SYNOPSIS

Name of Sponsor/Company	Janssen Research & Development*
Name of Investigational Product	CNTO 1959 (guselkumab)

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Status: Approved

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Prepared by: Janssen Research & Development, LLC

Protocol No.: CNTO1959NAP1002

Title of Study: Phase 1, Open-label, Single-dose Study to Characterize the Elimination of Guselkumab Glycoform Variants in Healthy Subjects

NCT No.: NCT02570373

Clinical Registry No.: CR107879

Principal Investigator(s): Danielle Armas, MD CPI Celerion [redacted], [redacted]

Study Center(s): United States (1 site)

Publication (Reference): None

Study Period: 05 October 2015 – 12 January 2016

Phase of Development: Phase 1

Objectives:

Primary Objective: To characterize the elimination of guselkumab glycoform variants following a single intravenous (IV) administration of guselkumab at a 10 mg/kg dose in healthy subjects.

Secondary Objective: To obtain additional safety and tolerability data following a single IV administration of guselkumab at a 10 mg/kg dose in healthy subjects.

Methodology: This was an open-label, single-dose study to gather serum samples and other data to support characterization of the elimination of guselkumab glycoform variants in healthy subjects. All subjects were to receive a single IV infusion of guselkumab at a dose of 10 mg/kg over 60 minutes on Day 1. The subjects were to stay in the clinical study unit until discharge after administration of the study drug for Day 2 assessments. Subjects were to return to the study center for outpatient visits including safety assessments through Day 85.

Number of Subjects (planned and analyzed): Planned: Approximately 8 healthy subjects were planned to be enrolled in the study.

Analyzed: A total of 8 healthy subjects were enrolled and dosed with guselkumab in the study.

Diagnosis and Main Criteria for Inclusion:

Healthy men and women between 18 and 55 years of age (inclusive), who had a body mass index (BMI) between 18.5 kg/m^2 to 30.0 kg/m^2 (inclusive), body weight in the range of 60.0 kg to 100.0 kg (inclusive), if male; and weight in the range of 50.0 kg to 90.0 kg (inclusive), if female were eligible for enrollment into the study.

Test Product, Dose and Mode of Administration, Batch No.: CNTO1959 was supplied as 100 mg (Batch EIS7D [expiry: 30 September 2016]) in 1mL prefilled syringes assembled with UltraSafe PLUS™ Passive Needle Guard (PFS-U).

Duration of Treatment: For each subject the total duration of the study was approximately 85 days (excluding screening). The Screening Phase was to be of approximately 28 days, followed by single IV infusion of guselkumab over 60 minutes on Day 1, and the final Follow-up visit on Day 85.

Criteria for Evaluation:

Glycoform Elimination: Serum samples were to be collected and analyzed to determine the potential change in the rate of elimination of each glycoform of guselkumab. The detailed methods and results of the glycoform analysis were to be presented in a separate technical report.

Serum Guselkumab Concentration and Antibodies to Guselkumab: Serum samples for the measurement of guselkumab concentration and detection of antibodies to guselkumab were to be collected at protocol specified time points throughout the study.

Safety: All subjects who received at least 1 dose of study drug were to be included in the safety analysis. Adverse events (AEs), concomitant medications, clinical laboratory tests, vital signs, physical examinations, and electrocardiogram (ECG) were to be assessed throughout the study at time points specified in the Time and Events Schedule of the protocol. A serum pregnancy test was to be done at screening, before guselkumab administration, at Day 43 visit, and at the end of the study.

Statistical Methods:

Sample Size Determination: There was no formal hypothesis to be tested. Therefore, no formal sample size power calculation was undertaken.

Serum Guselkumab Concentration Analysis: Descriptive statistics, including arithmetic mean, SD, coefficient of variation (CV%), median, minimum, and maximum were to be used to summarize serum guselkumab concentration data at each planned sampling time point. No data imputations were to be performed on missing data. Plots of the mean (SD) and individual serum guselkumab concentrations over time were to be provided. In addition, serum guselkumab concentrations by planned sampling time point were to be listed for each individual subject.

Immunogenicity analysis: The incidence of antibodies to guselkumab during the study period were to be summarized for all subjects who received an IV administration of guselkumab and had at least 1 serum sample obtained for the detection of antibodies to guselkumab after guselkumab administration. Subjects were classified as positive or negative for antibodies to guselkumab.

Safety Analyses: Count and percentages for treatment-emergent adverse events (TEAEs) and descriptive statistics for laboratory tests and 12-lead ECG by parameter and visit were to be provided. Listings of physical examinations and vital signs for individual subject were to be provided.

RESULTS:

STUDY POPULATION:

- Eight subjects were enrolled in the study and dosed with guselkumab. All 8 subjects completed the study and no discontinuation from the study was reported.
- Healthy subjects (6 women and 2 men) between 26 to 49 years of age (inclusive) were enrolled in the study. All 8 subjects received the study drug as per the treatment schedule.

PHARMACOKINETIC AND IMMUNOGENECITY RESULTS:

- After a single 60-minute IV infusion of guselkumab, serum guselkumab concentrations peaked at the end of IV infusion and declined in an apparently bi-exponential manner through Day 43.
- Mean (SD) serum guselkumab concentrations were 249.5 (25.9) µg/mL (range 251.8 to 312.8 µg/mL) at the end of infusion and 26.6 (6.6) µg/mL (range 18.1 to 36.2 µg/mL) on Day 43.
- None (0.0%) of 8 subjects were positive for antibodies to guselkumab during the study period.

SAFETY RESULTS:

- The most frequently reported TEAEs (occurring in at least 2 subjects) were: headache (5 subjects [62.5%]), oropharyngeal pain (3 subjects [37.5%]), upper respiratory tract infection (2 subjects [25%]), and musculoskeletal pain (2 subjects [25%]).
- No deaths, serious adverse events (SAEs), or discontinuations due to TEAEs occurred during the study.
- Overall, there were no clinically meaningful changes in clinical laboratory tests, vital signs, physical examinations, ECGs or concomitant medication use during the study. The findings in the study are comparable to those reported in healthy subjects in the previous studies.

STUDY LIMITATIONS: No notable study limitations were identified by the Sponsor.

CONCLUSION(S):

- A single IV dose of 10 mg/kg guselkumab was generally well tolerated in healthy subjects. The findings in the study are comparable to those reported in healthy subjects in the previous studies.
- Subjects received a single 60-minute IV infusion of 10 mg/kg guselkumab had high level of systemic exposure to guselkumab from the end of IV infusion through Day 43. The mean (SD) serum guselkumab concentration on Day 43 was 26.6 (6.6) µg/mL; range 18.1 to 36.2 µg/mL.
- Glycoforms of guselkumab were characterized after a single IV infusion of 10 mg/kg guselkumab in healthy subjects. The results of glycoform analysis were to be reported in a separate technical report.

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