 4 <br> Česká republika <br> France <br> KEYRUS <br> 155 rue Anatole France <br> Levallois-Perrett <br> 92300 <br> France <br> S.Korea <br> PAREXEL International <br> 9FL., Glass Tower, 534, <br> Teheran-ro, Gangnam-gu, <br> Seoul, Republic of Korea <br> (Zip Code: 06181) <br> Spain <br> -Parexel internacional <br> PLAZA DE CARLOS TRIAS BELTRAN, $7-7^{\text {a }}$ plta <br> 28020 Madrid <br> -MediTrial CRO <br> Avda. Nazaret, 4, Bajo Dcha. <br> 28009 Madrid <br> -Frelancers/unipersonal CRO <br> PPD (Sus\&Clinical Research) |


| Clinical Trial Activity | Performed by | Responsibilities and scope of activities | Site address |
| :---: | :---: | :---: | :---: |
|  |  |  | C/ Portal de la Rambla 3 local 4 08500 Vic (Barcelona) <br> United Kingdom GSK <br> B10, Stockley Park West, 1-3 Ironbridge Road, Uxbridge, Middlesex, UB11 1BT, United Kingdom |
| Data Management | Data Manager | Responsibilities involve: <br> - the design of the Case Report Form (CRF) <br> - the creation of data entry application <br> - the collection and handling of study data <br> - the cleaning of study data (in conjunction with the Clinical Research and Development Lead, Central Study and Local Monitors) in order to provide cleaned database for the statistical analysis | GlaxoSmithKline Biologicals SA, Rue de l'Institut 89, 1330 Rixensart (Belgium). |
| Statistics | Statistician | - is involved in the study design and is responsible for calculating the sample size, preparation of the randomisation list, identification of appropriate statistical tests to analyse the data, conducting the statistical analysis on the data collected, issuing the statistical report and interpretation of the statistical findings (GSK Biologicals, SA) <br> - reviews the final study report to ensure that all aspects of the statistical analysis and findings are accurately represented in the final report (GSK Biologicals, SA) <br> - Statistical analyses by an independent statistician (4Clinics and SClinica) for internal safety review committee (iSRC) reviews. | GlaxoSmithKline Biologicals SA, Rue de 'I'Institut 89, 1330 Rixensart (Belgium) <br> 4Clinics, <br> Drève Richelle 161 Bâtiment C, 1410 Waterloo (Belgium) <br> S-Clinica, <br> Chaussée de Boondael 6 , 1050 Brussels (Belgium) |


| Clinical Trial Activity | Performed by | Responsibilities and scope of activities | Site address |
| :---: | :---: | :---: | :---: |
| Laboratory assessments | GlaxoSmithKline <br> Biologicals Global Vaccine Clinical Laboratory; <br> CEVAC | - Testing for the analysis of the immune response <br> - Ab testing <br> - CMI (cell-mediated immunogenicity) | Ab testing GSK Biologicals, GVCL (CLS), Rue de I'Institut, 89 - B1330 Rixensart (Belgium) <br> Ghent University, Building A - De Pintelaan 185, 9000 Gent (Belgium) |
| Randomization | Department of Biometrics, Vaccine Supply Coordinator, Clinical Information Management Systems Team | - computer-generated randomisation list was used to number the vaccines <br> - A randomisation blocking scheme was used to ensure that the balance between vaccine groups was maintained. The randomisation number uniquely identified the vaccine dose to be administered to any subject. <br> - The randomization of supplies within blocks was performed at GSK Biologicals, using MATerial EXcellence (MATEX), a program developed for use in SAS (Statistical Analysis System) by GSK Biologicals. <br> - Using SBIR, the treatment numbers were allocated by kit. <br> - The randomization of subjects across study groups was performed using SBIR. | GlaxoSmithKline Biologicals SA, Rue de l'Institut 89, 1330 Rixensart (Belgium) |
| Medical writing | Scientific Writer | - In collaboration with the Clinical Development Team, prepares study protocols, Subject Information Sheet (SIS), Informed Consent Forms (ICFs), protocol amendments and the Clinical Study Reports (CSR). <br> - Co-ordinates the review of the final study report with the study team (including the investigators) to ensure that the report is an accurate account of the study and findings. | GlaxoSmithKline Biologicals, SA, Rue de l'Institut 89, 1330 Rixensart (Belgium) |


| Clinical Trial Activity | Performed by | Responsibilities and scope of activities | Site address |
| :---: | :---: | :---: | :---: |
| Central Safety | Central Safety Department | During the conduct of pre-licensure clinical studies, the Central Safety Department is responsible for: <br> - centralising collection, review and follow-up of all reported SAEs <br> - the issue of Expedited Investigator Safety Reports to inform all investigators in the programme and IRBs of unexpected and related SAEs <br> - the preparation and review of consolidated safety reports related to investigational vaccines <br> - the analysis of safety issues and review of the safety content of the final study report. | GlaxoSmithKline Biologicals SA, Rue de l'Institut 89, 1330 Rixensart (Belgium) |
| Other information |  |  |  |
| Location of trial master file | Local Study Monitor | The Sponsor's Trial Master file is composed of the following: <br> - The country monitoring study file. This part of the master file is located at the particular GSK or CRO office involved in the study and in an electronic repository. | Country monitoring study file: <br> Canada <br> GSK Canada Inc. <br> 7333 Mississauga Road North, Mississauga, Ontario, <br> L5N 6L4, Canada <br> Czech Republic <br> GSK <br> Hvězdova 1734/2c <br> 14000 Praha 4 <br> Česká republika <br> S. Korea <br> 39, Hwangsaemal 2-gil, Osan-ri, Jori-eup, Paju-si, <br> Gyeonggi-do, 10949, Republic of Korea <br> Spain <br> C/ Severo Ochoa, 2. 28760 Tres Cantos. Madrid <br> United Kingdom <br> PhlexGlobal <br> Manderville House <br> 62 The Broadway |


| Clinical Trial | Performed by | Responsibilities and scope of activities | Site address |  |
| :---: | :---: | :---: | :---: | :---: |
|  | Central Study Monitor | - The central study file. This part of the master file is located at the GSK offices and in an electronic repository. | Central study file: GlaxoSmithKline Biologicals SA, Rue de l'Institut 89, 1330 Rixensart (Belgium) |  |
| Site(s) of manufacture | GlaxoSmithKline Biologicals, SA | - | GlaxoSmithKline Biologicals, SA, Avenue Fleming, 20, <br> B-1300 Wavre (Belgium) |  |
| Site of release in Europe | GlaxoSmithKline Biologicals, SA | - | GlaxoSmithKline Biologicals, SA, Avenue Fleming, 20, <br> B-1300 Wavre (Belgium) |  |

## Statistical Analysis Plan

Study alias \& e-track number(s): Zoster-028 (116427)

| Detailed Title: |  |
| :---: | :---: |
|  | A phase II/III, randomised, observer-blind, placebocontrolled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster $\mathrm{HZ} / \mathrm{su}$ candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy |
| SAP version | Final |
| SAP date | 25-MAR-2013 |
| Scope: | Demographic and safety data as defined per iSRC Charter |
| Co-ordinating author: | PPD - SDAC Statistician |
| Other author(s): | PPD - Study statistician |
| Adhoc reviewers: | PPD - Director, Biostatistics |
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| Clinical Development Managert | PPD |
| Epidemiologist |  |
| Country |  |
| Medical Director |  |
| Study Statistician | PPD |
| Lead Statistician | PPD |

Statistical Analysis Plan
Study alias \& e-track number(s): Zoster-028 (116427)

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## Statistical Analysis Plan

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This document summarizes the planned statistical analyses for iSRC review as described in the charter dated 18MAR2013. This SAP is divided into 2 parts: the first part detailing the analyses to be performed (current document) and a second part, annex (called TFL) describing the flow and format of tables, figures and listings to be provided.

## 1. DOCUMENT HISTORY

| Date | Version | Description | Protocol Version |
| :--- | :--- | :--- | :--- |
| 25-MAR-2013 | 1 | Final | Amendment 1 Final: <br> 19 November 2012 |

## 2. STUDY DESIGN

All iSRC analyses will be unblinded. The following group names will be used:

| Group order in tables | Group label in tables | Group definition for footnote |
| :---: | :---: | :---: |
| 1 | HZ/su-PreChemo | Herpes Zoster subunit vaccine ( $1^{\text {st }}$ vaccination before start of chemotherapy) |
| 2 | Placeb-PreChemo | Placebo group ( $1^{\text {st }}$ vaccination before start of chemotherapy) |
| 3 | HZ/su-OnChemo | Herpes Zoster subunit vaccine ( $1^{\text {st }}$ vaccination at start of $1^{\text {st }}$ (or $2^{\text {nd }}$ ) chemotherapy cycle) |
| 4 | Placeb-OnChemo | Placebo group ( $1^{\text {st }}$ vaccination at start of $1^{\text {st }}$ (or $2^{\text {nd }}$ ) chemotherapy cycle) |

The third scheduled iSRC review meeting will occur after solicited (Days $0-6$ postdose 1) and unsolicited (Days 0-29 post-dose 1) adverse event (AE) data are available from the first 20 subjects in the "OnChemo" vaccination schedule group.

# Statistical Analysis Plan 

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## 3. OBJECTIVES

As per protocol

## 4. ENDPOINTS

As per protocol

## 5. STUDY POPULATION

The statistical analyses will be performed on the total vaccinated cohort, which includes all subjects with at least one visit/contact after vaccination.

## 6. STATISTICAL METHODS

TABLES:

- Demography summary
- Incidence of solicited symptoms of grade 3 reported up to seven days after each vaccination
- Incidence of unsolicited symptoms (all, grade 3, related) reported up to 30 days after each vaccination
- Incidence of Serious Adverse Events (SAEs) reported during the entire study period


## LISTING:

- Listing of Serious Adverse Events (SAEs) reported during the entire study period
- Listing of all potential Immune-Mediated Diseases (pIMDs) reported during the entire study period
- Listing of withdrawals from further vaccination/from the study due to $\mathrm{AE} / \mathrm{SAE}$ until study end
- Listing of SAEs detailed as Disease recurrences during the entire study period


# Statistical Analysis Plan 

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## 7. STATISTICAL CALCULATIONS

### 7.1. Derived and transformed data

### 7.1.1. Demography

Age: Age at the time of study entry, computed as the number of years between the date of birth and the date of first vaccination. In case of partial dates, consider:

- 15 th of month, if only the day is missing
- 30th of June, if day and month are missing.


### 7.1.2. Safety

For the analysis, temperatures (measured by oral, axillary or tympanic route) will be coded as follows:

| Grade | Temperature |
| :--- | :--- |
| 0 | $<37.5^{\circ} \mathrm{C}$ |
| 1 | $\geq 37.5^{\circ} \mathrm{C}-\leq 38^{\circ} \mathrm{C}$ |
| 2 | $\geq 38.1^{\circ} \mathrm{C}-\leq 39.0^{\circ} \mathrm{C}$ |
| 3 | $\geq 39.1^{\circ} \mathrm{C}$ |

The following conversion rule is used for the conversion of temperature to ${ }^{\circ} \mathrm{C}$ :
Temperature in ${ }^{\circ}$ Celsius $=\left(\left(\right.\right.$ Temperature in ${ }^{\circ}$ Fahrenheit -32 $\left.) * 5\right) / 9$
The result is rounded to 1 decimal.

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### 7.2. Numerators and denominators

For a given subject and the analysis of solicited symptoms within 7 days postvaccination, missing or non-evaluable measurements will not be replaced. Therefore the analysis of the solicited symptoms based on the total vaccinated cohort will include only vaccinated subjects for doses with documented safety data (i.e., symptom screen completed).

More specifically the following rules will be used:

- Subjects who documented the absence of a solicited symptom after one dose will be considered not having that symptom after that dose.
- Subjects who documented the presence of a solicited symptom and fully or partially recorded daily measurement over the solicited period will be included in the summaries at that dose and classified according to their maximum observed daily recording over the solicited period.
- Subjects who documented the presence of a solicited symptom after one dose without having recorded any daily measurement will be assigned to the lowest intensity category at that dose (i.e., $37.5^{\circ} \mathrm{C}$ for fever or grade 1 for other symptoms).
- Doses without symptom sheets documented will be excluded.

For analysis of unsolicited adverse events, such as serious adverse events or adverse events by primary MedDRA term, all vaccinated subjects will be considered. Subjects who did not report the event will be considered as subjects without the event.

Note that for safety tables, the way the percentage of subjects will be derived, will depend on the event analysed (see table below for details). As a result, the N value will differ from one table to another.

| Event | N used for deriving \% per subject for Vaccination phase |
| :--- | :--- |
| Solicited general symptom | All subjects with at least one solicited general symptom <br> documented as either present or absent (i.e., symptom <br> screen completed) |
| Solicited local symptom | All subjects with at least one solicited local symptom <br> documented as either present or absent (i.e., symptom <br> screen completed) |
| Unsolicited symptom | All subjects with study vaccine administered |

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### 7.3. Methods for Cls

The proportion of events will be tabulated with exact $95 \%$ Confidence Intervals (CI) 2 sided.

The exact $95 \%$ CIs for a proportion within a group will be calculated according to Clopper et al (1934).

### 7.4. Number of decimals

The following decimal description will be used for the demography and safety/reactogenicity analyses.

| Display Table | Parameters | Number of decimal <br> digits |
| :--- | :--- | :--- |
| Demographic <br> characteristics | Mean, median age | 1 |
| Demographic <br> characteristics | SD (age) | 1 |
| All summaries | \% of count, including LL \& UL <br> of CI | 2 |

## 8. CONDUCT OF ANALYSES

### 8.1. Sequence of analyses

| Description | Analysis ID (SDD sub-folder) |
| :--- | :--- |
| iSRC review x* | E1_0x* | * $\mathrm{x}=2, \ldots$

### 8.2. Statistical considerations for interim analyses

N.A.

## Statistical Analysis Plan

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## 9. CHANGES FROM PLANNED ANALYSES

N.A.

## 10. REFERENCES

Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of binomial. Biometrika. 1934;26:404-413

## 11. ABBREVIATIONS

AE Adverse event
CI Confidence Interval
GSK GlaxoSmithKline
iSRC internal Safety Review Committee
MedDRA Medical Dictionary for Regulatory Activities
N.A. Not Applicable

SAP Statistical Analysis Plan
SDAC Statistics Data Analysis Centre
SDD SAS Drug Development
TFL Tables Figures and Listing template annexed to SAP

## Statistical Analysis Plan

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| Detailed Title: | A phase II/III, randomised, observer-blind, placebocontrolled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster $\mathrm{HZ} / \mathrm{su}$ candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy. |
| :---: | :---: |
| SAP version | Version 1 |
| SAP date | 18-Nov-2014 |
| Scope: | All data pertaining to the above study |
| Co-ordinating author: | PPD |
| Other author(s): | PPD |
| Adhoc reviewers: | PPD (RA representative) |
|  | PPD (Safety representative) |
|  | PPD (Lead Stat. analyst) |
| Approved by: | PPD (CRDL) |
|  | PPD (Lead Stat.) |
|  | PPD (Lead Scientific Writer) |


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# Statistical Analysis Plan <br> Study alias \& e-track number(s): Zoster-028 (116427) <br> The complete statistical analysis plan and results presentation is divided into 2 parts: the first part detailing the analyses to be performed (known as SAP, current document) and a second part, annexes (called TFL) describing the flow and format of tables, figures and listings to be annexed to the SR. 

## LIST OF ABBREVIATIONS

| AE | Adverse event |
| :--- | :--- |
| ANCOVA | Analysis of Covariance |
| ATP | According-To-Protocol |
| CI | Confidence Interval |
| EL.U/ml | ELISA unit per milliliter |
| ELISA | Enzyme-linked immuno-sorbent assay |
| Eli Type | Internal GSK database code for type of elimination code |
| gE | Glycoprotein E |
| GMC | Geometric mean antibody concentration |
| GMF | Geometric mean frequency |
| GSK | GlaxoSmithKline |
| HZ | Herpes Zoster |
| HZ/su | Herpes Zoster subunit vaccine (50 $\mu \mathrm{g}$ gE/ AS01 B ) |
| IC | Immuno-Compromised |
| IU/ml | International units per milliliter |
| LL | Lower Limit of the confidence interval |
| MAR | Missing At Random |
| MCAR | Missing Completely At Random |
| MedDRA | Medical Dictionary for Regulatory Activities |
| NA | Not applicable |
| pIMD | Potential Immune-Mediated Disease |
| SAE | Serious adverse event |
| SAP | Statistical Analysis Plan |
| SBIR | GSK Biological's Internet Randomization System |
| SD | Standard Deviation |
| SR | Study Report |

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TFL Tables Figures and Listing template annexed to SAP
UL Upper Limit of the confidence interval
VRR Vaccine Response Rate
YOA Year of Age

| Date | Description | Protocol Version |
| :--- | :--- | :--- |
| 18-NOV-2014 | Version 1 | Amendment 2 Final, 11 August 2014 |

## 2. STUDY DESIGN

### 2.1. Study design overview


*The first dose of vaccine/ placebo will be administered to the groups in relation to a chemotherapy cycle. The Dose 1 scheduling windows for the study groups are indicated below:

- HZ/su-PreChemo and Placeb-PreChemo Groups - within a maximum of 1 month to a minimum of 10 days before the start of a chemotherapy cycle.
- $\mathrm{HZ} /$ su-OnChemo and Placeb-OnChemo Groups - at the first day (allowing a window of $+/-1$ day) of a chemotherapy cycle.
** The second dose of study vaccine/ placebo must be administered between 1 and 2 months after the first vaccination AND at the first day (allowing a window of $+/-1$ day) of a subsequent cycle of chemotherapy.
*** Visit 3 occurs approximately one month after the second vaccination.
+Visit 4 will occur within Months 4 to 13 for a Blood Sampling at the start of the last cycle of chemotherapy (if at least two months after the previous Blood Sampling (V3/M2)). Thus, the timing of this particular visit will be variable depending on the subject's chemotherapy schedule and also on when they started vaccination in relation to their chemotherapeutic regimen. This visit will coincide with the subject's lowest immune status.
$\ddagger$ Should Visit 4 coincide with Month 5 or Month 9, it will replace the Month 5 or the Month 9 Phone Contact, respectively.
${ }^{\Delta}$ Should Visit 4 coincide with Month 13, the Visit 5 procedures will be conducted (including a Blood Sampling for CMI).
$\neq$ Blood samples ( $\sim 8 \mathrm{~mL}$ ) will be collected from all subjects at Visit $1,2,3$, first day of last chemotherapy cycle at Visit 4 and Visit 5 to evaluate humoral immune responses.
§Blood samples ( $\sim 30 \mathrm{~mL}$ ) will be collected from a sub-cohort of subjects at Visit $1,2,3$ and 5 to evaluate cell-mediated immune responses (CMI sub-cohort).
$\mathrm{HZ} / \mathrm{su}=$ Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb $=$ Placebo; Vacc = Vaccination


## Statistical Analysis Plan

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### 2.2. Groups and sub-groups description

The Table 1 presents the group names that will be used for the statistical analyses:

Table 1 Study groups description

| Group order <br> in tables | Group label in <br> tables | Group definition for <br> footnote | Pooled Groups label in <br> tables |
| :--- | :--- | :--- | :--- |
| 1 | HZ/su | Herpes Zoster sub-unit <br> vaccine group | NA |
| 2 | Placebo | Placebo group | NA |

The Table 2 presents the sub-group names that will be used for the statistical analyses:

Table 2 Sub-groups description

| Sub-groups | Group order <br> in tables | Group label <br> in tables | Group definition for footnote |
| :--- | :--- | :--- | :--- |
| Age strata | 1 | $18-49 y s$ | Subjects aged between 18 and 49 years |
|  | 2 | $>=50$ ys | Subjects aged 50 years and older |
| Chemotherapy <br> schedule | 1 | PreChemo | first vaccination 8 days or more prior to the <br> start of a chemotherapy cycle |
|  | 2 | OnChemo | first vaccination at the start of a <br> chemotherapy cycle (+ or -1 day) |

All analyses will be performed per treatment actually administered. In case of the subject was vaccinated according to another study chemotherapy schedule (timing between Chemotherapy and vaccination), the analysis will be performed by the chemotherapy schedule actually followed.

### 2.3. Sub-cohort

Target enrolment is approximately 232 eligible adults diagnosed with solid tumours receiving chemotherapy.

The CMI sub-cohort will be comprised exclusively of subjects from the PreChemo Groups. This is a subgroup of the subjects in the study in selected countries at designated sites that have access to a peripheral blood mononuclear cells (PBMC) processing facility within the acceptable time window from sample collection to PBMC processing.

The sub-cohort foreseen for CMI analyses are described in Table 3.

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Table 3 Sub-cohorts

| Sub-cohort name | Description | Estimated number of <br> enrolled subjects |
| :--- | :--- | :--- |
| CMI sub-cohort* | Blood samples (approximately 30 mL ) collected at Visits <br> $1,2,3$ and 5 will be analysed to assess CMI response | 76 |

* This CMI sub-cohort will be comprised exclusively of subjects from the PreChemo Groups. $\mathrm{mL}=$ Millilitre; CMI = Cell-mediated Immunity


### 2.4. Method of blinding

Data will be collected in an observer-blind manner. By observer-blind, it is meant that during the course of the study, the vaccine recipient and those responsible for the evaluation of any study endpoint (e.g., safety and reactogenicity) will all be unaware of which vaccine was administered. To do so, vaccine preparation and administration will be done by authorised medical personnel who will not participate in any of the study clinical evaluation assays.

From study start until Month 2, the study is observer-blind. From Month 2 (Visit 3) until Month 13 (Visit 5, study end), the study remains blinded for the subjects and for the study staff to ensure that study-related procedures and observations performed at the study sites will continue to be conducted in a single-blind manner.

Beyond Month 2, the subjects will continue to be blinded and access to unblinded individual subject treatment assignments will be restricted to GSK study personnel only on an as-needed basis. The investigators will receive a copy of the report of the analysis for immunogenicity and safety data up to Month 2, and may thus be unblinded only with respect to any individual subject data summarized in the study report. However, the individual data listings and subject treatment assignments will not be provided to the investigators until after the conclusion of the study, following the completion of Month 13 (Visit 5, study end).

The laboratory in charge of the laboratory testing will be blinded to the treatment, and codes will be used to link the subject and study (without any link to the treatment attributed to the subject) to each sample.

## 3. OBJECTIVES

As per protocol.

## 4. ENDPOINTS

As per protocol.

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## 5. STUDY POPULATION

### 5.1. Study cohorts/ data sets to be analysed

### 5.1.1. Total vaccinated cohort

The Total Vaccinated cohort (TVC) will include all vaccinated subjects with respect to the vaccine actually administered.

The TVC for analysis of humoral immunogenicity will include vaccinated subjects for whom data related to humoral immunogenicity endpoints are available.

The TVC for analysis of CMI immunogenicity will include vaccinated subjects for whom data related to CMI immunogenicity endpoints are available and included in the CMI sub-cohort.

The TVC for analysis of safety will include all subjects with at least one vaccine administered.

The TVC for analysis of reactogenicity will include all subjects with at least one vaccine administration documented.

### 5.1.2. According-to-protocol cohort for analysis of safety - up to 30 days post last vaccination

The According To Protocol (ATP) cohort for analysis of safety will include all illegible subjects:

- who have received at least one dose of study vaccine/ placebo according to their random assignment;
- for whom administration site of study vaccine/ placebo is known;
- who have not received other vaccine forbidden in the protocol up to 30 days post last vaccination;
- for whom the randomisation code has not been broken.


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### 5.1.3. According-to-protocol cohort for analysis of safety - up to the study end

The According To Protocol (ATP) cohort for analysis of safety will include all illegible subjects:

- who have received at least one dose of study vaccine/ placebo according to their random assignment;
- for whom administration site of study vaccine/ placebo is known;
- who have not received other vaccine forbidden in the protocol during the entire study period;
- for whom the randomisation code has not been broken.


### 5.1.4. According-to-protocol cohort for analysis of humoral immunogenicity

The ATPc for analysis of humoral immunogenicity will include all evaluable subjects from the ATP cohort for analysis of safety - up to 30 days post last vaccination:

- Who meet all eligibility criteria :
- All inclusion/exclusion criteria are applicable;
- The following exclusion criterion is clarified :
- Previous chemotherapy course less than 28 days before first study vaccination.
- Who comply with the procedures and intervals defined below :

The intervals, as defined in Section 9.4.3 of the protocol, between vaccinations (dose 1 to dose 2) and between dose 2 and blood sample at Visit 3 (dose 2 to 1 month post dose 2 visit) for inclusion in the ATP cohort for immunogenicity will be defined respectively as 30-84 days and 21-63 days (see Table 4). The immune ATPc analysis will be based on the allowed intervals for Visit $1 \rightarrow$ Visit 2 and Visit $2 \rightarrow$ Visit 3 .

## Table 4 Intervals between study visits for the ATP cohort for analysis of immunogenicity

| Interval between visits | Allowed interval for the ATP cohort for analysis of immunogenicity |
| :--- | :--- |
| Visit $1 \rightarrow$ Visit 2 | $30-84$ days |
| Visit $2 \rightarrow$ Visit 3 | $21-63$ days |

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- Who do not meet any of the criteria for elimination from an ATP analysis up to Month 2 visit;
- Who did not receive a product leading to elimination from an ATP analysis up to Month 2 visit;
- Who did not present with a medical condition leading to elimination from an ATP analysis up to Month 2 visit;
- For whom data concerning immunogenicity endpoint measures are available up to Month 2 visit.


### 5.1.5. According-to-protocol cohort for analysis of humoral persistence

The ATPc for analysis of humoral persistence will include all evaluable subjects from the ATP cohort for safety analysis up to study end:

- Who meet all eligibility criteria :
- All inclusion/exclusion criteria are applicable;
- The following exclusion criterion is clarified:
- Previous chemotherapy course less than 28 days before first study vaccination.
- Who comply with the procedures and intervals defined below :

The intervals, as defined in Section 9.4.3 of the protocol, between vaccinations (dose 1 to dose 2) and between dose 2 and blood sample at Visit 3 (dose 2 to 1 month post dose 2 visit) for inclusion in the ATP cohort for immunogenicity/persistence will be defined respectively as 30-84 days and 21-63 days (see Table 5). The immune ATPc analysis will be based on the allowed intervals for Visit $1 \rightarrow$ Visit 2 , Visit $2 \rightarrow$ Visit 3 , and Visit $2 \rightarrow$ Visit 5 .

Table 5 Intervals between study visits for the ATP cohort for analysis of immunogenicity

| Interval between visits | Allowed interval for the ATP cohort for analysis of immunogenicity |
| :--- | :--- |
| Visit $1 \rightarrow$ Visit 2 | $30-84$ days |
| Visit $2 \rightarrow$ Visit 3 | $21-63$ days |
| Visit $2 \rightarrow$ Visit 5 | $335-425$ days |

- Who do not meet any of the criteria for elimination from an ATP analysis up to Month 13 visit,
- Who did not receive a product leading to elimination from an ATP analysis up to Month 13 visit,


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- Who did not present with a medical condition leading to elimination from an ATP analysis up to Month 13 visit.
- For whom data concerning immunogenicity endpoint measures are available up to Month 13 visit.


### 5.1.6. According-to-protocol cohort for analysis of CMI-immunogenicity

The ATPc for analysis of CMI-immunogenicity will include all evaluable subjects included in the ATP cohort for humoral immunogenicity analyses and included in the CMI sub-cohort.

### 5.1.7. According-to-protocol cohort for analysis of CMI-persistence

The ATPc for analysis of CMI-persistence will include all evaluable subjects included in the ATP cohort for humoral persistence analyses and included in the CMI sub-cohort.

### 5.2. Codes per study cohorts and analysis

The list of applicable elimination codes for each analysis can be found in the study specific form FORM-BIO-CLIN-9004-05 Elim code specifications.

| Analyses | Cohorts | Elimination codes | $\begin{array}{\|l} \hline \text { Eli } \\ \text { Type } \\ \hline \end{array}$ |
| :---: | :---: | :---: | :---: |
| Final analysis (active phase*) | Total vaccinated cohort | 900, 1030 | MA |
|  | ATP cohort for safety - up to 30 days post last vaccination | 900, 1030-1500 \& 1600 | MA |
|  | ATP cohort for Humoral immunogenicity | 900, 1030, 1050-2500 | MA |
|  | Total vaccinated cohort for CMI | 900, 1030 \& 4130 | MA |
|  | ATP cohort for CMI | $\begin{aligned} & 900,1030,1050-2500 \& \\ & 4130 \end{aligned}$ | MA |
| End of study+ analysis (extended safety FU and immunogenicity persistence**) | Total vaccinated cohort | 900, 1030 | FU |
|  | ATP cohort for safety up to the study end | 900, 1030-1500 \& 1600 | FU |
|  | ATP cohort for Humoral persistence | 900, 1030,1050-2500 | FU |
|  | Total vaccinated cohort for CMI | 900, 1030 \& 4130 | FU |
|  | ATP cohort for CMI persistence | $\begin{aligned} & 900,1030,1050-2500 \\ & \& 4130 \end{aligned}$ | FU |

*includes the immunogenicity data (humoral \& CMI) up to Month 2 and all safety data available
**includes all data, immunogenicity persistence (humoral \& CMI) and safety up to the study end +is the time of Month 13 visit

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## 6. STATISTICAL METHODS

The analyses by sub-groups are referring to the sub-groups described in section 2.2.

### 6.1. Analysis of demographics/baseline characteristics

Demographic characteristics (age at first study vaccination, gender, geographic ancestry and ethnicity), cohort description, ECOG performance status, Tumor diagnosis and withdrawal status will be summarized using descriptive statistics.

Frequency tables will be generated for categorical variables such as gender.
Mean, median and standard error will be provided for continuous data such as age.
The same tabulation will be performed by age strata and by duration between the first dose and the start of chemotherapy cycle (PreChemo/ OnChemo).

### 6.2. Analysis of immunogenicity

The primary analysis will be based on the ATP cohort for analysis of immunogenicity. If the percentage of subjects excluded from this ATP cohort be greater than $5 \%$ in any treatment group, a second analysis based on the Total vaccinated cohort will be performed to complement the ATP analysis.

The humoral descriptive analysis will be performed by treatment group, by age strata and by chemotherapy schedule (PreChemo and OnChemo).

The CMI descriptive analysis will be performed by treatment group and by age strata.

### 6.2.1. Humoral response:

The following parameters will be calculated for the humoral immune response in terms of Anti-gE antibody concentration as determined by ELISA:

### 6.2.1.1. within group assessment

- Geometric mean concentration (GMC) at Months $0,1,2,6$ and 13 with $95 \%$ confidence interval (CI).
- Seropositivity rate at Months $0,1,2,6$ and 13 with exact $95 \%$ confidence interval (CI).
- Vaccine response rate (VRR) at Months 1, 2, 6 and 13 with exact $95 \%$ confidence interval (CI).

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- Descriptive statistics of the fold over pre-vaccination at Month 1, 2, 6 and 13 (Mean, Standard deviation, Min, Q1, Median, Q3, Max)


### 6.2.1.2. Between group assessment

To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy, a repeated measurement model will be used to assess the geometric mean fold increase over placebo at month 2 .

For the assessment of the primary confirmatory objective "To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the HZ/su vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy (PreChemo Groups only)", the fixed-effect model will include the means for all levels of the visit by treatment interaction effect.

For the assessment of the secondary confirmatory objective "To evaluate the anti-gE humoral immunogenicity response at Month 2, following a two-dose administration of the $\mathrm{HZ} /$ su vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (all subjects)., the fixed-effect model will include the means for all levels of the visit by treatment interaction effect and for the 2 levels of the first vaccination schedule (Onchemo/Prechemo).

A likelihood-based approach will be used to analyze post-vaccination log-transformed anti-gE antibody concentrations (Month 1 to Month 2).

The pre-vaccination log-transformed antibody concentrations (Month 0 ) will be included as a continuous covariate.

The goodness-of-fit Bayesian information criterion (BIC) and Akaike information criteria AIC statistics will be used to assess the need of a separate residual variance for placebo group or for each treatment group. Geometric means of Month 2 post-vaccination antibody concentrations will be calculated conditionally to the means of the logtransformed concentrations at pre-vaccination calculated across the treatment groups. Adjusted means and difference of means between vaccines and placebo will be calculated together with 2 -sided confidence intervals and back-transformed to the original units to provide GMCs and GM ratios over Placebo.

A sensitivity analysis may include age strata and gender as fixed effect in the model if the data allows [age strata (2-levels, $<50 \mathrm{YOA}$ and $>=50 \mathrm{YOA}$ ), gender (male, female)]. Age strata and gender by treatment and activity interaction will be tested. The P-values higher than 0.1 , will be excluded from the model.

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### 6.2.2. Cell-mediated immune (CMI) response:

The following parameters will be calculated for the CMI response in terms of gE-specific CD4 ${ }^{+}$T-cell secreting at least two activation markers (from among IFN- $\gamma$, IL-2, TNF$\alpha, C D 40 \mathrm{~L}$ ) (Spec-CD4[2+]) and for CD4 ${ }^{+}$T-cell secreting at least two activation markers following induction with gE (Ind-CD4[2+]):

The calculation of the derived data Spec-CD4[2+] and Ind-CD4[2+] are described in section 7.1.3.2.

### 6.2.2.1. Within groups assessment

- Descriptive statistics of the frequency of the Spec-CD4[2+] and the Ind-CD4[2+] at Months 0, 1, 2 and 13.
- Descriptive statistics of the fold over pre-vaccination in the Spec-CD4[2+] and the Ind-CD4[2+] at Month 1, 2 and 13 (Mean, Standard deviation, Min, Q1, Median, Q3, Max)
- Vaccine response rate (VRR) in the Spec-CD4[2+] at Months 1, 2 and 13 with exact $95 \%$ confidence interval (CI).


### 6.2.2.2. Between groups assessment

The evaluation of the CMI responses at Month 2, following a two-dose administration of the $\mathrm{HZ} / \mathrm{su}$ vaccine, as compared to placebo, in subjects with solid tumours receiving chemotherapy (PreChemo Groups only), will be performed in term of Ind-CD4[2+] and Spec-CD4[2+].

## a. Evaluation of CMI immunogenicity response in term of Ind-CD4[2+]

A likelihood-based Repeated Measurement approach with repeated measurements model will be used to analyze the post-vaccination log-transformed frequencies of Ind-CD4 [2+] T-cells.

The fixed-effect model will include the means for all levels of the treatment effect by visits interaction. The continuous covariates will include the pre-vaccination logtransformed Ind-CD4 [2+] (Month 0) and the post-vaccination log-transformed CD4 T cell frequency under the background condition.

The goodness of fit Bayesian Information Criterion (BIC) and Akaike Information Criteria (AIC) statistics will be used to assess the need of a separate residual variance for each treatment group.

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Adjusted Geometric means (GMs) of Month 2 post-vaccination in Ind-CD4[2+] T cell frequency, will be calculated conditionally to the means of the pre-vaccination logtransformed Ind-CD4[2+] and the post-vaccination log-transformed CD4[2+] T cell frequency under background conditions. Adjusted means and difference of means between vaccines and placebo will be calculated together with 2 -sided confidence intervals and back-transformed to the original units to provide frequency adjusted GMs and frequency adjusted GM ratios.

The adjusted geometric means calculated as described above provide the effect of the vaccine on the sum of both antigen-specific and non-specific CD4[2+] frequencies.
b. Evaluation of CMI immunogenicity response in term of Spec-CD4[2+]

This procedure below allows the calculation of the geometric means for the Spec$C D 4[2+]$. These estimates better represent the net effect of the vaccines over the frequency of $\mathrm{CD} 4{ }^{2+}$ as caused by the vaccine.

The same model as described above will be used to analyze the log-transformed ratio between induction frequency and background frequency of CD4 [2+]. Least-square means and difference of least-squares means will then be back-transformed and used to provide estimates for the frequency difference divided by background ([induction background] / background). The log-transformation of the ratios of these estimates between treatments will be calculated. The confidence interval for ratio of Spec-CD4[2+] will be calculated using the Delta method following the procedure below. The confidence intervals are calculated on the $\log$ scale for $\log \left(\mathrm{W}_{\mathrm{jk}}\right)$ then back-transformed to the original units.

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$$
\begin{aligned}
Y_{i j k l}-x_{i j k} & =v_{j}+\mu_{j k}+\alpha_{j} \cdot y_{i 0 k}+\beta \cdot x_{i j k}+\varepsilon_{i j k} \\
(\hat{Y}-\bar{x})_{j k} \mid \bar{y}_{0}, \bar{x} & =v_{j}+\mu_{j k}+\alpha_{j} \cdot \bar{y}_{0}+\beta \cdot \bar{x} \\
\varepsilon_{i j k} & \approx N(0, \Sigma) \quad \Sigma \text { unstructured } \\
Y_{i j k} & =\text { log - transformed frequency following induction with antigen } \\
& \text { for subject } i, \text { visit } j \text { and treatment } k . \\
x_{i j k} & =\log \text { - transformed frequency in medium condition (background) } \\
\bar{y}_{0}= & \text { mean of log - transformed induction frequency at pre - vaccination } \\
\bar{x}= & \text { mean of log - transformed background frequency post - vaccination } \\
\hat{Z}_{j k}= & \operatorname{Exp}\left(\hat{Y}_{j k}-\bar{x}\right)-1=\frac{\operatorname{Exp}\left(\hat{Y}_{j k}\right)-\operatorname{Exp}(\bar{x})}{\operatorname{Exp}(\bar{x})} \\
\log \left[\hat{W}_{j k}\right]= & \log _{e}\left(\frac{\hat{Z}_{j k_{2}}}{\hat{Z}_{j k_{1}}}\right)=\log _{e}\left(\frac{\operatorname{Exp}\left(\hat{Y}_{j k 2}-\bar{x}\right)-1}{\operatorname{Exp}\left(\hat{Y}_{j k 1}-\bar{x}\right)-1}\right)=\log _{e}\left(\frac{\operatorname{Exp}\left(\hat{Y}_{j k_{2}}\right)-\operatorname{Exp}(\bar{x})}{\operatorname{Exp}\left(\hat{Y}_{j k_{1}}\right)-\operatorname{Exp}(\bar{x})}\right)
\end{aligned}
$$

$\hat{Z}_{j k}=$ mean increase from background frequency to induction frequency relative to background frequency at visit k for treatment k .
$\hat{W}_{j k}=$ Vaccine effect on the antigen - specific frequency of CD4 T cells producing cytokines, following adjustment for background frequency
1.1. The derivative of $\log (\mathrm{Wjk})$ with regards to the Yjk 2 is described below.

$$
\frac{\partial}{\partial Y_{j k 2}} \log _{e}\left(\frac{\operatorname{Exp}\left(\hat{Y}_{j k 2}-\bar{x}\right)-1}{\operatorname{Exp}\left(\hat{Y}_{j k 1}-\bar{x}\right)-1}\right)=\frac{\operatorname{Exp}\left(\hat{Y}_{j k 2}-\bar{x}\right)}{\operatorname{Exp}\left(\hat{Y}_{j k 2}-\bar{x}\right)-1}=1+\frac{1}{\operatorname{Exp}\left(\hat{Y}_{j k 2}-\bar{x}\right)-1}=1+\frac{1}{\hat{Z}_{j k 2}}
$$

1.2. The derivative of $\log (\mathrm{Wjk})$ with regards to the Yjk 1 is described below.

$$
\frac{\partial}{\partial Y_{j k 1}} \log _{e}\left(\frac{\operatorname{Exp}\left(\hat{Y}_{j k 2}-\bar{x}\right)-1}{\operatorname{Exp}\left(\hat{Y}_{j k 1}-\bar{x}\right)-1}\right)=-\left(\frac{\operatorname{Exp}\left(\hat{Y}_{j k 1}-\bar{x}\right)}{\operatorname{Exp}\left(\hat{Y}_{j k 1}-\bar{x}\right)-1}\right)=-1-\frac{1}{\operatorname{Exp}\left(\hat{Y}_{j k 1}-\bar{x}\right)-1}=-1-\frac{1}{\hat{Z}_{j k 1}}
$$

1.3. The vector of partial derivative contains only the derivative for the means involved in the comparison (ie. Yjk1 and Yjk2).

$$
\operatorname{Grad}_{\hat{Y}_{j k 1}, \hat{Y}_{j k 2}}\left(\log _{e}\left(\frac{\hat{Z}_{j k_{2}}}{\hat{Z}_{j k_{1}}}\right)\right)=\binom{-1-\frac{1}{\hat{Z}_{j k 1}}}{1+\frac{1}{\hat{Z}_{j k 2}}}
$$

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1.4. The covariance matrix of the means is pre multiplied and post-multiplied by the vector of partial derivative to provide the variance of the contrast.

$$
\operatorname{Var}\left(\log _{e}\left(\frac{\hat{Z}_{j k_{2}}}{\hat{Z}_{j k_{1}}}\right)\right)=T\left(\operatorname{Grad}_{\hat{Y}_{j k 1}, \hat{Y}_{j k 2}}(\bullet)\right) \cdot \sum \cdot \operatorname{Grad}_{\hat{Y}_{\hat{y}_{k 1}, \hat{Y}_{k 22}}}(\bullet)
$$

1.5. The $\log (\mathrm{Wjk})$ confidence interval is calculated based on the T -student percentile using the degrees of freedom provided by the MIXED procedure for the difference of means under consideration (eg Yjk2 and Yjk1) and the standard error calculated above.

$$
\log _{e}\left(\operatorname{LowerCI}\left(W_{j k}\right)\right)=\log _{e}\left(\frac{\hat{Z}_{j k_{2}}}{\hat{Z}_{j k_{1}}}\right)-\operatorname{TINV}(1-\operatorname{alpha} / 2, d f) \cdot \sqrt{\operatorname{Var}\left(\log _{e}\left(\frac{\hat{Z}_{j k_{2}}}{\hat{Z}_{j k_{1}}}\right)\right)}
$$

The confidence intervals are then back-transformed to the original units to provide the confidence intervals for $\mathrm{W}_{\mathrm{jk}}$.

A sensitivity analysis may include age strata and gender as fixed in the model, if the data allows [age strata (2-levels, $<50 \mathrm{YOA}$ and $>=50 \mathrm{YOA}$ ), gender (male, female)].

### 6.3. Analysis of safety

The primary analysis for safety will be based on the TVc. A second analysis based on the ATP c will be performed to complement the TVc analysis.

All safety analyses will be performed by age strata and by duration between the first dose and the start of chemotherapy cycle (Prechemo/Onchemo).

### 6.3.1. Within group assessment

When appropriate, tabulations will be presented overall and by time of occurrence relative to last vaccination (e.g., using windows such as Days $0-6$, Days $0-29$ and more than 30 days post-vaccination).

The results for the analysis of safety will be tabulated as:

- The percentage of subjects with at least one local AE (solicited and unsolicited), with at least one general adverse event (solicited and unsolicited) and with any AE during the solicited 7-day follow-up period will be tabulated with exact $95 \%$ Confidence Intervals (CI) after each vaccine dose and overall;

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- The percentage of subjects with at least one local solicited AE, with at least one general solicited AE and with any solicited AE during the solicited 7-day follow-up period will be tabulated with exact $95 \%$ Confidence Intervals (CI) after each vaccine dose and overall;
- The percentage of subjects reporting each individual solicited local and general AE during the solicited 7 -day-follow-up period will be tabulated with exact $95 \% \mathrm{CI}$;
- For all solicited symptoms, the same tabulation will be performed for grade 3 solicited AEs and for solicited general AEs with relationship to vaccination;
- The proportion of subjects with at least one report of unsolicited AE classified by the Medical Dictionary for Regulatory Activities (MedDRA) Preferred Terms and reported up to 30 days after each vaccination will be tabulated with exact $95 \% \mathrm{CI}$;
- The same tabulation will be performed for grade 3 unsolicited AEs and for unsolicited AEs with a relationship to vaccination. The proportion of AEs resulting in a medically attended visit will also be tabulated;
- Total number/percentages of doses (per dose and overall) followed by AEs will be tabulated;
- Number of subjects with pIMDs will be tabulated;
- SAEs and withdrawal due to $\mathrm{AE}(\mathrm{s})$ will be described in detail.


## 7. STATISTICAL CALCULATIONS

### 7.1. Derived and transformed variables

### 7.1.1. Handling of missing data

For a given subject and a given measurement, missing or non-evaluable measurements will not be imputed. The missing endpoint and censoring are supposed to occur independently, and the pattern of the missing value(s) being either Missing Completely At Random or Missing At Random only.

For the analysis of solicited symptoms, missing or non-evaluable measurements will not be replaced. Therefore the analysis of the solicited symptoms based on the TVC will include only subjects/doses with documented safety data (i.e., symptom screen/sheet completed).

For the analysis of unsolicited AEs/SAEs/pIMDs/concomitant medications, all vaccinated subjects will be considered and subjects who did not report an event will be considered as subjects without an event.

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For the analysis of immunogenicity, missing or non-evaluable measurements will not be replaced. Therefore, a subject will be excluded from an analysis if all measurements are missing or non-evaluable.

### 7.1.2. Demography

For a given subject and a given demographic variable, missing measurement will not be replaced except for age.

Age will be calculated as the number of years between the date of birth and the date of first vaccination.

In case of partial dates of any of these 2 dates:

- 15th of month, if only the day is missing
- 30th of June, if day and months are missing


### 7.1.3. Immunogenicity

### 7.1.3.1. Humoral immune response

- A seronegative subject is a subject whose Ab concentration is below the cut-off value.
- A seropositive subject is a subject whose Ab concentration is greater than or equal to the cut-off value.
- The seropositivity rate is defined as the percentage of seropositive subjects.
- The vaccine response rate for anti-gE is defined as the percentage of subjects who have at least a:
- 4-fold increase in the anti-gE antibodies concentration as compared to the prevaccination anti-gE antibodies concentration, for subjects who are seropositive at baseline, or,
- 4-fold increase in the anti-gE antibodies concentration as compared to the anti$g E$ antibodies cut-off value for seropositivity, for subjects who are seronegative at baseline.
- The Geometric Mean Concentrations (GMCs) calculations are performed by taking the anti-log of the mean of the log concentration transformations. For descriptive statistics only, Ab concentrations below the cut-off of the assay $(97 \mathrm{mIU} / \mathrm{mL})$ will be given an arbitrary value equal to half the cut-off for the purpose of GMC calculation.

For inferential analyses, the values below the cut-off will be considered as missing.

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### 7.1.3.2. Cellular-mediated immune response

- For the inferential analysis, the frequency of $\mathrm{CD} 4[2+]$ upon in vitro stimulation with the gE-antigen (Ind-CD4[2+]) is calculated by adding an offset of 0.5 to the number of activated $\mathrm{CD} 4^{+}$T-cells (numerator) divided by the total number of $\mathrm{CD} 4^{+}$T-cells involved (denominator). A similar calculation will be made for the frequency of CD4[2+] upon in vitro stimulation in medium only (background condition).

$$
\begin{aligned}
& \text { Freq }{ }_{\text {Induction }}^{C D 4[2+]}=\frac{n_{\text {Indunction }}^{2+}+0.5}{N_{\text {Induction }}^{C T}} \\
& \text { Freq }_{\text {Bachground }}^{C D 4[2+]}=\frac{n_{\text {Backrground }}^{2+}+0.5}{N_{\text {Bachrouround }}^{C D}}
\end{aligned}
$$

$$
\begin{aligned}
& \log \left(\text { Freq }_{\text {Induction }}^{C D 4}[2+]=\log \left(\frac{n_{\text {Induction }}^{2+}+0.5}{N_{\text {Induction }}^{C D 4}}\right)\right. \\
& \log \left(\text { Freq }_{\text {Background }}^{C D 4[2+]}\right)=\log \left(\frac{n_{\text {Background }}^{2+}+0.5}{N_{\text {Background }}^{C D 4}}\right)
\end{aligned}
$$

$n_{\text {Induction }}^{2+}=$ number of CD4 $\mathrm{T}-$ cells secreting at least 2 activations markers after inductions with the antigen
$n_{\text {Background }}^{2+}=$ number of CD4 T - cells secreting at least 2 activations markers in medium conditions
$N^{C D 4}=$ Total number of CD4 T - cells involved in the assay (induction or background)

- For the descriptive analyses, the frequency of CD4 [2+] T-cells upon in vitro stimulation with the antigen (induction condition) is calculated by dividing the number of activated CD4 [2+] T-cells (numerator) over the total number of CD4 Tcells involved (denominator).

$$
\text { Freq }_{\text {Induction }}^{C D 4[2+]}=\frac{n_{\text {Induction }}^{2+}}{N_{\text {Induction }}^{\text {CD }}}
$$

$n_{\text {Induction }}^{2+}=$ number of CD4 T cells secreting at least 2 activation markers after induction with the antigen
$N^{C D 4}=$ Total number of CD4 T cells involved in the assay (induction)

- The frequency of $\mathbf{g E}$-specific $\mathrm{CD}^{+}$T-cells (Spec-CD4[2+]) for each individual subject is calculated as the difference between the frequency of CD4[2+], upon in vitro stimulation with the gE-antigen (induction condition) minus the frequency of (CD4[2+] upon in vitro stimulation in medium only (background condition). The differences less or equal to one (1) are imputed to 1 gE -specific activation marker expressing CD4[2+] T-cell per $10^{6} \mathrm{CD} 4^{+}$T-cells.

Freq $q_{\text {Specific }}^{C D 4[2+]}=\frac{n_{\text {Induction }}^{2+}}{N_{\text {Induction }}^{C D 4}}-\frac{n_{\text {Background }}^{2+}}{N_{\text {Background }}^{C D 4}}$
Freq ${ }_{\text {Specific }}^{\text {CD4 }[2+]}=1$

$$
\begin{aligned}
& \text { if } \frac{n_{\text {Induction }}^{2+}}{N_{\text {Induction }}^{C D 4}}>1+\frac{n_{\text {Background }}^{2+}}{N_{\text {Background }}^{C D}} \\
& \text { if } \frac{n_{\text {Induction }}^{2+}}{N_{\text {Induction }}^{C D 4}} \leq 1+\frac{n_{\text {Background }}^{2+}}{N_{\text {Background }}^{C D 4}}
\end{aligned}
$$

$n_{\text {Induction }}^{2+}=$ number of CD4 T-cells secreting at least 2 activation markers after induction with the $\mathrm{gE}-$ antigen
$\boldsymbol{n}_{\text {Background }}^{2+}=$ number of CD4 T-cells secreting at least 2 activation markers in the medium conditions
$N^{C D 4}=$ Total number of CD4 T - cells involved in the assay (induction of background )

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- The Geometric Mean (GM) frequency calculations are performed by taking the antilog of the mean of the log frequency transformations;
- The CMI vaccine response to gE will be based on the gE-specific data as computed above. The lower limit of linearity (LLL) for the assay ( 320 positive events/106 CD4+ T-cells) will be used as threshold for vaccine response assessment. The vaccine response is defined as the percentage of subjects who have at least a:
- 2-fold increase as compared to the LLL, for subjects with pre-vaccination T-cell frequencies below the LLL.
- 2-fold increase as compared to pre-vaccination T-cell frequencies, for subjects with pre-vaccination above the LLL.


### 7.1.4. Safety

- For a given subject and the analysis of solicited symptoms within 7 days postvaccination, missing or non-evaluable measurements will not be replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated Cohort will include only vaccinated subjects for doses with documented safety data (i.e., symptom screen completed). More specifically the following rules will be used:
- Subjects who documented the absence of a solicited symptom after one dose will be considered not having that symptom after that dose.
- Subjects who documented the presence of a solicited symptom and fully or partially recorded daily measurement over the solicited period will be included in the summaries at that dose and classified according to their maximum observed daily recording over the solicited period.
- Subjects who documented the presence of a solicited symptom after one dose without having recorded any daily measurement will be assigned to the lowest intensity category at that dose (i.e., $37.5^{\circ} \mathrm{C}$ for fever or grade 1 for other symptoms).
- Doses without symptom sheets documented will be excluded.
- For analysis of unsolicited adverse events, such as serious adverse events, pIMDs or adverse events by primary MedDRA term and analysis of relapse, all vaccinated subjects will be considered. Subjects who did not report the event or the concomitant medication will be considered as subjects without the event or the concomitant medication respectively.
- For analysis of concomitant medications, all vaccinated subjects will be considered for the analysis of concomitant medication use. Subjects who did not report the use of a concomitant medication will be considered as subjects without medication. Subjects who started the use of a concomitant medication during the mentioned period and took at least one dose will be considered in these analyses.


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The way the percentage of subjects will be derived will depend on the event analysed (see the following table for details). As a result, the denominator $(\mathrm{N})$ will differ from one table to another.

| Event | N used for deriving \% | Terminology used in the tables for N |
| :--- | :--- | :--- |
| Concomitant <br> medication | All vaccinated subjects | Number of subjects with at least one <br> administered dose |
| Solicited general <br> symptom | All vaccinated subjects with <br> at least one solicited general <br> symptom documented as <br> either present or absent | For each dose and overall/subject: <br> $\mathrm{N}=$ number of subjects with at least <br> one documented dose <br> For overall/dose: <br> $\mathrm{N}=$ number of documented doses |
| Solicited local <br> symptom | All vaccinated subjects with <br> at least one solicited local <br> symptom documented as <br> either present or absent | For each dose and overall/subject: <br> $\mathrm{N}=$ number of subjects with at least <br> one documented dose <br> For overall/dose: <br> N= number of documented doses |
| Unsolicited <br> symptom from day <br> 0 to day 30 | All vaccinated subjects | Number of subjects with at least one <br> administered dose |
| SAE/pIMDs | All vaccinated subjects | Number of subjects with at least one <br> administered dose |

- All CI computed will be two-sided $95 \% \mathrm{CI}$.


### 7.1.4.1. Grading rule

The maximum intensity of local injection site redness/swelling will be scored at GSK Biologicals using GSK Biologicals' standard grading scale based on the US Food and Drug Administration (FDA) guidelines for Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers enrolled in Preventive Vaccine Clinical Trials" (see protocol).

| 0 | $:$ | $<20 \mathrm{~mm}$ diameter |
| :--- | :--- | :--- |
| 1 | $:$ | $\geq 20 \mathrm{~mm}$ to $\leq 50 \mathrm{~mm}$ diameter |
| 2 | $:$ | $>50 \mathrm{~mm}$ to $\leq 100 \mathrm{~mm}$ diameter |
| 3 | $:$ | $>100 \mathrm{~mm}$ diameter |

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The preferred route for recording temperature in this study is oral. When there is no other alternative, the temperature may be taken by another route. If the temperature is taken by another route (axillary, rectal or tympanic), that route should be documented. The following rules will be used for analysis including temperature:

- For the analysis of pooled solicited symptoms, pooled general symptoms that include Temperature and the analysis of temperature individually, all measurements will be converted to the preferred route scale (oral) according to the following rules:

|  | Temperature (route) |  |
| :--- | :--- | :--- |
| Grade | Oral/axillary/tympanic | rectal |
| 0 | $<37.5^{\circ} \mathrm{C}$ | $<38.0^{\circ} \mathrm{C}$ |
| 1 | $\geq 37.5^{\circ} \mathrm{C}-\leq 38.0^{\circ} \mathrm{C}$ | $\geq 38.0^{\circ} \mathrm{C}-\leq 38.5^{\circ} \mathrm{C}$ |
| 2 | $>38.0^{\circ} \mathrm{C}-\leq 39.0^{\circ} \mathrm{C}$ | $>38.5^{\circ} \mathrm{C}-\leq 39.5^{\circ} \mathrm{C}$ |
| 3 | $>39.0^{\circ} \mathrm{C}$ | $>39.5^{\circ} \mathrm{C}$ |

Note that Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C} / 99.5^{\circ} \mathrm{F}$ for oral, axillary or tympanic route, or $\geq 38.0^{\circ} \mathrm{C} / 100.4^{\circ} \mathrm{F}$ for rectal route. The preferred route for recording temperature in this study is oral.

- An additional analysis will be performed on temperature broken down by route. The summary of temperature will be broken by $0.5^{\circ}$ increase starting from $37.5^{\circ}$.


### 7.1.4.2. Conversion of temperature to ${ }^{\circ} \mathrm{C}$

The following conversion rule is used for the conversion of temperature to ${ }^{\circ} \mathrm{C}$
Temperature in ${ }^{\circ}$ Celsius $=\left(\left(\right.\right.$ Temperature in ${ }^{\circ}$ Fahrenheit -32 $\left.) * 5\right) / 9$
The result is rounded to 1 decimal digit.

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### 7.2. Number of decimals

The following decimal description from the decision rules will be used for the demography, immunogenicity and safety/reactogenicity.

| Display Table | Parameters | Number of <br> decimal digits |
| :--- | :--- | :--- |
| Demographic <br> characteristics | Mean, median age | 1 |
| Demographic <br> characteristics | SD (age) | 2 |
| Immunogenicity | Ratio of GMC | 2 |
| Immunogenicity | GMC | 1 |
| All summaries | Mean, Min, Q1, Median, Q3, Max for duration | 1 |
| All summaries | \% of count, including LL \& UL of Cl | 1 |
| All summaries | \% of difference, including LL \& UL of CI | 2 |
| All summaries | p-value | 3 |

### 7.3. Methods for Cls

All p-values reported are related to the null hypothesis test parameter $=0$ or absence of effect of the vaccine.

Unless otherwise mentioned, the confidence intervals will be 2 sided $95 \%$ CI and calculated according to the following methods:

### 7.3.1. Binomial Data

The exact $95 \%$ CIs for a proportion within a group will be calculated according to Clopper \& al. (1934).

### 7.3.2. Continuous Data

The $95 \%$ CI for geometric mean concentrations/frequencies analyses will be obtained. The $95 \%$ CI for the mean of log-transformed concentration/frequency will be first obtained assuming that log-transformed values were normally distributed with unknown variance. The $95 \%$ CI for the GMCs will be then obtained by exponential-transformation of the $95 \%$ CI for the mean of log-transformed titre/concentration.

Refer to dedicated methods for inferential methods.

## Statistical Analysis Plan

Study alias \& e-track number(s): Zoster-028 (116427)

### 7.4. Inferential analysis and statistical models

### 7.4.1. Humoral response endpoints with treatment comparison

The SAS code will resemble the following:

```
For the primary analysis on the PREchemo group only the following SAS code will be
used :
PROC MIXED DATA=file METHOD=ML NOCLPRINT=10 SCORING=3 CL;
    CLASS pid trt activity;
    MODEL anti-ge response(M1 and 2) = trt trt*activity
            Anti_gE_pre
            / DDFM=KR OUTPRED=predict RESIDUALS;
One of the 2 statements:
    REPEATED activity / TYPE=UNR SUBJECT=pid R;
    REPEATED activity / TYPE=UNR SUBJECT=pid GROUP=trt R;
For the primary analysis on all subjects the following SAS code will be used :
PROC MIXED DATA=file METHOD=ML NOCLPRINT=10 SCORING=3 CL;
    CLASS pid trt activity chemo_schedule;
    MODEL anti-ge_response(M1 and 2) = chemo_schedule trt trt*activity
trt*activity*chemo_schedule
    Anti_gE_pre
    / DD\overline{FM=}=\overline{K}R OUTPRED=predict RESIDUALS;
One of the 2 statements:
    REPEATED activity / TYPE=UNR SUBJECT=pid R;
    REPEATED activity / TYPE=UNR SUBJECT=pid GROUP=trt R;
For the sensitivity analysis, the following SAS code will be used if the analysis
doesn't include an effect (EX: Prechemo group only), that variable will be excluded
from the model:
/* agestrat gender chemo_schedule will be added as fixed effect in the model, the
effect with P-values below 0.1 will be removed from the model*/
PROC MIXED DATA=file METHOD=ML NOCLPRINT=10 SCORING=3 CL;
    CLASS pid trt activity agestrat gender chemostatus;
    MODEL anti-ge response(M1 and 2) = agestrat chemostatus gender
            trt trt*activity trt*activity*agestrat trt*activity*chemostatus
            trt*activity*gender
            Anti_gE_pre
            / DDFM=KR OUTPRED=predict RESIDUALS;
One of the 2 statements:
    REPEATED activity / TYPE=UNR SUBJECT=pid R;
    REPEATED activity / TYPE=UNR SUBJECT=pid GROUP=trt R;
```

- Anti_ge_response and anti_ge_pre will be used in logarithm scale.


## Statistical Analysis Plan

gsk
GlaxoSmithKline
Study alias \& e-track number(s): Zoster-028 (116427)

### 7.4.2. CMI response endpoints with treatment comparison

The SAS code will resemble the following

### 7.4.2.1. $\quad \mathrm{gE}-\mathrm{CD}^{2+}$ following induction frequency

```
PROC MIXED DATA=file METHOD=ML NOCLPRINT=10 SCORING=3 CL;
    CLASS pid trt activity;
    MODEL lninduction = trt trt*activity
        Lninduction_pre
            lnbackgroun\overline{d}
            / DDFM=KR OUTPRED=predict RESIDUALS;
One of the 2 statements:
    REPEATED activity / TYPE=UNR SUBJECT=pid R;
    REPEATED activity / TYPE=UNR SUBJECT=pid GROUP=trt R;
```

Lninduction $=\log \left(\mathrm{CD} 4^{2+}\right.$ following induction frequency $)$.
Lnbackground $=\log \left(\mathrm{CD} 4^{2+}\right.$ following background frequency $)$.

### 7.4.2.2. gE-specific $C D 4^{2+}$ frequency

```
For the primary analysis the following SAS code will be used :
MODEL lninduction - lnbackground = trt trt*activity
    Lninduction_pre
    Lninduction_pre*activity
    lnbackgroun\overline{d}
    / DDFM=KR OUTPRED=predict RESIDUALS;
For the sensitivity analysis, the following SAS code will be used.
/* agestrat gender will be added as fixed effect in the model, the effect with
P-values below 0.1 will be removed from the model*/
MODEL lninduction - lnbackground = chemostatus
    trt trt*activity trt*activity*gender trt*activity*agestrat
    Lninduction_pre
    lnbackground
    / DDFM=KR OUTPRED=predict RESIDUALS;
```

| Statistical Analysis Plan | gSk |
| :--- | :--- |
| ClaxoSmithKline |  |
| Study alias \& e-track number(s): Zoster-028 (116427) |  |

## 8. CONDUCT OF ANALYSES

### 8.1. Sequence of analyses

Two formal analyses are planned: a first analysis and an end of study analysis.
The first analysis of immunogenicity and reactogenicity/safety data will be performed when all data up to and including Month 2 ( 30 days post dose 2 ) will be available after completion of Visit 3.

The end of study analysis of persistence of immunogenicity and safety data will be performed when all data up to and including Month 13 will be available.

| Description | Analysis ID (SDD sub-folder) | TFL short title |
| :--- | :--- | :--- |
| Analysis active phase - Immunogenicity <br> (Month 2) and safety follow up | Analysis_E1_07 | Annex 1 |
| Analysis of persistence and Extended <br> safety follow-up | Analysis_E1_01 | Annex 2 |

### 8.2. Statistical considerations for interim analyses

No interim analysis has been planned.

## Statistical Analysis Plan

Study alias \& e-track number(s): Zoster-028 (116427)

## 9. CHANGES FROM PLANNED ANALYSES

- For the analysis purpose, the "Prechemo" sub-group is defined as "first vaccination at least 10 days before 8 days or more prior to the start of a chemotherapy cycle".
- The following exclusion criterion has been clarified:
- Previous chemotherapy course less than one month-28 days before first study vaccination.
- A clarification is done on CMI analysis by sub-group. No analysis by "by duration between the first dose and the start of chemotherapy cycle (PreChemo and OnChemo)" could be done on CMI sub-cohort.

All descriptive immmnegenicity analyses will be performed by age strata and by duration between the first dose and the start of chemotherapy cycle (PreChemo and OnChemo) as appropriate. This will be further detailed in the Statistical Analysis Plan (SAP).

The humoral descriptive analysis will be performed by treatment group, by age strata and by chemotherapy schedule (PreChemo and OnChemo).

The CMI descriptive analysis will be performed by treatment group and by age strata.

## Statistical Analysis Plan

Study alias \& e-track number(s): Zoster-028 (116427)

## 10. REFERENCES

Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of binomial. Biometrika. 1934;26:404-413

## Signature of principal or coordinating investigator

## GlaxoSmithKline Biologicals

Vaccines R\&D
Investigator Approval Page
STUDY TITLE: A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy.

Study: 116427 (ZOSTER-028) Development Phase: II/III
I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

| Name of Investigator: | Ignacio Delgado Mingorance |  |
| :--- | :--- | :--- |
| Affiliation /investigational | Hospital Infanta Cristina, |  |
| centre: | Unidad De Cuidados IntenPPD , SPD |  |$\quad$, de Flvas

Signature of Investigator:
Date:


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0573lc8487ce255d05ee5ald7a9alld9ae627f56 2.0 5/8/2017 10:49:33 AM - .

## CONFIDENTIAL

## GlaxoSmithKline Biologicals Vaccines R\&D <br> Sponsor Signatory Approval Page

Please note that by signing this page, you take responsibility for the content of the Study Report including appendices
STUDY TITLE: A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster $\mathrm{HZ} /$ su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $\geq 18$ years of age with solid tumours receiving chemotherapy

Study: 116427 (ZOSTER-028) Development Phase: II/III
I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

Name of Sponsor Signatory: Lidia Oostvogels

Title of Sponsor Signatory:
Director, Clinical and Epidemiology Project Leader
Zoster Program
Belgian Research and Development Care
GlaxoSmithKline Vaccines


Signature:
Date:


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[^0]:    ${ }^{1}$ Specific laboratory tests performed in the course of VZV-infection medical evaluation include VZVpositive polymerase chain reaction (PCR), culture, immunohistochemical staining, or other tests that strongly suggest of VZV

[^1]:    ${ }^{2}$ Interferon gamma, interleukin-2, tumour necrosis factor alpha and CD40 ligand

[^2]:    ${ }^{3}$ Interferon gamma, interleukin-2, tumour necrosis factor alpha and CD40 ligand

[^3]:    Narrative: This 67-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 24th July 2013, for prophylaxis.

    Concomitant products included enoxaparin (Clexane) and metamizole magnesium (Nolotil).
    On PPD 108 days after receiving Herpes zoster vs Placebo, the subject developed severe - grade 3 perianal abscess. Serious criteria included hospitalization and GSK medically significant. The

[^4]:    Narrative: This 71-year-old male subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 1st dose of Herpes zoster vs Placebo (intramuscular) on 11th April 2013, for prophylaxis.

    On PPD 4 days after receiving Herpes zoster vs Placebo, the subject developed severe grade 3 seizure cerebral. Serious criteria included hospitalization and GSK medically significant. The subject was treated with LEVETIRACETAM, BEMIPARIN and BETAMETHASONE DIPROPIONATE (DIPRODERM). The outcome of seizure cerebral was recovered/resolved on 15th April 2013.

[^5]:    Narrative: This 54-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 9th October 2013, for prophylaxis.

    Previously administered products included FLU VACCINE. Concurrent medical conditions included colon carcinoma.

[^6]:    Narrative: This 66-year-old female subject was enrolled in a blinded study titled A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' herpes zoster HZ/su candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults $=18$ years of age with solid tumours receiving chemotherapy. The subject received the 2nd dose of Herpes zoster vs Placebo (intramuscular) on 27th September 2013, for prophylaxis.

    Co-suspect products included paclitaxel for cancer.
    On PPD 8 days after receiving Herpes zoster vs Placebo, the subject developed not

[^7]:    18-49ys = Subjects aged between 18 and 49 years
    $\geq 50 y s=$ Subjects aged 50 years and older
    HZ/su = Herpes Zoster sub-unit vaccine group
    Placebo = Placebo group
    $N=$ number of subjects with available results
    Nmiss = number of subjects with missing results
    SD = Standard Deviation
    Q1, Q3 = First and third quartiles
    Min/Max = Minimum/Maximum
    PI(M1) = Post-vaccination Dose I (Month 1)
    PII(M2) = Post-vaccination Dose II (Month 2)
    PII(M6) = Post-vaccination Dose II (Month 6)
    PII(M13) = Post-vaccination Dose II (Month 13)

[^8]:    18-49ys = Subjects aged between 18 and 49 years
    $\geq 50 y s=$ Subjects aged 50 years and older
    HZ/su = Herpes Zoster sub-unit vaccine group
    Placebo = Placebo group
    $\mathrm{N}=$ number of subjects with available results
    Nmiss = number of subjects with missing results
    SD = Standard Deviation
    Q1,Q3 = First and third quartiles
    Min/Max = Minimum/Maximum
    PI(M1) = Post-vaccination Dose I (Month 1)
    PII(M2) = Post-vaccination Dose II (Month 2)
    PII(M6) = Post-vaccination Dose II (Month 6)
    PII(M13) = Post-vaccination Dose II (Month 13)

[^9]:    HZ/su = Herpes Zoster sub-unit vaccine group
    Placebo = Placebo group
    $\mathrm{N}=$ number of subjects with available results
    Nmiss = number of subjects with missing results
    SD = Standard Deviation
    Q1,Q3 = First and third quartiles
    Min/Max = Minimum/Maximum
    PRE = Pre-vaccination (Month 0)
    PI(M1) = Post-vaccination Dose I (Month 1)
    PII(M2) = Post-vaccination Dose II (Month 2)
    PII(M13) = Post-vaccination Dose II (Month 13)

[^10]:    18-49ys = Subjects aged between 18 and 49 years
    $\geq 50 y s=$ Subjects aged 50 years and older
    HZ/su = Herpes Zoster sub-unit vaccine group
    Placebo = Placebo group
    $\mathrm{N}=$ number of subjects with available results
    Nmiss = number of subjects with missing results
    SD = Standard Deviation
    Q1, Q3 = First and third quartiles
    Min/Max = Minimum/Maximum
    PRE = Pre-vaccination (Month 0)
    PI(M1) = Post-vaccination Dose I (Month 1)
    PII(M2) = Post-vaccination Dose II (Month 2)
    PII(M13) = Post-vaccination Dose II (Month 13)

[^11]:    $\mathrm{N}=$ number of subjects with at least one documented dose
    $\mathrm{n} / \%=$ number/percentage of subjects reporting the symptom at least once For Overall/dose:
    $\mathrm{N}=$ number of documented doses
    $\mathrm{n} / \%=$ number/percentage of doses followed by at least one type of symptom
    $95 \% \mathrm{Cl}=$ Exact $95 \%$ confidence interval; $\mathrm{LL}=$ lower limit, UL = upper limit
    $\left(^{*}\right)=$ Temperature is measured by oral, axillary or tympanic routes
    Fever is defined as temperature $\geq 37.5^{\circ} \mathrm{C}$ for oral, axillary or tympanic route

[^12]:    - ----------------Checksum----------------!Ver.!Created On - -

    100c090ea30ccf4add295e32205f6c2221d28acd 2.0 8/14/2014 12:52:34 PM - -

[^13]:    * The first dose of vaccine/ placebo will be administered to the groups in relation to a chemotherapy cycle. The Dose 1 scheduling windows for the study groups are indicated below:
    - HZ/su-PreChemo and Placeb-PreChemo Groups - within a maximum of 1 month to a minimum of 10 days before the start of a chemotherapy cycle.
    - HZ/su-OnChemo and Placeb-OnChemo Groups - at the first day (allowing a window of $+/-1$ day) of a chemotherapy cycle. (Amended: 11 August 2014)
    ** The second dose of study vaccine/ placebo must be administered between 1 and 2 months after the first vaccination AND at the first day (allowing a window of $+/-1$ day) of a subsequent cycle of chemotherapy.
    *** Visit 3 occurs approximately one month after the second vaccination.
    †Visit 4 will occur within Months 4 to 13 for a Blood Sampling at the start of the last cycle of chemotherapy (if at least two months after the previous Blood Sampling (V3/M2)). Thus, the timing of this particular visit will be variable depending on the subject's chemotherapy schedule and also on when they started vaccination in relation to their chemotherapeutic regimen. This visit will coincide with the subject's lowest immune status.
    $\ddagger$ Should Visit 4 coincide with Month 5 or Month 9, it will replace the Month 5 or the Month 9 Phone Contact, respectively (see Table 7).
    ${ }^{\Delta}$ Should Visit 4 coincide with Month 13, the Visit 5 procedures will be conducted (including a Blood Sampling for CMI). ${ }^{*}$ Blood samples ( $\sim 8 \mathrm{~mL}$ ) will be collected from all subjects at Visit $1,2,3$, first day of last chemotherapy cycle at Visit 4 and Visit 5 to evaluate humoral immune responses.
    §Blood samples ( $\sim 30 \mathrm{~mL}$ ) will be collected from a sub-cohort of subjects at Visit 1, 2, 3 and 5 to evaluate cell-mediated immune responses (CMI sub-cohort).
    HZ/su = Herpes Zoster subunit vaccine; Chemo = Chemotherapy; Placeb = Placebo; Vacc = Vaccination

[^14]:    * The first dose of vaccine/ placebo will be administered to the groups in relation to a chemotherapy cycles. The Dose 1 scheduling windows for the study groups are indicated below:

[^15]:    CRF template version 14 - May 22 2013 - System page 17 - Workbook 1 : with pre-vacc before V1

[^16]:    CRF template version 14 - May 22 2013 - System page 31-Workbook 2 : with pre-vacc during V1

[^17]:    WHO TO CONTACT IN CASE OF QUESTIONS?
    If you have any questions, please contact your study doctor or the study staff on the following phone number: [insert phone $n^{\circ}$ of the study doctor or study staff]

[^18]:    * Subjects of the Total Enrolled Cohort

[^19]:    - -----------------Checksum----------------!Ver.!Created On - -
    b465a295ff1052639c83532c14dde2d066808ff2 1.0 5/5/2017 9:51:27 AM - 8d279edacde44410fc45ba114b0df8e17076e979 1.0 5/5/2017 9:45:23 AM - daba4aff27e6bf628dc183e1c53bf8f6a2efe680 1.0 5/5/2017 9:48:38 AM - 35a6c488f6b4c8c3efb64d015c91808ccc7b568b 1.0 5/5/2017 9:42:45 AM - 675304ebb9d3c73efb4ec30731701982ac3b4e27 1.0 5/5/2017 9:55:47 AM - 2b87a6752df47199bcbdbf942ab51ac8e6412642 1.0 5/5/2017 9:55:54 AM - eb9cb3eaa748c8e274d118c6e8658dd0fc234fb8 1.0 5/5/2017 9:56:03 AM - 3ae030f20d589589526c2061234e0edcf4fd22d4 1.0 5/5/2017 10:12:37 AM - 72882f09a8716b7f17cb06416b6228ad36bafee1 1.0 5/5/2017 9:56:14 AM - 8afa84a25406ed7185de348219f5ebd628544550 1.0 5/5/2017 10:05:15 AM - 89b4d339521bf8127837ec1213fc4e227a53eead 1.0 5/5/2017 9:42:52 AM - 028e95245217169cc5f37fa185ce8a0b145a94c3 1.0 5/5/2017 10:13:05 AM - ae85f260577d01a6ab55ff9b595bc9659b3af876 1.0 5/5/2017 10:25:11 AM - f9ed1d775a620ababfbb0b46b00b5aac8835498b 1.0 5/5/2017 9:51:23 AM - 3f58a40232927844425b6cf7984260537add4e7d 1.0 5/5/2017 10:12:50 AM - 7ff3e3772dc01flbe13e24500a9382ble2826916 1.0 5/5/2017 10:13:00 AM - 05731c8487ce255d05ee5a1d7a9a11d9ae627f56 2.0 5/8/2017 10:49:33 AM - -

[^20]:    - -----------------Checksum----------------!Ver.!Created On - -
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