PASS Study Report

Active substance	AZD1222
Product reference	D8111R00003
Version number	1.0
Date	07 March 2022

A Phase IV Non-Interventional Enhanced Active Surveillance Study of Adults Vaccinated with AZD1222

Marketing Authorisation Holder

Marketing authorisation holder	AstraZeneca AB, 151 85 Södertälje, Sweden
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EU PAS register number	EUPAS41335 (View Study (encepp.eu))

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Approved by:

PPD

Dr. Frederico Martinon Torres, PPD
Principal Investigator

PPD

Date

PASS INFORMATION

Title	A Phase IV Non-Interventional Enhanced Active Surveillance Study of Adults Vaccinated with AZD1222
Version identifier of the final study report	1.0
Date of last version of the final study report	07 March 2022
EU PAS register number	EUPAS41335
Active substance	AZD1222
Medicinal product	Vaxzevria
Product reference	CCI
Procedure number	CCI
Marketing authorisation holders	AstraZeneca AB
Joint PASS	No
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. **Primary objective:** • To estimate the incidence of SAEs, AESIs, and medically-attended AEFIs after at least one IM dose of AZD1222 for 3 months after vaccination. **Secondary objectives:** • 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.
Countries of study	Germany, Spain, and Sweden
Author	PPD PPD, AstraZeneca AB

AESI: adverse event of special interest; AEFI: adverse event following immunisation; EU: European Union; IM: intramuscular; PAS: post-authorisation studies; PASS: post-authorisation safety study; SAE: serious adverse event.

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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

Dr. Frederico Martinon Torres, PPD

2. LIST OF ABBREVIATIONS

Abbreviation or special term	Explanation
AE	Adverse event
AEFI	Adverse event following immunisation
AESI	Adverse event of special interest
AZD1222	COVID-19 Vaccine AstraZeneca
BMI	Body mass index
CI	Confidence interval
COVID-19	Coronavirus disease 2019
CRO	Contract research organisation
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU	European Union
FAS	Full analysis set
GPP	Good Pharmacoepidemiology Practices
HCP	Healthcare provider
CCI	CCI
IEC	Independent Ethics Committee
IM	Intramuscular
MedDRA	Medical Dictionary for Regulatory Activities
NITAG	National Immunisation Technical Advisory Group
PASS	Post-authorisation safety studies
CCI	CCI
PT	Preferred term
SAE	Serious adverse event
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SOC	System Organ Class
UK	United Kingdom

3. INVESTIGATORS

The investigators involved in the study are listed in Table 1.

Table 1 Investigators

Principal Investigator	Dr. Frederico Martinon Torres, PPD
Co-investigator	PPD Germany
	PPD , Germany
	PPD Spain
	PPD Spain
	PPD Sweden
	PPD Sweden

4. OTHER RESPONSIBLE PARTIES

Not applicable.

5. MILESTONES

Table 2 Milestones

Milestone	Planned date [a]	Actual date
Start of data collection	08 June 2021	31 May 2021
End of data collection	31 March 2024	15 December 2021
Registration in the EU PAS register	May 2021	31 May 2021
Interim report with data cut-off 1 month after first enrolment	Q3 2021	15 September 2021
Interim report with data cut-off 3 months after first enrolment	Q3 2021	03 December 2021
Final report of study results	25 June 2024	07 March 2022

[a] Planned dates are the Sponsor's best estimates based on circumstances at the time of writing the protocol. As the COVID-19 pandemic is a dynamic situation, milestones and dates may be amended if recruitment forecasts change.

EU: European Union; PAS: post-authorisation studies.

6. RATIONALE AND BACKGROUND

Safe, effective, and accessible vaccines to prevent COVID-19 are needed to reduce the spread of the disease and mitigate the public health and socioeconomic crises that have resulted from the pandemic. The COVID-19 Vaccine AstraZeneca (AZD1222; formerly ChAdOx1 nCoV 19) helped prevent COVID-19 in Phase II and III clinical studies.

Coronaviruses are enveloped viruses with positive-sense single-stranded ribonucleic acid genomes. The spike glycoprotein is a coronavirus surface protein involved in receptor binding and mediating virus entry into host cells during infection (Li 2016). AZD1222 is a recombinant replication defective chimpanzee adenovirus expressing the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike glycoprotein. Development of AZD1222 was initiated by the University of Oxford with subsequent transfer of development activities to the Sponsor. AZD1222 received emergency authorisation in the UK in Dec 2020.

7. 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. Table 3 lists the study objectives and outcome measures.

Table 3 Study objectives and outcome measures

Objective	Outcome measures
Primary objective	
To estimate the incidence of SAEs, AESIs, and medically-attended AEFIs after at least one IM dose of AZD1222 for 3 months after vaccination.	• Serious adverse events • Adverse events of special interest • Medically-attended AEFIs
Secondary objectives	
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.	• Serious adverse events • Adverse events of special interest • Medically-attended AEFIs
To estimate the incidence of SAEs, AESIs, and medically-attended AEFIs after at least one IM dose of AZD1222 in participants by age group.	• Serious adverse events • Adverse events of special interest • Medically-attended AEFIs
To estimate the incidence of SAEs, AESIs, and medically-attended AEFIs after at least one IM dose of AZD1222 in participants with select comorbidities.	• Serious adverse events • Adverse events of special interest • Medically-attended AEFIs
To estimate the frequency of select pregnancy outcomes in women vaccinated with AZD1222 during pregnancy or within 45 days of the estimated conception date.	Events within the AESI medical concept "Pregnancy outcome – Maternal", including: • Spontaneous abortions • Stillbirths • Preterm births
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.	Events within the AESI medical concept "Pregnancy outcome – Neonates", including: • Major congenital malformations • Small for gestational age
Exploratory objectives	
CCI [redacted]	CCI [redacted]
CCI [redacted]	CCI [redacted]
CCI [redacted]	CCI [redacted]

AE: adverse event; AEFI, adverse event following immunisation; AESI: adverse event of special interest; CCI [redacted]; IM: intramuscular; CCI [redacted]; SAE: serious adverse event.

8. AMENDMENTS AND UPDATES

Important amendments to the original study protocol are shown in Table 4. See Appendix 16.1.1 for full details of protocol amendments.

Table 4 Amendments and key updates

Number	Date	Section of study protocol	Amendment or update	Reason
1	11 May 2021	Section 6.2	The text describing the important identified risks and important potential risks of AZD1222 was updated.	To align the protocol with the updated Safety Specification in the EU RMP (version 3), including changes to risks.
		Section 8.2	Text added to clarify that participants may also receive messages to maintain contact and ensure study retention.	Clarification.
		Section 8.4.1	In the footnotes to Table 3, Data Collection Plan, the time interval for participants to receive reminders for the safety outcome follow-ups was revised from “2 to 8 weeks” to “1 to 12 weeks”.	Correction.
		Section 8.4.3; Section 8.8	A new subsection (Section 8.4.3.5) concerning antipyretic/pain-reliever use was added to the variables section. Also, in the data analysis description (Section 8.8), “Use of antipyretics/pain-reliever medication” was added to the subgroup analyses.	Clarification.
		Section 10.1.4	Table 5, the list of AESI for AZD1222 was updated to replace “stroke and other cerebrovascular events, venous thromboembolism” with “embolic and thrombotic events”, and to add “capillary leak syndrome” as an AESI.	To align the protocol with the updated AESI list in the EU RMP (version 3).
1	11 May 2021	Section 10.1.4	Table 5, the list of Adverse Events of Special Interest for AZD1222 was updated to clarify that the AESI “multisystem inflammatory syndrome” applies to both children and adults.	To align the protocol with the updated AESI list in the EU RMP (version 3).

Number	Date	Section of study protocol	Amendment or update	Reason
		Sections 10.2 and 10.6	The statement in Section 10.6 suggesting the Independent Adjudication Committee would advise study personnel on specific events was removed and a related statement in Section 10.2 was revised to state that study personnel with medical expertise will fulfil this role.	Correction.
		Section 10.6	The list of events to be reviewed by the Independent Adjudication Committee was updated to include embolic and thrombotic events, thrombosis in combination with thrombocytopenia, and thrombocytopenia.	These events will now be independently adjudicated.

AESI: adverse event of special interest; EU: European Union, RMP: risk management plan.

9. RESEARCH METHODS

9.1 Study design

This was a Phase IV real-world, observational, non-interventional, prospective cohort study of adults who received the AZD1222 vaccine. Vaccine recipients ≥ 18 years old were recruited for the study at vaccination sites in Germany, Spain, and Sweden. Awareness of the study was raised through social media and traditional media (television, print, and radio).

In this study, vaccination sites did not act as traditional study investigators and were not responsible for participant screening or safety follow-up. Rather, participants self-enrolled in the study using the study app, web portal, or call centre and submitted answers to study questionnaires using those methods. Event follow-up and assessment, where needed, were also performed remotely by study personnel. The digital platform also included an investigator dashboard where investigators and selected study personnel could view and track, in real-time, all AEs submitted. Role-based permissions ensured only authorised personnel could view identifying confidential data like participant names.

Participants enrolled in the study after vaccination with AZD1222. Enrolment was permitted within 28 days of the first dose of AZD1222 and could be completed at the vaccination site or remotely. Both digital and non-digital participants had the option to select a proxy, ie, a caregiver, family member, or other trusted individual, with permission to complete study questionnaires on behalf of the participant.

If a vaccine recipient chose to enrol in the study at the vaccination site, a study research coordinator was present and able to assist by:

- Providing information about the study.
- Explaining the study participation options: study app, web portal, or telephone communication with the call centre.
- Assisting the participant with the informed consent process.
- Checking if participants met the eligibility criteria and providing vaccination details.
- Recording contact information for the participant, the emergency contact (in case of apparent loss to follow-up), and the participant's proxy, if needed.
- Providing the proxy with instructions on how to assist the participant with reporting.

For vaccine recipients who preferred to enrol remotely, up to 28 days after the first vaccine dose, a study information brochure was available that included instructions to remotely enrol (including electronic informed consent completion, where permitted) and their vaccination details (if a vaccination card was not already provided).

Study personnel confirmed each participants' receipt of AZD1222 using the vaccination card, reported batch/lot number of the vaccine dose, and/or regional vaccination register details. The batch/lot number of the vaccine dose was recorded whenever possible. The enrolment questionnaires also asked participants demographic information, medical history, pregnancy status, breastfeeding status (Figure 1). CCI [redacted]

After enrolment, participants received study reminders and reported outcomes using the app, web portal, or study call centre. Participants received study notifications at predefined time intervals for up to 18 months after the first AZD1222 dose. Study notifications included prompts for safety outcomes at 1, 4, 8, and 14 weeks and 6, 9, 12, and 18 months following the first vaccine dose. Due to the early close out, the study follow-up period was restricted to a maximum of 14 weeks vs the 18 months originally planned. Participants were also able to submit unscheduled, unprompted AE information, with focus on the AE types specified for this study: SAEs, AESIs, and medically-attended AEFIs, including COVID-19 cases that were medically-attended. Any other AE types reported were also collected, managed accordingly, and presented in this study report.

CCI [redacted] were sent at 4.5 months and 15 months, after the first vaccine dose. Participants also received messages to maintain contact and ensure study retention.

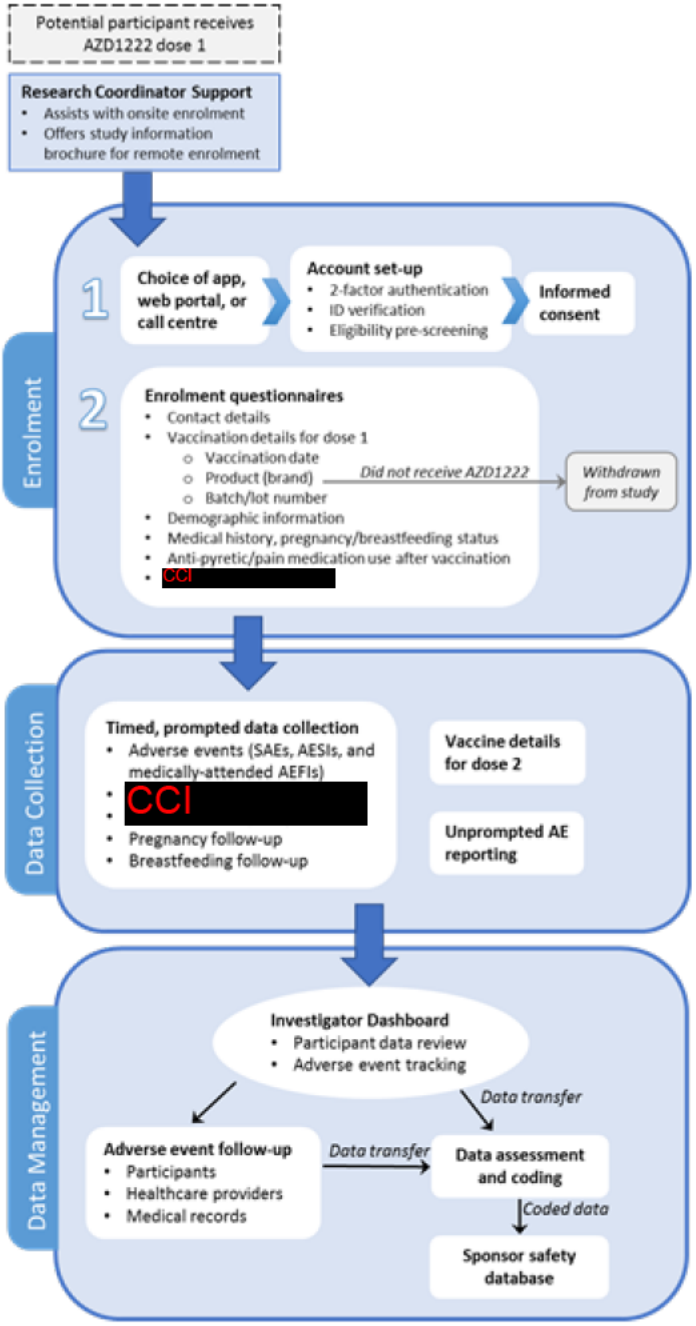
When a participant reported an AE, a flag was raised in the investigator dashboard and study personnel performed event follow-up and assessment. Study personnel requested medical

records from the participant's HCP and study personnel assessed if the event was serious and/or an adverse drug reaction (see Protocol Section 10 [Appendix 16.1.1]). For events without an HCP contact, study personnel assessed AEs based on details provided from the participants.

Participants who were pregnant at the time of vaccination or were vaccinated within 45 days prior to the estimated date of conception were asked to provide additional information to assess pregnancy and neonatal/infant outcomes. Pregnant women were asked for pregnancy outcomes 12 months after their last menstrual period and for infant outcomes up to 12 months of age or at 24 months post-first dose for the last participant enrolled in the study, whichever was first. Participants who were breastfeeding were asked for additional information (see Section 9.4.3.3).

This study was closed out early due to age and usage restrictions for AZD1222 that were recommended by the NITAGs in the participating countries. For more details, please see Section 9.4.4.

Figure 1 Overview of the study design



If a participant is unable to directly provide requested information, a proxy can do so on the participant's behalf.
AE: adverse event; AESI: adverse event of special interest, AEFIs: adverse events following immunisation; CCI [redacted]; SAE: serious adverse event.

9.2 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 .

9.3 Subjects

9.3.1 Eligibility criteria

Participants were eligible to be included in the study only if all the following criteria applied:

- Aged 18 years or older at the time of vaccination.
- Received AZD1222 as the first dose of COVID-19 vaccination in the prior 28 days.
- The participant had provided sufficient details to validate the vaccination (vaccination card, batch/lot number, and/or regional vaccination register details).
- Provided informed consent to participate in the study, either personally or through a legal representative.
- Able and willing to respond to study notifications using the mobile device app, web portal, or call centre or have a proxy (a caregiver, family member, or other trusted individual) who could do so on their behalf.
- Able and willing to grant, personally or through a legal representative, permission to contact the participant's healthcare providers and to access the participant's medical records at the time of vaccination and during the post-vaccination follow-up period.

9.3.2 Key subpopulations

This real-world, non-interventional study enrolled all eligible participants but especially sought to enrol older adults, with a target of 50% of participants aged ≥ 65 years. The study also aimed to have an equal enrolment of male and female participants. Additional subpopulations of interest in this study included:

- Pregnant women, breastfeeding women
- Immunocompromised participants
- Participants with autoimmune or inflammatory disorders
- Frail participants with comorbidities (eg, chronic obstructive pulmonary disease, diabetes, chronic neurological disease, cardiovascular disorders)

9.3.3 Participant withdrawal and lost to follow-up

A participant could withdraw from the study at any time at his/her own request or may have been withdrawn at any time at the discretion of the investigator for safety, behavioural, compliance, or administrative reasons. If the participant withdrew consent for disclosure of future information, the Sponsor retained and continued to use any data collected before such a

withdrawal of consent. Participants who chose to withdraw were asked for the reason they were leaving the study.

A participant was considered lost to follow-up if he or she failed to respond to the study notifications and did not respond to subsequent follow-up attempts. At least 2 follow-up attempts were made, at least one week apart.

For participants who were lost to follow-up, study personnel attempted to collect the vital status of the participant within legal and ethical boundaries for all participants enrolled. Participant's emergency contact, provided at enrolment, was contacted, and asked for the status of the participant, and, if appropriate, the reason the participant had not responded to study notifications. Public sources could be searched for vital status information. If vital status was determined as deceased, this would be documented, and the participant would not be considered lost to follow-up. Sponsor personnel were not involved in any attempts to collect vital status information.

9.4 Variables

9.4.1 Definitions

In this study report, the following terms are used as defined here:

Participants: Individuals who had enrolled in the study.

Vaccination site: Any location where a participant was administered an AZD1222 vaccination. Vaccination sites are not study investigators.

Research coordinators: Research coordinators would assist with study recruitment and enrolment at vaccination sites. Research coordinators would generally be employees or contractors of the vaccination site. Where this was not feasible, study personnel acting on behalf of the Sponsor would contract with the vaccination site to permit a research coordinator not otherwise associated with the site to be present at the site.

Healthcare provider: Healthcare providers are medically qualified individuals who treat participants for a health issue during the study. Healthcare providers are not study investigators. For some participants, their vaccination site could also be their HCP.

Investigators: Investigators are responsible for the overall conduct of the study.

9.4.2 Study variables to be collected

Table 5 summarises the data collection plan.

Table 5 Data collection plan for key variables and information

Procedure or variable	Enrolment (post-vaccine dose 1) [b]	Post-vaccination follow-up with participants via the app, email, or phone call (months, weeks after first vaccine dose)										Data source(s)	Data capture format
		1 wk	4 wk	8 wk	14 wk	4.5 m 20 wk	6 m 26 wk	9 m 39 wk	12 m 52 wk	15 m 65 wk	18 m 78 wk		
Consent and Contact Details													
Informed consent [a]	X											Participant	ICF form
Choice of digital or non-digital participation	X											Participant	Profile questionnaire
Personal contact information, including emergency contact	X												
Primary HCP and contact information	X												
Name and contact information for proxy, if needed	X											Participant	App or web portal interface
Vaccination Details													
Vaccine product (brand)	X		Starting at Week 4, participants can complete a post-vaccination questionnaire for their second dose. Second doses are expected between Week 4 and Week 14 based on recommended schedules.									Vaccination site, RC, participant	Vaccination details questionnaire
Vaccination date	X												
Vaccine batch/lot number	X												
Type of vaccination site	X												
Photo of vaccination card [c]	X											Participant	Vaccine card photo
Any antipyretic/pain-reliever within 5 days of vaccination		X										Participant	Antipyretic/ pain-reliever questionnaire
Participant Background Information													
Age	X											Participant	Background questionnaire
Sex/gender	X												
Height/weight	X												
Race/ethnicity [d]	X												

Procedure or variable	Enrolment (post-vaccine dose 1) [b]	Post-vaccination follow-up with participants via the app, email, or phone call (months, weeks after first vaccine dose)										Data source(s)	Data capture format
		1 wk	4 wk	8 wk	14 wk	4.5 m 20 wk	6 m 26 wk	9 m 39 wk	12 m 52 wk	15 m 65 wk	18 m 78 wk		
Country of birth/residence	X											Participant, medical records	Medical history questionnaire
Employment status	X												
Smoking status/history	X												
Medical History													
Prior infection with SARS-CoV-2 or prior COVID-19 disease, including symptoms	X												
Recent non-AZD1222 vaccination	X	X	X	X	X		X	X	X		X		
Select comorbidities and medications [e]	X												
Safety Outcomes													
SAEs, AESIs, and medically-attended AEFIs [f] • Symptoms • Diagnosis • Onset date/duration • Intensity • Resolution • Treatment • Seriousness [g] • Causality [g]		X	X	X	X		X	X	X		X	Participant, HCP, medical records	CCI [redacted], AESI form (when applicable)
CCI [redacted]		X	X	X	X		X	X	X		X	Participant, medical records	CCI [redacted]

Procedure or variable	Enrolment (post-vaccine dose 1) [b]	Post-vaccination follow-up with participants via the app, email, or phone call (months, weeks after first vaccine dose)										Data source(s)	Data capture format
		1 wk	4 wk	8 wk	14 wk	4.5 m 20 wk	6 m 26 wk	9 m 39 wk	12 m 52 wk	15 m 65 wk	18 m 78 wk		
Death												Emergency contact, proxy, HCP, medical records	Safety database
Pregnancy Status and Outcomes (Pregnant and Breastfeeding Women Only)													
Pregnancy status, including maternal medical and obstetric history	X	X	X	X	X		X	X	X		X	Participant, medical records	Pregnancy status questionnaire
Pregnancy/infant outcomes, pregnant participants		Participants who report pregnancy at the time of vaccination were to be followed-up at 12 months after their estimated last menstrual period and, for those reporting live-birth, at infant age up to 12 months to assess pregnancy/infant outcomes [j]										Participant, medical records	Pregnancy follow-up questionnaire
Breastfeeding status, including infant outcomes	X	X	X	X	X		X	X	X			Participant, medical records	Breastfeeding status questionnaire
Parent/caregiver informed consent [i]	X											Participant	Parent/caregiver ICF
Patient-reported Quality of Life Outcomes													
CCI [redacted]	X [k]					X [k]				X [k]		Participant	CCI [redacted]
CCI [redacted]						X [k]				X [k]		Participant	CCI [redacted]

[a] Informed consent included consent to participate in the study as well as to contact HCPs and for the release of medical records relevant to the study.

[b] Participants could enrol up to 16 weeks after their first vaccine dose.

[c] For digital participants only. For non-digital participants, vaccination details would be validated by the call centre.

[d] Were to be collected in countries where permitted.

[e] Selected medical conditions: neuroimmune condition, other neurological condition, bleeding disorder, asthma, chronic obstructive pulmonary disease, diabetes, cerebrovascular conditions, heart disease, other cardiovascular diseases, chronic kidney disease cancer, autoimmune disease, solid organ transplant recipient, other condition affecting immune system, liver disease, history of allergic conditions, depression/anxiety, viral/bacterial infection leading to hospital admission, and other chronic condition or conditions for which participant received treatment or medication in last month. If a participant indicated having any of these conditions, the participant was asked if they were currently taking any medication or being treated for it. Specific medication would not be asked unless the participant indicated they were taking an immunosuppressant.

[f] Adverse event reports could be scheduled (timed follow-ups) or unscheduled. At the scheduled timepoints, participants would be asked if they've had any new or worsening health issues resulting in consultation with a medical doctor, an emergency room visit or hospitalisation, or a significant or long-term disability or incapacitation. When a participant responded "yes", the participant was asked for more details. For reported COVID-19 cases, this would include patient-reported symptoms.

[g] Healthcare providers would provide input and study personnel would assess the seriousness and causality of AEs.

[h] CCI [redacted]

[i] Participants vaccinated with AZD1222 during pregnancy or up to 45 days before the estimated date of conception would be asked to follow outcomes in their child for up to 12 months after birth. Breastfeeding participants were also be asked to follow-up on their child's health. Before any request for a child's medical records, the participant would be asked for additional informed consent. The child's other parent may also be asked for consent, depending on local requirements.

[j] Outcomes in infants were requested up to 12 months of age. However, follow-up of pregnancy and infant outcomes were not continued past 24 months post-first dose for the last participant enrolled in the study.

[k] CCI [redacted]

As a data source, participant meant either the participant directly or the participant's designated proxy.
For the safety outcome follow-ups at Weeks 1, 4, 8, 14, and Month 6, 9, 12, and 18, depending on the interval between scheduled contacts, participants received reminders for 1 to 12 weeks after the initial notification to complete the questionnaire.
AE: adverse event; AEFI: adverse event following immunisation; AESI: adverse event of special interest; CSP: clinical study protocol; HCP: healthcare provider, CCI [redacted]; ICF: informed consent form; m: month; NA: not applicable; CCI [redacted]; CCI [redacted]; RC: research coordinator; SAE: serious adverse event; wk: week.

9.4.3 Variables for identifying subpopulations

9.4.3.1 Adults aged ≥ 65 years and other age groups

Participants' age was recorded at enrolment and were categorised accordingly.

9.4.3.2 Pregnant women

At enrolment, females aged < 50 years were asked the date of their last menstrual period and if they were currently pregnant. Those who had not reported pregnancy, were prompted for this information at each safety follow-up. Women who reported pregnancy were asked for their expected due date. Their estimated date of conception was calculated, and those vaccinated (either first or second dose) between 45 days prior to the estimated date of conception and, any other point during pregnancy, were included in the pregnant women subpopulation.

9.4.3.3 Breastfeeding women

At enrolment and at all safety follow-ups (except at 18 months), females aged < 50 years were asked if they were currently breastfeeding. Participants who reported they were breastfeeding when they received either vaccine dose (first or second) were included in the breastfeeding women subpopulation.

9.4.3.4 Immunocompromised participants and participants with autoimmune or inflammatory disorders

At enrolment, participants were asked if they had ever been diagnosed with certain medical conditions and if they were currently taking immunosuppressant medication. Study personnel confirmed medical conditions and immunosuppressant medications with medical records. Confirmed medical conditions and medications were used to categorise participants as immunocompromised and/or as having an autoimmune or inflammatory disorder.

The subpopulation of immunocompromised participants included participants taking an immunosuppressant (eg, tacrolimus, cyclosporine, corticosteroids, and methotrexate), participants with a diagnosis of an autoimmune disease, neuroimmune condition, or another condition affecting the immune system, and participants currently taking medication for cancer or being treated for cancer.

The subpopulation of participants with an autoimmune or inflammatory disorder included participants diagnosed with an autoimmune disease or neuroimmune condition.

9.4.3.5 Frail participants with comorbidities

The EMA's reflection paper on physical frailty had defined the concept of frailty "as a state of increased vulnerability resulting from aging and often disease-associated decline … leading to increased risk of adverse health outcomes…" (EMA 2015).

For this study, physical frailty was identified at baseline using participant answers to the enrolment questionnaire as well as to the CCI [redacted]. Comorbidities were reported by participants at enrolment and then confirmed by study personnel through medical record reviews.

Only participants with physical frailty and comorbidities at baseline were included in this subpopulation.

9.4.4 Early study termination

This study was closed out early due to age and usage restrictions for AZD1222 that were recommended by the NITAGs in the participating countries. This made study recruitment very challenging, rendering the study unable to generate meaningful safety data in a timely manner. The safety of AZD1222 continues to be monitored through the implementation of other studies and established safety reporting platforms across Europe.

9.5 Data sources and measurement

Adverse events were planned to be collected from the time of informed consent through 18 months post-first dose for participants. However, due to the early close out of study, AEs were collected only for maximum 14 weeks.

Participants received timed notifications via push notification, email, or phone call asking for any new or worsening health issues that had resulted in consultation with a medical doctor, an emergency room visit or hospitalisation, or a significant or long-term disability or incapacitation.

If the participant indicated an AE may be related to COVID-19 or if they received a diagnosis for COVID-19, they were asked about any COVID-19 testing and results.

Participants also submitted unprompted AE information at any time through the app, web portal, or call centre. All AEs collected during this study were considered solicited AEs, regardless of if they were prompted or unprompted.

If a participant indicated a new or worsened health problem, the participant was asked additional questions about the issue, intensity, treatment, and outcome. Adverse events collected for this study, both prompted and unprompted, focused on the events of interest for the study assessments and analyses: SAEs, AESIs, and medically-attended AEFIs, including COVID-19 infections. If other AE types were reported, these were also collected and managed accordingly and are presented in the study report.

All collected events were immediately available to study personnel in the investigator dashboard, where new events were flagged. Study personnel validated the cases, provided

medical records, and assessed seriousness and causality with input from HCPs and the medical records.

Study personnel confirmed all collected AEs with the participant, the proxy, the emergency contact, and/or through the review of medical records. If the participant received care from an HCP aside from their primary care physician, study personnel was to follow-up to obtain contact information for that HCP to permit a medical record request. Follow-up for AESIs with the HCP included the completion of a targeted safety questionnaire. Study personnel with medical expertise were available to advise on whether any reported symptoms or events may be a suspected AESI and/or require adjudication.

Additionally, data was collected for pregnancy outcomes and infant outcomes. For pregnancy outcomes, events within the AESI medical concept "Pregnancy outcome – Maternal" were collected, including spontaneous abortions, still births, and preterm births. For infant outcomes, events within the AESI medical concept "Pregnancy outcome – Neonates" were collected, including major congenital malformations and small size for gestational age.

CCI

Furthermore, participants were asked to complete the CCI and an additional CCI, as per the data collection schedule described in Table 5.

CCI

CCI

CCI

CCI [redacted]

9.6 Bias

Strategies for the mitigation of bias included:

- To account for possible sampling bias due to the recruitment of vulnerable populations first (residual confounding), in the risk assessment analyses, in addition to the expected background event rate, the rates had been multiplied by 1.2, 1.5, and 2.0 times, for example.
- Subgroup analyses within risk assessment analyses was also be performed, if feasible. If characteristics were found that both were related to differences in AE risk and to differences between study participants and the overall vaccinated population, weighting was to be added.

9.7 Study size

This study planned to enrol 15,000 participants in at least 3 countries in the EU (Germany, Spain, and Sweden). The Sponsor aimed for at least 50% of participants to be 65 years of age or older and approximately equal proportions of male and female participants.

As the COVID-19 pandemic is a dynamic situation, the enrolment target was to be amended if recruitment forecasts change.

9.8 Data transformation

Data management was performed by a CRO according to the Data Management Plan.

All data entered into the study app or web portal was integrated in the digital platform and was tracked by reporting method (app or web portal), who reported it (participant, proxy, or emergency contact), and who entered it (participant, proxy, or call centre). The digital platform also included an investigator dashboard where investigators and selected study personnel could view and track, in real-time, all AEs submitted. Role-based permissions ensured only authorised personnel could view identifying confidential data like participant names.

The study app and web portal were validated and compliant with good practice guidelines and regulations and the EU General Data Protection Regulation. The app support iOS and Android operating systems. The app and web portal were approved by local IECs and translated into local languages.

9.9 Statistical methods

9.9.1 Main summary measures

Demographic and baseline characteristics including

- Age (years)
- Sex (Female/Male)
- Height/weight (cm/kg)
- Body mass index (kg/m^2)
- Country of birth
- Country of residence
- Employment status
- Smoking status and history

were presented by descriptive statistics for all study populations.

To address the issue of missing data, the demographics and baseline characteristics were also presented for participants who were lost to follow-up at study end. The differences between the baseline characteristics for the FAS versus the group lost to follow-up were related to the subgroup analyses to assess for a possible impact on AE risk, if feasible.

The quantitative variables were described at study end by the number of observed data, arithmetic mean and asymptotic 95% CI, median and interquartile range, minimum and maximum.

The qualitative variables were described by proportions with asymptotic 95% CI.

The following additional characteristics were reported at study end for all defined subpopulations of special interest at baseline:

- Medical History (as captured in-patient questionnaires):
  - Prior infection with SARS-CoV-2 or prior COVID-19 disease including informed date and symptoms
  - Recent non-AZD1222 vaccination for study-defined follow-up intervals

The primary analysis included participants who enrolled within 7 days of vaccination with the first dose of AZD1222 and was performed for the following study-defined follow-up intervals: 1 week, 4 weeks, 8 weeks, and 14 weeks follow-up.

For all reported SAEs, AESIs and medically-attended AEFIs the following statistics were calculated for each study-defined follow-up interval at study end:

- total number of events reported in the considered follow-up interval
- number of participants who experienced at least one event in the considered follow-up interval
- number of all AZD1222 vaccinated participants who completed considered follow-up interval
- incidence rate expressed by the patient-year statistic with asymptotic 95% CI, defined as the total number of events reported in the considered follow-up interval divided by the total participant-time at risk, ie, the time period between first dose of AZD1222 and the end of the considered follow-up interval.

The secondary analysis was performed after completion of the study surveillance period.

The secondary analysis was performed for the following study-defined follow-up intervals, which included participants with at least: 1-, 4-, 8-, 14 weeks follow-up, 6-, 9-, 12- and 18 months follow-up.

The analysis was performed for all defined populations who completed the considered follow-up interval, ie, the FAS, the FAS for primary analysis and subpopulations of special interest including the subpopulations of pregnant and breastfeeding woman, subpopulation of immunocompromised participants, subpopulation of participants with autoimmune or inflammatory disorders, and subpopulation of frail participants.

For all reported SAEs, AESIs and medically-attended AEFIs the following statistics was calculated for all participants who completed the considered follow-up interval at study end:

- total number of events reported in the considered follow-up interval
- number of all AZD1222 vaccinated participants

- number of participants who experienced at least one event
- incidence rate with asymptotic 95% CI, calculated as the proportion of participants who reported an event among all AZD1222 vaccinated participants in the considered follow-up interval
- incidence rate expressed by the patient-year statistic with asymptotic 95% CI, defined as the total number of events reported in the considered follow-up interval divided by the total participant-time at risk, ie, the time period between first dose of AZD1222 and the end of the considered follow-up interval.
- incidence rate expressed by the patient-year statistic with asymptotic 95% CI among all AZD1222 vaccinated participants regardless of completing status of the considered follow-up interval

Also, the following analysis was performed for all events reported in the considered follow-up interval

- distribution of intensity (mild, moderate, severe) of reported events – numbers and percentages of mild, moderate, and severe
- distribution of outcomes (resolved, unresolved, fatal, unknown) of reported events – numbers and percentages
- distribution of causality of reported events – numbers and percentages of
  - cases with adequate information for causality conclusion (Consistent causal association to immunisation, Indeterminate, Inconsistent causal association to immunisation [coincidental])
  - cases without adequate information for causality conclusion
- duration of the issues (in days) – mean, asymptotic 95% CI for mean, median, interquartile range, min, max
- distribution of the number of events in consecutive weeks of the follow-up period

For AESIs and medically-attended AEFIs there was to be reported additionally:

- the proportion of SAEs within the reported number of events

Where feasible the incidence rate of SAEs, AESIs and medically-attended AEFIs were to be analysed using the cumulative incidence function with asymptotic 95% CI, where death was considered as competing event and withdrawal from the study/loss to follow-up as a censoring event. Kaplan-Meier curves were used for this analysis where appropriate.

The analysis of outcomes reported in the subpopulation of pregnant women was to include pregnancy outcomes.

9.9.2 Main statistical methods

Due to the early termination of this study, the number of participants and follow-up period was limited. No primary, secondary, or exploratory analyses were performed. The statistical methods described in statistical analysis plan were not applied for data analysis. Only descriptive statistics were produced for demographic and baseline characteristics and the number of AEs.

9.9.2.1 Analysis sets

Full analysis set

Full analysis set consisted of all enrolled participants fulfilling the eligibility criteria and who received first dose of the AZD1222 vaccine.

Safety analysis set

Safety analysis set was same as FAS.

Safety analysis set for primary analysis

This analysis set comprised the subset of FAS which included participants who enrolled within 7 days of vaccination with the first dose of AZD1222 and performed with data cut-off 3 months after the end of accrual period.

9.9.3 Missing values

See section 9.9.2.

9.9.4 Sensitivity analyses

Due to the early close out of the study and small number of participants sensitivity analysis was not performed.

9.9.5 Amendments to the statistical analysis plan

Not applicable.

9.10 Quality control

This study followed all applicable international and local quality regulations, including GPP. AstraZeneca standard operating procedures were also used to ensure the quality of the data and study. These procedures included internal quality audits, rules for secure and confidential data storage, methods to maintain and archive project documents, quality control procedures for study monitoring, standards for writing a statistical analysis plan, and requirements for senior scientific review.

9.10.1 Data quality assurance

- Vaccination sites and study personnel maintained accurate documentation and permitted study-related monitoring, audits, IEC review, and regulatory agency inspections, and provided direct access to study documents.
- Monitoring details describing strategy (eg, risk-based initiatives in operations and quality such as Risk Management and Mitigation Strategies and Analytical Risk-Based Monitoring), methods, responsibilities, and requirements, including handling of noncompliance issues and monitoring techniques, were provided in the Site Monitoring Plan.
- The Sponsor assumed accountability for actions delegated to other individuals (eg, CROs).
- In-person monitoring of vaccination sites was only to be performed if a specific cause required investigation.
- Records and documents, including signed informed consent forms, pertaining to the conduct of this study must be retained by the Sponsor or designee for 5 years after study completion unless local regulations or institutional policies required a longer retention period. No records were to be destroyed during the retention period without the written approval of the Sponsor. No records were to be transferred to another location or party without written notification to the Sponsor.

9.10.2 Audits and inspections

The Sponsor or designee were permitted to conduct a quality assurance assessment and/or audit of study records, and the regulatory agencies may conduct a regulatory inspection at any time during or after completion of the study.

10. RESULTS

10.1 Participants

Results are presented by participants population. Summary tables and appendices are presented in Appendix B.

10.1.1 Disposition

A summary of subject disposition is presented in Table 6.

A total of 27 participants were enrolled to this study of which 6 (22.2%) did enrol within 7 days of 1st dose of AZD1222. 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 (due to technical issues with the study app) from the study and the remaining 23 (85.2%) participants were discontinued by the Sponsor due to study termination.

Table 6 Disposition

	Overall (N=27) n(%)
All participants enrolled [a]	27
Participants enrolled within 7 days after first dose of Vaxzevria (AZD1222) [a]	6 (22.2)
Participants who completed follow-up period:	
1 week	26 (96.3)
4 weeks	23 (85.2)
8 weeks	17 (63.0)
14 weeks	15 (55.6)
Participants who discontinued the study	27 (100.0)
Reason for discontinuation	
Study terminated by Sponsor	23 (85.2)
Withdrawal by participant	4 (14.8)

[a] Informed consent received.

[b] Percentages are determined using number of participants enrolled as denominator.

Source: Table 14.1.1

10.1.2 Participants analysed (analysis sets)

Definitions of the analysis sets are given in Section 9.9.2.1.

The analysis sets by age group are summarised in Table 7. All 27 (100%) participants enrolled in the study were included in the FAS. The primary analysis set included 6 (22.2%) participants. PPD

Table 7 Analysis sets by age group

	<60 years (N=16) n(%)	≥60 years (N=11) n(%)	Overall (N=27) n(%)
Full analysis set [a]	16	11	27
Primary analysis set [b]	1 (6.3)	5 (45.5)	6 (22.2)
PPD			
PPD			

[a] Defined as all participants enrolled.

[b] Defined as all participants enrolled within 7 days of first dose of Vaxzevria (AZD1222).

Source: Table 14.1.2

No participant was included in the subpopulations of pregnant women (Table 14.2.3), breastfeeding women (Table 14.2.4), and frail participants with comorbidities (Table 14.2.7).

10.2 Descriptive data

10.2.1 Demographic characteristics

The demographic and baseline characteristics of participants in the FAS are summarised in Table 8 and listed by participant in Appendix B.

All 27 (100%) participants enrolled had entered information about demographic and baseline characteristics. Most of the participants were male (16 [59.3%] participants). The median (range) age of the study participants was 57 (PPD) years and a mean (95% CI) BMI of 28.9 (26.6, 31.2) kg/m^2. PPD

Table 8 Key demographic and baseline characteristics by age group - Full analysis set

		<60 years (N=16) n(%)	≥60 years (N=11) n(%)	Total (N=27) n(%)
Age (years)	Mean (95% CI)	48.4 (44.4-52.5)	64.0 (61.9-66.1)	54.8 (50.9-58.7)
	Min	PPD	PPD	PPD
	Median	50.0	65.0	57.0
	Max	PPD	PPD	PPD
Gender, n (%)	Female	5 (31.3)	6 (54.5)	11 (40.7)
	Male	11 (68.8)	5 (45.5)	16 (59.3)

		<60 years (N=16) n(%)	≥60 years (N=11) n(%)	Total (N=27) n(%)
PPD				
PPD				
Height (cm)	Mean (95% CI)	179.8 (174.8-184.8)	172.1 (166.9-177.3)	176.7 (173.0-180.4)
	Min	PPD	PPD	PPD
	Median	179.5	171.0	177.0
	Max	PPD	PPD	PPD
Weight (kg)	Mean (95% CI)	94.9 (79.3-110.6)	85.0 (76.6-93.4)	90.9 (81.3-100.5)
	Min	PPD	PPD	PPD
	Median	87.5	84.0	85.0
	Max	PPD	PPD	PPD
BMI (kg/m^2)	Mean (95% CI)	29.1 (25.3-32.9)	28.7 (26.3-31.0)	28.9 (26.6-31.2)
	Min	PPD	PPD	PPD
	Median	27.4	29.9	29.4
	Max	PPD	PPD	PPD
Country of birth, n (%)	PPD			
Country of residence, n (%)	PPD			
Employment status, n (%)	PPD			
				)
Smoking status/Smoking history, n (%)	PPD			

Abbreviations: Max: maximum; Min: minimum; N: number of subjects in analysis set; n: number of subjects included in analysis.

Sources: Table 14.2.2

Primary analysis set

The demographic and baseline characteristics of participants in primary analysis set are summarised in Table 9.

The participants were balanced between male and female (3 [50%] participants, each). The median (range) age of the study participants was PPD (PPD) years and a mean (95% CI) BMI of 27.7 (24.4, 31.0) kg/m^2. PPD

Table 9 Key demographic and baseline characteristics by age group - Primary analysis set

		<60 years PPD n(%)	≥60 years (N=5) n(%)	Total [a] (N=6) n(%)
Age (years)	Mean (95% CI) [b]	PPD	63.6 (60.5-66.7)	59.8 (49.9-69.8)
	Min	PPD	PPD	PPD
	Median	PPD	PPD	PPD
	Max	PPD	PPD	PPD
Gender, n (%)	Female	0	3 (60.0)	3 (50.0)
	Male	1 (100.0)	2 (40.0)	3 (50.0)
PPD				
Height (cm)	Mean (95% CI) [b]	PPD	172.6 (161.0-184.2)	175.7 (163.9-187.5)
	Min	PPD	PPD	PPD
	Median	PPD	PPD	PPD
	Max	PPD	PPD	PPD
Weight (kg)	Mean (95% CI) [b]	PPD	85.2 (74.0-96.4)	85.0 (76.6-93.4)
	Min	PPD	PPD	PPD
	Median	PPD	PPD	PPD
	Max	PPD	PPD	PPD
BMI (kg/m^2)	Mean (95% CI) [b]	PPD	28.6 (25.7-31.6)	27.7 (24.4-31.0)
	Min	PPD	PPD	PPD
	Median	PPD	PPD	PPD
	Max	PPD	PPD	PPD
Country of birth, n (%)	PPD			
Country of residence, n (%)	PPD			)
Employment status, n (%)	PPD			

		<60 years PPD n(%)	≥60 years (N=5) n(%)	Total [a] (N=6) n(%)
	PPD			
Smoking status/Smoking history, n (%)	PPD			
				)

[a] Informed consent received.

[b] Not calculated due to low participant number.

Abbreviations: Max: maximum; Min: minimum; N: number of subjects in analysis set; n: number of subjects included in analysis; NC: not calculated.

Sources: Table 14.2.1

PPD

The demographic and baseline characteristics of PPD are summarised in Table 10.

PPD . The majority of the participants were male PPD . PPD

Table 10 Key demographic and baseline characteristics by age group - PPD

		<60 years PPD n(%)	≥60 years PPD n(%)	Total PPD n(%)
Age (years)	Mean (95% CI) [a]	PPD		
	Min			
	Median			
	Max			
Gender, n (%)	Female			
	Male			
PPD	PPD			
Height (cm)	Mean (95% CI) [a]			
	Min			
	Median			
	Max			
Weight (kg)	Mean (95% CI) [a]			

		<60 years PPD n(%)	≥60 years PPD n(%)	Total PPD n(%)
	Min	PPD		
	Median			
	Max			
BMI (kg/m^2)	Mean (95% CI) [a]			
	Min			
	Median			
	Max			
Country of birth, n (%)	PPD			
Country of residence, n (%)	PPD			
Employment status, n (%)	PPD			
	PPD			
	PPD			
Smoking status/Smoking history, n (%)	PPD			
	PPD			
	PPD			

[a] Not calculated due to low participant number.

Abbreviations: Max: maximum; Min: minimum; N: number of subjects in analysis set; n: number of subjects included in analysis; NC: not calculated.

Sources: Table 14.2.5

PPD

The demographic and baseline characteristics of participants PPD are summarised in Table 11.

PPD . PPD were male, and PPD

Table 11 **Key demographic and baseline characteristics by age group - PPD**

		<60 years PPD n(%)	≥60 years PPD n(%)	Total PPD n(%)
Age (years)	Mean (95% CI) [a]	PPD		
	Min			
	Median			
	Max			
Gender, n (%)	Male			
Height (cm)	Mean (95% CI) [a]			
	Min			
	Median			
	Max			
Weight (kg)	Mean (95% CI) [a]			
	Min			
	Median			
	Max			
BMI (kg/m^2)	Mean (95% CI) [a]			
	Min			
	Median			
	Max			
Country of birth, n (%)	PPD			
Country of residence, n (%)	PPD			
Employment status, n (%)	PPD			
	PPD			
	PPD			
Smoking status/Smoking history, n (%)	PPD			
	PPD			
	PPD			

[a] Not calculated due to low participant number.

Abbreviations: Max: maximum; Min: minimum; N: number of subjects in analysis set; n: number of subjects included in analysis; NC: not calculated.

Sources: Table 14.2.6

10.2.2 Medical history

Primary analysis set

The prior infection with SARS-CoV-2 virus or prior COVID-19 disease and non-AZD1222 vaccination for study-defined follow-up is summarised in Table 14.3.1. Medical history of participants is summarised by MedDRA SOC and PT in Table 14.4.1.

Full analysis set

The prior infection with SARS-CoV-2 virus or prior COVID-19 disease and non-AZD1222 vaccination for study-defined follow-up is summarised in Table 14.3.2 and listed by subject in Appendix B. Medical history of participants is summarised by MedDRA SOC and PT in Table 14.4.2 and listed by subject in Appendix B.

Seventeen participants received their initial dose of AZD1222 vaccine. However, due to changes in vaccination usage in PPD (where participants were enrolled), they received a second dose of non-AZD1222 vaccine (for details see Section 9.4.4). This was classed as off-label use. No AEs were reported for these off-label use cases.

PPD (Table 14.3.2).

PPD

The prior infection with SARS-CoV-2 virus or prior COVID-19 disease and non-AZD1222 vaccination for study-defined follow-up is summarised in Table 14.3.5. Medical history of participants is summarised by MedDRA SOC and PT in Table 14.4.5.

PPD

The prior infection with SARS-CoV-2 virus or prior COVID-19 disease and non-AZD1222 vaccination for study-defined follow-up is summarised in Table 14.3.6. Medical history of participants is summarised by MedDRA SOC and PT in Table 14.4.6.

10.3 Outcome data

No efficacy evaluation was done for this study.

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

10.4 Main results

See section 10.3.

10.5 Other analyses

The primary, secondary, and exploratory analyses were not performed due to insufficient data.

10.6 Adverse events/adverse reactions

No AEs were reported.

11. DISCUSSION

This report summarises final data for participants enrolled in the Phase IV non-interventional enhanced active surveillance study of adults vaccinated with AZD1222.

11.1 Key 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 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.

11.2 Limitations

The main limitation is the early termination of the study and safety could not be evaluated overall. Given the early close out of the study, the number of participants in key subpopulations was limited. In total 27 participants have been enrolled vs 15,000 planned participants. Consequently, the number of participants was also limited in primary analysis set, PPD .

The study follow-up period was restricted to a maximum of 14 weeks vs the 18 months originally planned.

Given all the above-mentioned limitations and the result of 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.

11.3 Interpretation

Given the results of the primary endpoint (ie, no AEs), the interpretation is limited due to low participant number and restricted follow-up period.

11.4 Generalisability

Not applicable.

12. OTHER INFORMATION

Not applicable.

13. CONCLUSION

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.

14. REFERENCES

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Li F. Structure, Function, and Evolution of Coronavirus Spike Proteins. Annu Rev Virol. 2016;3(1):237-61.

Appendix A List of stand-alone documents

Table 12 List of stand-alone documents

Number	Document reference number	Date	Title
1	16.1.1	10 March 2021	Protocol
2	16.1.1	11 May 2021	Protocol amendment
3	16.1.3	15 March 2021	Sample participant information sheet and informed consent form
4	16.1.9	14 December 2021	Statistical Analysis Plan

Appendix B Additional information

Participant data listings/final tables and listings.

SIGNATURE PAGE

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Document Name: d8111r00003-clinical-study-report		
Document Title:	D8111R00003 Clinical Study Report	
Document ID:	CCI [redacted]	
Version Label:	1.0 CURRENT LATEST APPROVED	
Server Date **(dd-MMM-yyyy HH:mm 'UTC'Z)**	**Signed by**	**Meaning of Signature**
05-Apr-2022 13:45 UTC	PPD [redacted]	Content Approval
01-Apr-2022 14:24 UTC	PPD [redacted]	Qualified Person Approval
07-Apr-2022 09:39 UTC	PPD [redacted]	Content Approval

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