1. ABSTRACT

Title

A Phase IV Non-Interventional Enhanced Active Surveillance Study of Adults Vaccinated with AZD1222, dated 07 March 2022 by PPD , AstraZeneca AB.

Keywords

AstraZeneca (AZD1222), Post-authorisation, Active Surveillance, Safety

Rationale and background

Safe, effective, and accessible vaccines are needed to prevent Coronavirus disease 2019 (COVID-19). The COVID-19 Vaccine AstraZeneca (AZD1222) is a recombinant replication defective chimpanzee adenovirus expressing the severe acute respiratory syndrome coronavirus 2 spike protein. In Phase II and III clinical studies, AZD1222 helped to prevent COVID-19. In addition to ongoing Phase III studies and routine pharmacovigilance, the benefit-risk profile of AZD1222 was assessed in regional post-authorisation studies. This Phase IV enhanced safety surveillance study aimed to collect safety and tolerability data from adults vaccinated with AZD1222 in real-world settings in the European Union (Germany, Spain, and Sweden).

Research question and objectives

The purpose of this study was to assess the safety and tolerability of AZD1222 in adults vaccinated in real-world settings.

The primary objective of the study was to estimate the incidence of serious adverse events (SAEs), adverse events of special interest (AESIs), and medically-attended adverse events following immunisation (AEFIs) after at least one intramuscular (IM) dose of AZD1222 for 3 months after vaccination.

The secondary objectives were:

- To estimate the incidence of SAEs, AESIs, and medically-attended AEFIs after at least one IM dose of AZD1222 for up to 18 months after vaccination.
- To estimate the incidence of SAEs, AESIs, and medically-attended AEFIs after at least one IM dose of AZD1222 in participants by age group.
- To estimate the incidence of SAEs, AESIs, and medically-attended AEFIs after at least one IM dose of AZD1222 in participants with select comorbidities.
- To estimate the frequency of select pregnancy outcomes in women vaccinated with AZD1222 during pregnancy or within 45 days of the estimated conception date.

- To estimate the frequency of select outcomes at birth and up to 12 months of age in neonates/infants born to mothers vaccinated with AZD1222 during pregnancy or within 45 days of the estimated conception date.

Study design

This was a Phase IV real-world, observational, non-interventional, prospective cohort study of adults vaccinated with AZD1222. The study used an innovative digital platform (study app and web portal) as well as a traditional call centre to collect participants' responses to a series of health and well-being questionnaires over an 18-months. This study was closed out early due to age and usage restrictions for AZD1222 that were recommended by the national immunisation technical advisory groups in the participating countries. Due to the early close out of the study, participant responses were collected only for a maximum of 14 weeks. Investigators and study personnel had real-time access to enrolment trends and reported adverse events (AEs) via an investigator dashboard within the digital platform.

Research coordinators at vaccination sites invited vaccinated adults to join the study. Participants could enrol at the vaccination site with assistance from a research coordinator or could take home a study information brochure and enrol within 28 days after the first dose of AZD1222. Research coordinators and the study call centre were available to assist with enrolment and informed consent, as needed. Electronic consent using the study app could be an option where permitted.

Participants using the digital platform set up secure accounts, completed the enrolment questionnaires, and provided details of their vaccination to confirm eligibility. Non-digital participants completed the enrolment questionnaires and confirmed eligibility at a vaccination site or by a telephone call to the call centre. After enrolment, participants were contacted to complete follow-up questionnaires at timed intervals over an 18-month period (extended to 24 months for pregnant women and infant outcomes) after their first AZD1222 dose. Digital participants received push notifications or emails and non-digital participants received phone calls. Participants could also submit unscheduled AE reports through the digital platform and call centre.

Adverse events reported by participants were reviewed, followed-up, and assessed by study personnel. Participants granted permission for study personnel to contact their healthcare providers and obtain medical records. All participant data was coded and personal identifying information removed before the data was transferred to the Sponsor’s safety database. Role-based permissions ensured only authorised personnel could view data and records containing participant identities.

Setting

Planned vaccination sites included various healthcare settings such as general/primary care practices, hospitals, vaccination centres, mobile vaccination units, and long-term care facilities. The types of sites may have differed over time and between countries, reflecting differences in local practices and vaccination policies. To boost enrolment of older adults (≥ 65 years of age), the choice of vaccination sites for the study targeted locations likely to administer vaccines to older adults and geographical areas with higher populations of older adults. PPD .

Subjects and study size, including dropouts

Participants were adults ≥ 18 years of age who received the AZD1222 vaccine in PPD and were able and willing to consent to participate in the study. This study enrolled all eligible participants but sought to enrol older adults, with a target of 50% of participants being aged ≥ 65 years. Other subpopulations of interest included pregnant women, women who were breastfeeding, PPD , and frail persons with comorbidities. The study also aimed for an approximately equal enrolment of male and female participants. Target enrolment was 15,000 participants.

Variables and data sources

The information collected at enrolment included: AZD1222 vaccination details (date, batch/lot), exposure to any other vaccines, demographics, relevant medical history (select comorbidities, smoking history, prior COVID-19 infection), pregnancy status, breastfeeding status, and a self-reported global health assessment score.

The primary and secondary objectives assessing the safety and tolerability of AZD1222 (up to 3 months, up to 18 months, by age group, and in participants with select comorbidities) were planned to be measured by the incidence of SAEs, AESIs, and medically-attended AEFIs. Medically-attended AEFIs are AEs after immunisation leading to consultation with a medical doctor, hospitalisation, or an emergency room visit. Due to early close out of the study, these were measured for a maximum of 14 weeks. The additional secondary objectives (estimating the frequency of select pregnancy outcomes and neonatal/infant outcomes) were measured by events within the AESI medical concept “Pregnancy outcome – Maternal” (including spontaneous abortions, stillbirths, and preterm births) and within the AESI medical concept “Pregnancy outcome – Neonates” (including major congenital malformations and infants small for gestational age).

The main data sources for the study were participants and their medical records. Vaccination details were verified by a vaccination card, batch/lot number, and/or using a regional vaccination register. Participants reported all study outcomes using the study app, web portal, or call centre. Participants had the option to select a proxy to communicate on their behalf: a

caregiver, family member, or other trusted individual. Participants were asked for an emergency contact in case of death or incapacity.

Results

A total of 27 participants were eligible and provided consent. Twenty-six (96.3%) participants completed Week 1 of follow-up, 23 (85.2%) completed Week 4 of follow-up, 17 (63.0%) completed Week 8 of follow-up, and 15 (55.6%) completed Week 14 of follow-up. Four (14.8%) participants withdrew from the study (due to technical issues with the study app) and the remaining 23 (85.2%) participants were discontinued by the Sponsor due to study termination.

All 27 (100%) participants enrolled in the study were included in the full analysis set (FAS). The primary analysis set included 6 (22.2%) participants. PPD There were no pregnant women, women who became pregnant during the study, or breastfeeding women enrolled in the study.

Most of the participants in the FAS were male (16 [59.3%] participants). The median (range) age of the study participants was 57 (PPD) years. PPD

As for the safety evaluation of the study, no deaths and no AEs were reported.

Given the early close out of the study, the number of participants in key subpopulations was limited. The study follow-up period was restricted to a maximum of 14 weeks vs the 18 months originally planned.

Due to limited data for primary endpoint analysis and the result of the primary endpoint (ie, no AEs) the primary, secondary, and exploratory analyses were not performed, and the analysis was restricted to demographic and baseline characteristics of the considered population and subpopulations of participants.

Discussion

This report summarises the final data for participants enrolled in the non-interventional enhanced active surveillance study of adults vaccinated with AZD1222. For the safety evaluation, no deaths and no AEs were reported. Due to the premature termination of the study, the data collected are insufficient to provide a meaningful conclusion regarding the safety data of AZD1222.

Marketing authorisation holders

AstraZeneca AB

Names and affiliations of the principal investigator

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