Clinical trial results:
A Phase II/III Partially Double-Blinded, Randomised, Multinational, Active-Controlled Study in Both Previously Vaccinated and Unvaccinated Adults to Determine the Safety and Immunogenicity of AZD2816, a Vaccine for the Prevention of COVID-19 Caused by Variant Strains of SARS-CoV-2

Summary

EudraCT number	2021-002530-17
Trial protocol	PL
Global end of trial date	02 August 2022

Results information

Result version number	v1
This version publication date	13 August 2023
First version publication date	13 August 2023

Trial information

Trial identification

Sponsor protocol code	D7220C00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04973449
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	One MedImmune Way, Gaithersburg, Maryland, United States, 20878
Public contact	Global Clinical Lead, AstraZeneca Clinical study Information Center, +1 8772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca Clinical study Information Center, +1 8772409479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objectives of the study are in seronegative participants as follows:
1. To characterize safety and tolerability of a 2-dose primary vaccination with AZD2816 (4-week dosing interval [4]) in previously unvaccinated participants and one booster dose of AZD2816 in participants previously vaccinated with AZD1222 or messenger ribronucleic acid (mRNA) primary series vaccination.
2. To determine the non-inferiority of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) neutralizing antibody (nAb) geometric mean titre (GMT) response and seroresponse:
(a) Against B.1.351 variant elicited by a 2-dose primary vaccination with AZD2816 (4) versus (vs) original Wuhan-Hu-1 strain elicited by a 2-dose primary vaccination with AZD1222 (4).
(b) Against original Wuhan-Hu-1 strain elicited by AZD1222 booster dose in participants previously vaccinated with AZD1222 or mRNA primary vaccination vs 2-dose AZD1222 vaccination administered to previously unvaccinated participants.

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements. Participants signed an informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 June 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 966
Country: Number of subjects enrolled	South Africa: 464
Country: Number of subjects enrolled	Poland: 58
Country: Number of subjects enrolled	United Kingdom: 1346
Worldwide total number of subjects	2834
EEA total number of subjects	58

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	2251
From 65 to 84 years	571
85 years and over	12

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 2843 participants were randomized in this study of which 2834 participants were treated (9 participants were randomized but not treated). Results are presented for 2834 treated participants only.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Primary Vaccination Cohort:- AZD1222 (4)

Arm description:

Previously unvaccinated participants received intramuscular (IM) AZD1222 5*10^10 viral particles (vp) on Days 1 and 29 (4-week dosing interval).

Arm type	Experimental
Investigational medicinal product name	AZD1222
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular (IM) AZD1222 5*10^10 viral particles (vp) on Days 1 and 29.

Arm title	Primary Vaccination Cohort:- AZD2816 (4)

Arm description:

Previously unvaccinated participants received IM AZD2816 5*10^10 vp on Days 1 and 29 (4-week dosing interval).

Arm type	Experimental
Investigational medicinal product name	AZD2816
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IM AZD2816 5*10^10 vp on Days 1 and 29.

Arm title	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)

Arm description:

Previously unvaccinated participants received IM AZD1222 5*10^10 vp on Day 1 and IM AZD2816 5*10^10 vp on Day 29 (4-week dosing interval).

Arm type	Experimental

Investigational medicinal product name	AZD2816
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IM AZD2816 5*10^10 vp on Day 29.

Investigational medicinal product name	AZD1222
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IM AZD1222 5*10^10 vp on Day 1.

Arm title	Primary Vaccination Cohort:- AZD2816 (12)

Arm description:

Previously unvaccinated participants received IM AZD2816 5*10^10 vp on Days 1 and 85 (12-week dosing interval).

Arm type	Experimental
Investigational medicinal product name	AZD2816
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IM AZD2816 5*10^10 vp on Days 1 and 85.

Arm title	Booster Cohort:- AZD1222:AZD1222

Arm description:

Participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD1222 5*10^10 vp on Day 1.

Arm type	Experimental
Investigational medicinal product name	AZD1222
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IM AZD1222 5*10^10 vp on Day 1.

Arm title	Booster Cohort:- AZD1222:AZD2816

Arm description:

Participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.

Arm type	Experimental
Investigational medicinal product name	AZD2816
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IM AZD2816 5*10^10 vp on Day 1.

Arm title	Booster Cohort:- mRNA:AZD1222

Arm description:

Participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD1222 5*10^10 vp on Day 1.

Arm type	Experimental
Investigational medicinal product name	AZD1222
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IM AZD1222 5*10^10 vp on Day 1.

Arm title	Booster Cohort:- mRNA:AZD2816

Arm description:

Participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.

Arm type	Experimental
Investigational medicinal product name	AZD2816
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IM AZD2816 5*10^10 vp on Day 1.

Number of subjects in period 1	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)
Started	409	413	411
Completed	389	393	391
Not completed	20	20	20
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	3	3	2
Unspecified	1	1	2
Lost to follow-up	15	16	16

Number of subjects in period 1	Primary Vaccination Cohort:- AZD2816 (12)	Booster Cohort:- AZD1222:AZD1222	Booster Cohort:- AZD1222:AZD2816
Started	208	373	377
Completed	189	359	366
Not completed	19	14	11
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	5	5	4
Unspecified	1	4	-
Lost to follow-up	13	5	6

Number of subjects in period 1	Booster Cohort:-mRNA:AZD1222	Booster Cohort:-mRNA:AZD2816
Started	322	321
Completed	303	308
Not completed	19	13
Adverse event, serious fatal	-	-
Consent withdrawn by subject	7	5
Unspecified	2	2
Lost to follow-up	10	6

Baseline characteristics

Reporting groups	
Reporting group title	Primary Vaccination Cohort:- AZD1222 (4)
Reporting group description:	
Previously unvaccinated participants received intramuscular (IM) AZD1222 5*10^10 viral particles (vp) on Days 1 and 29 (4-week dosing interval).	
Reporting group title	Primary Vaccination Cohort:- AZD2816 (4)
Reporting group description:	
Previously unvaccinated participants received IM AZD2816 5*10^10 vp on Days 1 and 29 (4-week dosing interval).	
Reporting group title	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)
Reporting group description:	
Previously unvaccinated participants received IM AZD1222 5*10^10 vp on Day 1 and IM AZD2816 5*10^10 vp on Day 29 (4-week dosing interval).	
Reporting group title	Primary Vaccination Cohort:- AZD2816 (12)
Reporting group description:	
Previously unvaccinated participants received IM AZD2816 5*10^10 vp on Days 1 and 85 (12-week dosing interval).	
Reporting group title	Booster Cohort:- AZD1222:AZD1222
Reporting group description:	
Participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD1222 5*10^10 vp on Day 1.	
Reporting group title	Booster Cohort:- AZD1222:AZD2816
Reporting group description:	
Participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.	
Reporting group title	Booster Cohort:- mRNA:AZD1222
Reporting group description:	
Participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD1222 5*10^10 vp on Day 1.	
Reporting group title	Booster Cohort:- mRNA:AZD2816
Reporting group description:	
Participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.	

Reporting group values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)
Number of subjects	409	413	411
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0

Adults (18-64 years)	392	391	394
From 65-84 years	16	22	17
85 years and over	1	0	0
Age Continuous			
Units: Years			
arithmetic mean	29.1	29.7	28.0
standard deviation	± 12.48	± 12.95	± 12.23
Sex: Female, Male			
Units: Participants			
Female	171	169	166
Male	238	244	245
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	4	0	2
Asian	3	5	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	202	192	214
White	161	166	151
More than one race	11	23	10
Unknown or Not Reported	28	27	30
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	239	246	257
Not Hispanic or Latino	143	148	137
Unknown or Not Reported	27	19	17

Reporting group values	Primary Vaccination Cohort:- AZD2816 (12)	Booster Cohort:- AZD1222:AZD1222	Booster Cohort:- AZD1222:AZD2816
Number of subjects	208	373	377
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	198	199	203
From 65-84 years	10	173	173
85 years and over	0	1	1
Age Continuous			
Units: Years			
arithmetic mean	28.8	59.7	60.4
standard deviation	± 12.98	± 13.72	± 13.30
Sex: Female, Male			
Units: Participants			
Female	85	172	172
Male	123	201	205

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	0	0
Asian	0	10	14
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	98	2	1
White	86	325	328
More than one race	6	0	1
Unknown or Not Reported	16	36	33
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	131	8	10
Not Hispanic or Latino	70	322	331
Unknown or Not Reported	7	43	36

Reporting group values	Booster Cohort:-mRNA:AZD1222	Booster Cohort:-mRNA:AZD2816	Total
Number of subjects	322	321	2834
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	238	236	2251
From 65-84 years	83	77	571
85 years and over	1	8	12
Age Continuous Units: Years			
arithmetic mean	55.3	55.9	
standard deviation	± 13.19	± 13.73	-
Sex: Female, Male Units: Participants			
Female	197	192	1324
Male	125	129	1510
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	8
Asian	8	13	57
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	2	714
White	290	288	1795
More than one race	2	0	53
Unknown or Not Reported	19	18	207
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	6	901

Not Hispanic or Latino	291	292	1734
Unknown or Not Reported	27	23	199

End points

End points reporting groups

Reporting group title	Primary Vaccination Cohort:- AZD1222 (4)
Reporting group description:	
Previously unvaccinated participants received intramuscular (IM) AZD1222 5*10^10 viral particles (vp) on Days 1 and 29 (4-week dosing interval).	
Reporting group title	Primary Vaccination Cohort:- AZD2816 (4)
Reporting group description:	
Previously unvaccinated participants received IM AZD2816 5*10^10 vp on Days 1 and 29 (4-week dosing interval).	
Reporting group title	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)
Reporting group description:	
Previously unvaccinated participants received IM AZD1222 5*10^10 vp on Day 1 and IM AZD2816 5*10^10 vp on Day 29 (4-week dosing interval).	
Reporting group title	Primary Vaccination Cohort:- AZD2816 (12)
Reporting group description:	
Previously unvaccinated participants received IM AZD2816 5*10^10 vp on Days 1 and 85 (12-week dosing interval).	
Reporting group title	Booster Cohort:- AZD1222:AZD1222
Reporting group description:	
Participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD1222 5*10^10 vp on Day 1.	
Reporting group title	Booster Cohort:- AZD1222:AZD2816
Reporting group description:	
Participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.	
Reporting group title	Booster Cohort:- mRNA:AZD1222
Reporting group description:	
Participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD1222 5*10^10 vp on Day 1.	
Reporting group title	Booster Cohort:- mRNA:AZD2816
Reporting group description:	
Participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.	
Subject analysis set title	Historical Control
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants from study D8110C00001 who were treated with 2 doses of AZD1222 and well-matched with the AZD1222 cohort in this study, with respect to at least age, gender, and presence of baseline comorbidities.	
Subject analysis set title	Primary Vaccination Cohort:- AZD2816 (4) (Comparator)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Previously unvaccinated seronegative participants received IM AZD2816 5*10^10 vp on Days 1 and 29 (4-week dosing interval).	
Subject analysis set title	Primary Vaccination Cohort:- AZD2816 (4) (Reference)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Previously unvaccinated seronegative participants received IM AZD2816 5*10^10 vp on Days 1 and 29 (4-week dosing interval).	

Subject analysis set title	Primary Vaccination Cohort:- AZD1222+AZD2816 (4) (Comparator)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Previously unvaccinated seronegative participants received IM AZD1222 5*10^10 vp on Day 1 and IM AZD2816 5*10^10 vp on Day 29 (4-week dosing interval).

Subject analysis set title	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) (Reference)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Previously unvaccinated seronegative participants received IM AZD1222 5*10^10 vp on Day 1 and IM AZD2816 5*10^10 vp on Day 29 (4-week dosing interval).

Subject analysis set title	Booster Cohort:- AZD1222:AZD2816 (Comparator)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Seronegative participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.

Subject analysis set title	Booster Cohort:- AZD1222:AZD2816 (Reference)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Seronegative participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.

Subject analysis set title	Booster Cohort:- AZD1222:AZD1222 (Comparator)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Seronegative participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD1222 5*10^10 vp on Day 1.

Subject analysis set title	Booster Cohort:- AZD1222:AZD1222 (Reference)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Seronegative participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD1222 5*10^10 vp on Day 1.

Subject analysis set title	Booster Cohort:- AZD1222:AZD2816 (Comparator)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Seronegative participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.

Subject analysis set title	Booster Cohort:- AZD1222:AZD2816 (Reference)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Seronegative participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.

Subject analysis set title	Booster Cohort:- mRNA:AZD2816 (Comparator)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Seronegative participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.

Subject analysis set title	Booster Cohort:- mRNA:AZD2816 (Reference)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Seronegative participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.

Subject analysis set title	Booster Cohort:- mRNA:AZD1222 (Comparator)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Seronegative participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD1222 5*10^10 vp on Day 1.

Subject analysis set title	Booster Cohort:- mRNA:AZD1222 (Reference)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Seronegative participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD1222 5*10^10 vp on Day 1.

Subject analysis set title	Booster Cohort:- mRNA:AZD2816 (Comparator)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Seronegative participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.

Subject analysis set title	Booster Cohort:- mRNA:AZD2816 (Reference)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Seronegative participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.

Primary: Number of Participants With Local and Systemic Solicited Treatment Emergent Adverse Events (TEAEs) in Primary Vaccination Cohort (PVC):- AZD2816 (4), Booster Cohorts:-AZD1222:AZD2816, and mRNA:AZD2816

End point title	Number of Participants With Local and Systemic Solicited Treatment Emergent Adverse Events (TEAEs) in Primary Vaccination Cohort (PVC):- AZD2816 (4), Booster Cohorts:-AZD1222:AZD2816, and mRNA:AZD2816[1][2]

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. Solicited AEs: local or systemic predefined events for assessment of reactogenicity. An e-diary was used to collect information on timing and severity of solicited AEs. Local AEs included pain, redness/erythema, tenderness, induration/swelling at site of injection. Systemic AEs included fever, chills, muscle pains, fatigue, headache, malaise, nausea, and vomiting. Seronegative safety analysis set: all participants who received at least 1 dose of study treatment, were analysed according to treatment actually received, and were seronegative at baseline. Here, number of subjects analyzed denotes those participants who were evaluated for solicited symptoms.

End point type	Primary

End point timeframe:

During the 7-day follow-up period after vaccination (vaccines administered on Days 1 and 29 [only for primary vaccination cohort])

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD2816 (4)	Booster Cohort:- AZD1222:AZD2816	Booster Cohort:- mRNA:AZD2816	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	375	343	299	
Units: Participants				
Any solicited AEs	319	275	277	
Any local solicited AEs	278	225	236	
Any systemic solicited AEs	289	211	253	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Unsolicited TEAEs, Treatment-emergent Serious AEs (TESAEs), Medically Attended AEs (MAAEs), and Adverse Events of Special Interest (AESIs) in PVC:- AZD2816 (4), Booster Cohorts:- AZD1222:AZD2816, and mRNA:AZD2816

End point title	Number of Participants With Unsolicited TEAEs, Treatment-emergent Serious AEs (TESAEs), Medically Attended AEs (MAAEs), and Adverse Events of Special Interest (AESIs) in PVC:- AZD2816 (4), Booster Cohorts:- AZD1222:AZD2816, and mRNA:AZD2816[3][4]

End point description:

Unsolicited AEs (AEs other than solicited AEs) were collected by "open question" at study visits. TEAEs: AEs present at baseline that worsened in intensity after administration of study drug or AEs absent at baseline that emerged after administration of study drug. SAE: AE resulting in any of following outcomes/deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience; persistent or significant disability/incapacity; congenital anomaly. MAAE: AE leading to non-routine/unscheduled medically-attended visit, to or from medical doctor for any reason. AESI: AE of scientific/medical interest specific to further understanding of study drug safety profile and require close monitoring and rapid communication by investigators to Sponsor. Seronegative safety analysis set: all participants who received at least 1 dose of study treatment, were analysed according to treatment actually received, and were seronegative at baseline.

End point type	Primary

End point timeframe:

During the 28-day follow-up period after vaccination (vaccines administered on Days 1 and 29 [only for primary vaccination cohort])

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD2816 (4)	Booster Cohort:- AZD1222:AZD2816	Booster Cohort:- mRNA:AZD2816	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	379	348	302	
Units: Participants				
Any unsolicited TEAEs	96	70	79	

Any TESAEs	1	0	1	
Any MAAEs	31	26	24	
Any AESIs	10	1	6	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Abnormal Laboratory Parameters Reported as TEAEs in Primary Vaccination Cohort:- AZD2816 (4), Booster Cohorts:- AZD1222:AZD2816 and mRNA:AZD2816

End point title	Number of Participants With Abnormal Laboratory Parameters Reported as TEAEs in Primary Vaccination Cohort:- AZD2816 (4), Booster Cohorts:-AZD1222:AZD2816 and mRNA:AZD2816[5][6]

End point description:

Number of participants with abnormal laboratory parameters reported as TEAEs are reported. Laboratory tests included haematology and clinical chemistry. Seronegative safety analysis set included all participants who received at least 1 dose of study treatment, were analysed according to treatment actually received, and were seronegative at baseline.

End point type	Primary

End point timeframe:

During the 28-day follow-up period after vaccination (vaccines administered on Days 1 and 29 [only for primary vaccination cohort])

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.
[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD2816 (4)	Booster Cohort:- AZD1222:AZD2816	Booster Cohort:- mRNA:AZD2816	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	379	348	302	
Units: Participants				
Anaemia	1	0	0	
Eosinophilia	1	0	1	
Iron deficiency anaemia	2	0	1	
Hypercholesterolaemia	1	0	0	
Alanine aminotransferase increased	1	0	0	
Fibrin D dimer increased	1	2	4	
Haematocrit decreased	1	0	0	
Haemoglobin decreased	2	0	0	
Transaminases increased	1	0	0	
Lymphopenia	0	1	0	
Normochromic normocytic anaemia	0	1	0	
Thrombocytopenia	0	1	0	
Hyponatraemia	0	1	0	

Blood creatine increased	0	1	0	
White blood cell count increased	0	2	0	
Aspartate aminotransferase increased	0	0	1	
Blood alkaline phosphatase increased	0	0	1	
Blood fibrinogen increased	0	0	2	
Vitamin D decreased	0	0	1	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titre (GMT) of SARS-CoV-2 Neutralizing Antibodies (nAb) Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD2816 (4) and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 (4)

End point title	Geometric Mean Titre (GMT) of SARS-CoV-2 Neutralizing Antibodies (nAb) Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD2816 (4) and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 (4)[7]

End point description:

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of log-transformed titre, where 'n' was the number of participants with titre information. PVC:- AZD2816 (4) with response against B.1.351 variant is comparator group and PVC:- AZD1222 (4) with response against the original Wuhan-Hu-1 strain is reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Primary

End point timeframe:

28 days after second dose (Day 57)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	348	342		
Units: 1/dilution				
geometric mean (confidence interval 95%)	661.29 (617.16 to 708.57)	790.96 (735.29 to 850.85)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using analysis of covariance (ANCOVA).

Comparison groups	Primary Vaccination Cohort:- AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	690
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	GMT ratio
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	1.32

Notes:

[8] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% confidence interval (CI) of the GMT ratio of the comparator group and reference group was > 0.67.

Primary: GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD1222 and AZD1222 in Historical Control

End point title	GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD1222 and AZD1222 in Historical Control[9]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- AZD1222:AZD1222 is the comparator group and AZD1222 in Historical Control is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Primary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- AZD1222:AZD1222	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	329	508		
Units: 1/dilution				
geometric mean (confidence interval 95%)	246.45 (227.39 to 267.12)	242.80 (224.82 to 262.23)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD1222 v Historical Control
Number of subjects included in analysis	837
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	GMT ratio
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.14

Notes:

[10] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group is > 0.67.

Primary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD2816 (4) and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 (4)

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD2816 (4) and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 (4)[11]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Primary Vaccination Cohort:- AZD2816 (4) with response against B.1.351 variant is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Primary

End point timeframe:

28 days after second dose (Day 57)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	342		
Units: Percentage of participants				
number (confidence interval 95%)	87.79 (83.86 to 91.06)	89.47 (85.73 to 92.52)		

Statistical analyses

Statistical analysis title	Seroresponse difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	686
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Parameter estimate	Seroresponse difference
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.11
upper limit	6.49

Notes:

[12] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Primary: GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD1222 and AZD1222 in Historical Control

End point title	GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD1222 and AZD1222 in Historical Control[13]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- mRNA:AZD1222 is the comparator group and AZD1222 in Historical Control is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Primary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- mRNA:AZD1222	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	280	508		
Units: 1/dilution				
geometric mean (confidence interval 95%)	841.96 (790.34 to 896.96)	242.80 (224.82 to 262.23)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD1222 v Historical Control
Number of subjects included in analysis	788
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
Parameter estimate	GMT ratio
Point estimate	3.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.09
upper limit	3.89

Notes:

[14] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group is > 0.67.

Secondary: Number of Participants With Local and Systemic Solicited TEAEs

End point title	Number of Participants With Local and Systemic Solicited TEAEs[15]

End point description:

AE: any untoward medical occurrence in participant who received study drug without regard to possibility of causal relationship. TEAEs: AEs present at baseline that worsened in intensity after administration of study drug or AEs absent at baseline that emerged after administration of study drug. Solicited AEs are local or systemic predefined events for assessment of reactogenicity. An e-diary was used to collect information on timing and severity of solicited AEs. Local AEs included pain, redness/erythema, tenderness, induration/swelling at the site of the injection. Systemic AEs included fever (>100°F/37.8°C), chills, muscle pains, fatigue, headache, malaise, nausea, and vomiting. Seronegative safety analysis set included all participants who received at least 1 dose of study treatment, were analysed according to treatment actually received, and were seronegative at baseline. Here, number of subjects analyzed denotes those participants who were evaluated for solicited symptoms.

End point type	Secondary

End point timeframe:

During the 7-day follow-up period after vaccination (vaccines administered on Days 1 and 29 or Day 85 [only for primary vaccination cohorts])

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)	Primary Vaccination Cohort:- AZD2816 (12)	Booster Cohort:- AZD1222:AZD1222	Booster Cohort:- mRNA:AZD1222
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	373	188	340	299
Units: Participants				
Any solicited AEs	322	168	266	269
Any local solicited AEs	285	146	209	228
Any systemic solicited AEs	296	153	206	238

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Unsolicited TEAEs, TESAEs, MAAEs, and AESIs

End point title	Number of Participants With Unsolicited TEAEs, TESAEs, MAAEs, and AESIs[16]

End point description:

Unsolicited AEs (AEs other than solicited AEs) were collected by "open question" at study visits. TEAEs: AEs present at baseline that worsened in intensity after administration of study drug or AEs absent at baseline that emerged after administration of study drug. SAE: AE resulting in any of following outcomes/deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience; persistent or significant disability/incapacity; congenital anomaly. MAAE: AE leading to non-routine/unscheduled medically-attended visit, to or from medical doctor for any reason. AESI: AE of scientific/medical interest specific to further understanding of study drug safety profile and require close monitoring and rapid communication by investigators to Sponsor. Seronegative safety analysis set: all participants who received at least 1 dose of study treatment, were analysed according to treatment actually received, and were seronegative at baseline.

End point type	Secondary

End point timeframe:

During the 28-day follow-up period after vaccination (vaccines administered on Days 1 and 29 or Day 85 [only for primary vaccination cohorts])

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)	Primary Vaccination Cohort:- AZD2816 (12)	Booster Cohort:- AZD1222:AZD1222	Booster Cohort:- mRNA:AZD1222
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	380	191	349	300
Units: Participants				

Any unsolicited TEAEs	93	67	81	73
Any TESAEs	2	0	0	0
Any MAAEs	37	25	34	16
Any AESIs	9	7	3	6

Statistical analyses

No statistical analyses for this end point

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)[17]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of log-transformed titre, where 'n' was the number of participants with titre information. Primary Vaccination Cohort:- AZD2816 (4) is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	348	342		
Units: 1/dilution				
geometric mean (confidence interval 95%)	269.89 (260.72 to 279.37)	865.48 (837.85 to 894.02)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)

Number of subjects included in analysis	690
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Parameter estimate	GMT ratio
Point estimate	3.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.06
upper limit	3.36

Notes:

[18] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 (4)

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 (4)[19]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of log-transformed titre, where 'n' was the number of participants with titre information. PVC:- AZD1222 + AZD2816 (4) with response against B.1.351 variant is the comparator group and PVC:- AZD1222 (4) with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	348	334		
Units: 1/dilution				
geometric mean (confidence interval 95%)	800.92 (745.59 to 860.36)	405.20 (373.64 to 439.43)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	682
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
Parameter estimate	GMT ratio
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	0.56

Notes:

[20] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)

End point title	GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)[21]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of log-transformed titre, where 'n' was the number of participants with titre information. Primary Vaccination Cohort:-AZD2816 (4) is comparator group and Primary Vaccination Cohort:- AZD1222 (4) is reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre,and no protocol deviations judged to have potential to interfere with antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	348	342		
Units: 1/dilution				
geometric mean (confidence interval 95%)	719.37 (654.68 to 790.46)	222.75 (201.60 to 246.12)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	690
Analysis specification	Pre-specified
Analysis type	non-inferiority[22]
Parameter estimate	GMT ratio
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	0.35

Notes:

[22] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD2816 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD2816 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control[23]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- AZD1222:AZD2816 with response against B.1.351 variant is the comparator group and AZD1222 in Historical Control with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- AZD1222:AZD2816	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	322	508		
Units: 1/dilution				
geometric mean (confidence interval 95%)	341.96 (315.48 to 370.66)	242.80 (224.82 to 262.23)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD2816 v Historical Control
Number of subjects included in analysis	830
Analysis specification	Pre-specified
Analysis type	non-inferiority[24]
Parameter estimate	GMT ratio
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.25
upper limit	1.58

Notes:

[24] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD2816 and Booster Cohort:- AZD1222:AZD1222

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD2816 and Booster Cohort:- AZD1222:AZD1222[25]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- AZD1222:AZD2816 is the comparator group and Booster Cohort:- AZD1222:AZD1222 is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after booster dose (Day 29)

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end

point.

End point values	Booster Cohort:- AZD1222:AZD 1222	Booster Cohort:- AZD1222:AZD 2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	329	322		
Units: 1/dilution				
geometric mean (confidence interval 95%)	185.70 (169.32 to 203.66)	341.96 (315.48 to 370.66)		

Statistical analyses

Statistical analysis title	GMT Ratio
Statistical analysis description:	
The analyses were derived using ANCOVA.	
Comparison groups	Booster Cohort:- AZD1222:AZD2816 v Booster Cohort:- AZD1222:AZD1222
Number of subjects included in analysis	651
Analysis specification	Pre-specified
Analysis type	non-inferiority[26]
Parameter estimate	GMT ratio
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.63
upper limit	2.08

Notes:

[26] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD2816 and AZD1222 in Historical Control

End point title	GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD2816 and AZD1222 in Historical Control[27]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- AZD1222:AZD2816 is the comparator group and AZD1222 in Historical Control is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second

dose (Day 57)

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- AZD1222:AZD2816	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	322	508		
Units: 1/dilution				
geometric mean (confidence interval 95%)	213.26 (197.45 to 230.34)	242.80 (224.82 to 262.23)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD2816 v Historical Control
Number of subjects included in analysis	830
Analysis specification	Pre-specified
Analysis type	non-inferiority[28]
Parameter estimate	GMT ratio
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	0.99

Notes:

[28] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against the original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD2816 and Booster Cohort:- AZD1222:AZD1222

End point title	GMT of SARS-CoV-2 nAb Against the original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD2816 and Booster Cohort:- AZD1222:AZD1222[29]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- AZD1222:AZD2816 is the comparator group and Booster Cohort:- AZD1222:AZD1222 is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after booster dose (Day 29)

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- AZD1222:AZD1222	Booster Cohort:- AZD1222:AZD2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	329	322		
Units: 1/dilution				
geometric mean (confidence interval 95%)	246.45 (227.39 to 267.12)	213.26 (197.45 to 230.34)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD2816 v Booster Cohort:- AZD1222:AZD1222
Number of subjects included in analysis	651
Analysis specification	Pre-specified
Analysis type	non-inferiority[30]
Parameter estimate	GMT ratio
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	0.97

Notes:

[30] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD2816 and Primary Vaccination Cohort:- AZD1222 (4)

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD2816 and Primary Vaccination Cohort:- AZD1222 (4)[31]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- AZD1222:AZD2816 is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations

judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Primary Vaccination Cohort: 28 days after the second dose (Day 57)

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Booster Cohort:- AZD1222:AZD 2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	348	322		
Units: 1/dilution				
geometric mean (confidence interval 95%)	360.43 (324.90 to 399.84)	341.96 (315.48 to 370.66)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD2816 v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	non-inferiority[32]
Parameter estimate	GMT ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.08

Notes:

[32] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD2816 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD2816 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control[33]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean

of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- mRNA:AZD2816 with response against B.1.351 variant is the comparator group and AZD1222 in Historical Control with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- mRNA:AZD2816	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	280	508		
Units: 1/dilution				
geometric mean (confidence interval 95%)	1587.58 (1463.98 to 1721.61)	242.80 (224.82 to 262.23)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD2816 v Historical Control
Number of subjects included in analysis	788
Analysis specification	Pre-specified
Analysis type	non-inferiority[34]
Parameter estimate	GMT ratio
Point estimate	6.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.82
upper limit	7.4

Notes:

[34] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD2816 and Booster Cohort:- mRNA:AZD1222

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD2816 and Booster Cohort:- mRNA:AZD1222[35]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- mRNA:AZD2816 is the comparator group and Booster Cohort:- mRNA:AZD1222 is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after booster dose (Day 29)

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- mRNA:AZD1222	Booster Cohort:- mRNA:AZD2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	280	280		
Units: 1/dilution				
geometric mean (confidence interval 95%)	718.90 (670.46 to 770.84)	1587.58 (1463.98 to 1721.61)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD2816 v Booster Cohort:- mRNA:AZD1222
Number of subjects included in analysis	560
Analysis specification	Pre-specified
Analysis type	non-inferiority[36]
Parameter estimate	GMT ratio
Point estimate	2.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.99
upper limit	2.47

Notes:

[36] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD2816 and AZD1222 in Historical Control

End point title	GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD2816 and AZD1222 in Historical Control[37]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- mRNA:AZD2816 is the comparator group and AZD1222 in Historical Control is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- mRNA:AZD2816	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	280	508		
Units: 1/dilution				
geometric mean (confidence interval 95%)	1052.73 (974.55 to 1137.19)	242.80 (224.82 to 262.23)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD2816 v Historical Control
Number of subjects included in analysis	788
Analysis specification	Pre-specified
Analysis type	non-inferiority[38]
Parameter estimate	GMT ratio
Point estimate	4.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.86
upper limit	4.9

Notes:

[38] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group is > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD2816 and Booster Cohort:- mRNA:AZD1222

End point title	GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD2816 and Booster Cohort:- mRNA:AZD1222[39]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- mRNA:AZD2816 is the comparator group and Booster Cohort:- mRNA:AZD1222 is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after booster dose (Day 29)

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- mRNA:AZD1222	Booster Cohort:- mRNA:AZD2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	280	280		
Units: 1/dilution				
geometric mean (confidence interval 95%)	841.96 (790.34 to 896.96)	1052.73 (974.55 to 1137.19)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD2816 v Booster Cohort:- mRNA:AZD1222
Number of subjects included in analysis	560
Analysis specification	Pre-specified
Analysis type	non-inferiority[40]
Parameter estimate	GMT ratio
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	1.39

Notes:

[40] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD2816 and Primary Vaccination Cohort:- AZD1222 (4)

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD2816 and Primary Vaccination Cohort:- AZD1222 (4)[41]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- mRNA:AZD2816 is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Primary Vaccination Cohort: 28 days after the second dose (Day 57)

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Booster Cohort:- mRNA:AZD2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	348	280		
Units: 1/dilution				
geometric mean (confidence interval 95%)	360.43 (324.90 to 399.84)	1587.58 (1463.98 to 1721.61)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD2816 v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	628
Analysis specification	Pre-specified
Analysis type	non-inferiority[42]
Parameter estimate	GMT ratio
Point estimate	4.42

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.85
upper limit	5.08

Notes:

[42] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD2816 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD2816 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control[43]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- AZD1222:AZD2816 with response against B.1.351 variant is the comparator group and AZD1222 in Historical Control with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- AZD1222:AZD2816	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	320	508		
Units: Percentage of participants				
number (confidence interval 95%)	82.81 (78.22 to 86.78)	84.06 (80.58 to 87.13)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD2816 v Historical Control

Number of subjects included in analysis	828
Analysis specification	Pre-specified
Analysis type	non-inferiority[44]
Parameter estimate	Seroresponse difference
Point estimate	-1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.62
upper limit	3.84

Notes:

[44] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD2816 and Booster Cohort:- AZD1222:AZD1222

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD2816 and Booster Cohort:- AZD1222:AZD1222[45]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- AZD1222:AZD2816 is the comparator group and Booster Cohort:- AZD1222:AZD1222 is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after booster dose (Day 29)

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- AZD1222:AZD1222	Booster Cohort:- AZD1222:AZD2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	329	320		
Units: Percentage of participants				
number (confidence interval 95%)	65.96 (60.56 to 71.07)	82.81 (78.22 to 86.78)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD2816 v Booster Cohort:- AZD1222:AZD1222
Number of subjects included in analysis	649
Analysis specification	Pre-specified
Analysis type	non-inferiority[46]
Parameter estimate	Seroresponse difference
Point estimate	16.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.18
upper limit	23.32

Notes:

[46] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD2816 and AZD1222 in Historical Control

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD2816 and AZD1222 in Historical Control[47]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- AZD1222:AZD2816 is the comparator group and AZD1222 in Historical Control is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[47] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- AZD1222:AZD2816	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	320	508		
Units: Percentage of participants				
number (confidence interval 95%)	65.94 (60.46 to 71.12)	84.06 (80.58 to 87.13)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD2816 v Historical Control
Number of subjects included in analysis	828
Analysis specification	Pre-specified
Analysis type	non-inferiority[48]
Parameter estimate	Seroresponse difference
Point estimate	-18.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.22
upper limit	-12.07

Notes:

[48] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD2816 and Booster Cohort:- AZD1222:AZD1222

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD2816 and Booster Cohort:- AZD1222:AZD1222[49]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- AZD1222:AZD2816 is the comparator group and Booster Cohort:- AZD1222:AZD1222 is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after booster dose (Day 29)

Notes:

[49] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- AZD1222:AZD1222	Booster Cohort:- AZD1222:AZD2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	329	320		
Units: Percentage of participants				
number (confidence interval 95%)	65.96 (60.56 to 71.07)	65.94 (60.46 to 71.12)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD2816 v Booster Cohort:- AZD1222:AZD1222
Number of subjects included in analysis	649
Analysis specification	Pre-specified
Analysis type	non-inferiority[50]
Parameter estimate	Seroresponse difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.28
upper limit	7.23

Notes:

[50] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD2816 and Primary Vaccination Cohort:- AZD1222 (4)

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD2816 and Primary Vaccination Cohort:- AZD1222 (4)[51]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- AZD1222:AZD2816 is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Primary Vaccination Cohort: 28 days after the second dose (Day 57)

Notes:

[51] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Booster Cohort:- AZD1222:AZD2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	320		
Units: Percentage of participants				
number (confidence interval 95%)	51.45 (46.03 to 56.85)	82.81 (78.22 to 86.78)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD2816 v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	664
Analysis specification	Pre-specified
Analysis type	non-inferiority[52]
Parameter estimate	Seroresponse difference
Point estimate	31.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	24.44
upper limit	37.82

Notes:

[52] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD2816 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD2816 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control[53]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- mRNA:AZD2816 with response against B.1.351 variant is the comparator group and AZD1222 in Historical Control with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[53] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- mRNA:AZD2816	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	277	508		
Units: Percentage of participants				
number (confidence interval 95%)	80.51 (75.34 to 85.00)	84.06 (80.58 to 87.13)		

Statistical analyses

Statistical analysis title	Seroresponse Difference
Statistical analysis description:	
The analyses were derived using ANCOVA.	
Comparison groups	Booster Cohort:- mRNA:AZD2816 v Historical Control
Number of subjects included in analysis	785
Analysis specification	Pre-specified
Analysis type	non-inferiority[54]
Parameter estimate	Seroresponse difference
Point estimate	-3.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.4
upper limit	1.9

Notes:

[54] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD2816 and AZD1222 in Historical Control

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD2816 and AZD1222 in Historical Control[55]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- mRNA:AZD2816 is the comparator group and AZD1222 in Historical Control is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[55] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end

point.

End point values	Booster Cohort:- mRNA:AZD2816	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	277	508		
Units: Percentage of participants				
number (confidence interval 95%)	49.82 (43.78 to 55.86)	84.06 (80.58 to 87.13)		

Statistical analyses

Statistical analysis title	Seroresponse Difference
Statistical analysis description:	
The analyses were derived using ANCOVA.	
Comparison groups	Booster Cohort:- mRNA:AZD2816 v Historical Control
Number of subjects included in analysis	785
Analysis specification	Pre-specified
Analysis type	non-inferiority[56]
Parameter estimate	Seroresponse difference
Point estimate	-34.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.77
upper limit	-27.45

Notes:

[56] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD2816 and Booster Cohort:- mRNA:AZD1222

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD2816 and Booster Cohort:- mRNA:AZD1222[57]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- mRNA:AZD2816 is the comparator group and Booster Cohort:- mRNA:AZD1222 is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after booster dose (Day 29)

Notes:

[57] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- mRNA:AZD1222	Booster Cohort:- mRNA:AZD2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	280	277		
Units: Percentage of participants				
number (confidence interval 95%)	57.50 (51.48 to 63.36)	80.51 (75.34 to 85.00)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD2816 v Booster Cohort:- mRNA:AZD1222
Number of subjects included in analysis	557
Analysis specification	Pre-specified
Analysis type	non-inferiority[58]
Parameter estimate	Seroresponse difference
Point estimate	23.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.41
upper limit	30.23

Notes:

[58] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD2816 and Primary Vaccination Cohort:- AZD1222 (4)

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD2816 and Primary Vaccination Cohort:- AZD1222 (4)[59]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- mRNA:AZD2816 is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Primary Vaccination Cohort: 28 days after the second dose (Day 57)

Notes:

[59] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Booster Cohort:- mRNA:AZD2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	277		
Units: Percentage of participants				
number (confidence interval 95%)	51.45 (46.03 to 56.85)	80.51 (75.34 to 85.00)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD2816 v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	621
Analysis specification	Pre-specified
Analysis type	non-inferiority[60]
Parameter estimate	Seroresponse difference
Point estimate	29.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.76
upper limit	35.81

Notes:

[60] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD2816 and Booster Cohort:- mRNA:AZD1222

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD2816 and Booster Cohort:- mRNA:AZD1222[61]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- mRNA:AZD2816 is the comparator group and Booster Cohort:- mRNA:AZD1222 is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at

baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after booster dose (Day 29)

Notes:

[61] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- mRNA:AZD1222	Booster Cohort:- mRNA:AZD2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	280	277		
Units: Percentage of participants				
number (confidence interval 95%)	42.86 (36.99 to 48.88)	49.82 (43.78 to 55.86)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD2816 v Booster Cohort:- mRNA:AZD1222
Number of subjects included in analysis	557
Analysis specification	Pre-specified
Analysis type	non-inferiority[62]
Parameter estimate	Seroresponse difference
Point estimate	6.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	15.1

Notes:

[62] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Number of Participants With TESAEs, MAAEs, and AESIs From Day 1 Through 6 Months Post Last Dose

End point title	Number of Participants With TESAEs, MAAEs, and AESIs From Day 1 Through 6 Months Post Last Dose[63]

End point description:

TEAEs: AEs present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. SAE: an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. MAAEs: AEs leading to medically-attended visits that were unscheduled visits to or from medical doctor for any reason. AESIs: AEs of scientific/medical interest specific to the further understanding of study drug safety profile and require close monitoring and rapid

communication by the investigators to the Sponsor. Seronegative safety analysis set: all participants who received at least 1 dose of study treatment, were analysed according to treatment actually received, and were seronegative at baseline.

End point type	Secondary

End point timeframe:

During the 6 months follow-up period after vaccination (vaccines administered on Days 1 and 29 or Day 85 [only for primary vaccination cohorts])

Notes:

[63] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD2816 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)	Primary Vaccination Cohort:- AZD2816 (12)	Booster Cohort:- AZD1222:AZD 1222
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	379	380	191	349
Units: Participants				
Any TESAEs	2	5	2	6
Any MAAEs	69	82	50	72
Any AESIs	48	51	32	41

End point values	Booster Cohort:- AZD1222:AZD 2816	Booster Cohort:- mRNA:AZD122 2	Booster Cohort:- mRNA:AZD281 6	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	348	300	302	
Units: Participants				
Any TESAEs	7	3	4	
Any MAAEs	65	47	58	
Any AESIs	42	31	33	

Statistical analyses

No statistical analyses for this end point

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)[64]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against B.1.351 variant.

Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

Notes:

[64] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	348	334		
Units: 1/dilution				
geometric mean (confidence interval 95%)	329.46 (319.47 to 339.76)	446.63 (432.91 to 460.78)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	682
Analysis specification	Pre-specified
Analysis type	non-inferiority[65]
Parameter estimate	GMT ratio
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	1.42

Notes:

[65] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)

End point title	GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)[66]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of log-transformed titre, where 'n' was the number of participants with titre information. Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against the Original Wuhan-Hu-1 Strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

Notes:

[66] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	348	334		
Units: 1/dilution				
geometric mean (confidence interval 95%)	769.03 (731.95 to 808.00)	581.78 (553.12 to 611.92)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	682
Analysis specification	Pre-specified
Analysis type	non-inferiority[67]
Parameter estimate	GMT ratio
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.81

Notes:

[67] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant and the Original

Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD2816 (4)	
End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD2816 (4)

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of log-transformed titre, where 'n' was the number of participants with titre information. Primary Vaccination Cohort:- AZD2816 (4) with response against B.1.351 variant is comparator group and Primary Vaccination Cohort:- AZD2816 (4) with response against the original Wuhan-Hu-1 strain is reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

End point values	Primary Vaccination Cohort:- AZD2816 (4) (Comparator)	Primary Vaccination Cohort:- AZD2816 (4) (Reference)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	342	342		
Units: 1/dilution				
geometric mean (confidence interval 95%)	718.10 (662.58 to 778.27)	185.70 (168.16 to 205.07)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD2816 (4) (Comparator) v Primary Vaccination Cohort:- AZD2816 (4) (Reference)
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	non-inferiority[68]
Parameter estimate	GMT ratio
Point estimate	3.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.4
upper limit	4.39

Notes:

[68] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against the B.1.351 Variant and the Original Wuhan-Hu-1 Strain by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)

End point title	GMT of SARS-CoV-2 nAb Against the B.1.351 Variant and the Original Wuhan-Hu-1 Strain by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of mean of log-transformed titre, where 'n' was number of participants with titre information. Primary Vaccination Cohort:-AZD1222+AZD2816 (4) with response against B.1.351 variant is comparator group and Primary Vaccination Cohort:-AZD1222+AZD2816 (4) with response against the original Wuhan-Hu-1 strain is reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, no protocol deviations judged to have potential to interfere with antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

End point values	Primary Vaccination Cohort:- AZD1222+AZD 2816 (4) (Comparator)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) (Reference)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	334	334		
Units: 1/dilution				
geometric mean (confidence interval 95%)	392.13 (380.34 to 404.28)	586.00 (566.15 to 606.54)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD1222+AZD2816 (4) (Comparator) v Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) (Reference)
Number of subjects included in analysis	668
Analysis specification	Pre-specified
Analysis type	non-inferiority[69]
Parameter estimate	GMT ratio
Point estimate	0.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.7

Notes:

[69] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)[70]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Primary Vaccination Cohort:- AZD2816 (4) is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame. The arbitrary number 999 signified the upper limit of 95% confidence interval was not evaluable as all participants had seroresponse for the specified arm.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

Notes:

[70] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	342		
Units: Percentage of participants				
number (confidence interval 95%)	99.42 (97.92 to 99.93)	100 (98.73 to 999)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)

Number of subjects included in analysis	686
Analysis specification	Pre-specified
Analysis type	non-inferiority[71]
Parameter estimate	Seroresponse difference
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	2.09

Notes:

[71] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)[72]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Primary Vaccination Cohort:- AZD2816 (4) is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

Notes:

[72] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	342		
Units: Percentage of participants				
number (confidence interval 95%)	84.59 (80.34 to 88.24)	49.42 (44.00 to 54.85)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:	
The analyses were derived using ANCOVA.	
Comparison groups	Primary Vaccination Cohort:- AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	686
Analysis specification	Pre-specified
Analysis type	non-inferiority[73]
Parameter estimate	Seroresponse difference
Point estimate	-35.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.46
upper limit	-28.44

Notes:

[73] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)[74]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

Notes:

[74] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	334		
Units: Percentage of participants				
number (confidence interval 95%)	99.42 (97.92 to 99.93)	99.40 (97.85 to 99.93)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	678
Analysis specification	Pre-specified
Analysis type	non-inferiority[75]
Parameter estimate	Seroresponse difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.63
upper limit	1.56

Notes:

[75] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) and the Original Wuhan Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 (4)

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) and the Original Wuhan Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 (4)[76]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) with response against B.1.351 variant is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

Notes:

[76] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	334		
Units: Percentage of participants				
number (confidence interval 95%)	87.50 (83.53	62.57 (57.14		

to 90.80)	to 67.78)

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	678
Analysis specification	Pre-specified
Analysis type	non-inferiority[77]
Parameter estimate	Seroresponse difference
Point estimate	-24.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.06
upper limit	-18.56

Notes:

[77] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD2816 (4)

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD2816 (4)

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Primary Vaccination Cohort:- AZD2816 (4) with response against B.1.351 variant is the comparator group and Primary Vaccination Cohort:- AZD2816 (4) with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

End point values	Primary Vaccination Cohort:- AZD2816 (4) (Comparator)	Primary Vaccination Cohort:- AZD2816 (4) (Reference)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	342	342		
Units: Percentage of participants				
number (confidence interval 95%)	88.60 (84.74 to 91.76)	49.42 (44.00 to 54.85)		

Statistical analyses

Statistical analysis title	Seroresponse Difference
Statistical analysis description:	
The analyses were derived using ANCOVA.	
Comparison groups	Primary Vaccination Cohort:- AZD2816 (4) (Comparator) v Primary Vaccination Cohort:- AZD2816 (4) (Reference)
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	non-inferiority[78]
Parameter estimate	Seroresponse difference
Point estimate	39.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	32.68
upper limit	45.21

Notes:

[78] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4)[79]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

Notes:

[79] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	334		
Units: Percentage of participants				
number (confidence interval 95%)	99.42 (97.92 to 99.93)	80.24 (75.56 to 84.38)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	678
Analysis specification	Pre-specified
Analysis type	non-inferiority[80]
Parameter estimate	Seroresponse difference
Point estimate	-19.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.8
upper limit	-14.98

Notes:

[80] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) with response against B.1.351 variant is the comparator group and Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary
End point timeframe:	
28 days after second dose (Day 57)	

End point values	Primary Vaccination Cohort:- AZD1222+AZD2816 (4) (Comparator)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) (Reference)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	334	334		
Units: Percentage of participants				
number (confidence interval 95%)	99.40 (97.85 to 99.93)	99.40 (97.85 to 99.93)		

Statistical analyses

Statistical analysis title	Seroresponse Difference
Statistical analysis description:	
The analyses were derived using ANCOVA.	
Comparison groups	Primary Vaccination Cohort:- AZD1222+AZD2816 (4) (Comparator) v Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) (Reference)
Number of subjects included in analysis	668
Analysis specification	Pre-specified
Analysis type	non-inferiority[81]
Parameter estimate	Seroresponse difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.62
upper limit	1.62

Notes:

[81] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD1222 and Primary Vaccination Cohort:- AZD1222 (4)

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD1222 and Primary Vaccination Cohort:- AZD1222 (4)[82]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- AZD1222:AZD1222 is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment

actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Primary Vaccination Cohort: 28 days after the second dose (Day 57)

Notes:

[82] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Booster Cohort:- AZD1222:AZD1222		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	348	329		
Units: 1/dilution				
geometric mean (confidence interval 95%)	360.43 (324.90 to 399.84)	185.70 (169.32 to 203.66)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD1222 v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	677
Analysis specification	Pre-specified
Analysis type	non-inferiority[83]
Parameter estimate	GMT ratio
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	0.59

Notes:

[83] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD1222 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD1222 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control[84]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:-

AZD1222:AZD1222 with response against B.1.351 variant is the comparator group and AZD1222 in Historical Control with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[84] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- AZD1222:AZD1222	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	329	508		
Units: 1/dilution				
geometric mean (confidence interval 95%)	185.70 (169.32 to 203.66)	242.80 (224.82 to 262.23)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD1222 v Historical Control
Number of subjects included in analysis	837
Analysis specification	Pre-specified
Analysis type	non-inferiority[85]
Parameter estimate	GMT ratio
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.86

Notes:

[85] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against the B.1.351 Variant and the Original Wuhan-Hu-1 Strain by Booster Cohort:- AZD1222:AZD2816

End point title	GMT of SARS-CoV-2 nAb Against the B.1.351 Variant and the Original Wuhan-Hu-1 Strain by Booster Cohort:- AZD1222:AZD2816

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- AZD1222:AZD2816 with response against B.1.351 variant is the comparator group and Booster Cohort:- AZD1222:AZD2816 with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

End point values	Booster Cohort:- AZD1222:AZD2816 (Comparator)	Booster Cohort:- AZD1222:AZD2816 (Reference)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	322	322		
Units: 1/dilution				
geometric mean (confidence interval 95%)	341.96 (315.48 to 370.66)	213.26 (197.45 to 230.34)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD2816 (Comparator) v Booster Cohort:- AZD1222:AZD2816 (Reference)
Number of subjects included in analysis	644
Analysis specification	Pre-specified
Analysis type	non-inferiority[86]
Parameter estimate	GMT ratio
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.43
upper limit	1.79

Notes:

[86] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD1222 and AZD1222 in Historical Control

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2

	nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD1222 and AZD1222 in Historical Control[87]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- AZD1222:AZD1222 is the comparator group and AZD1222 in Historical Control is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[87] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- AZD1222:AZD1222	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	329	508		
Units: Percentage of participants				
number (confidence interval 95%)	65.96 (60.56 to 71.07)	84.06 (80.58 to 87.13)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD1222 v Historical Control
Number of subjects included in analysis	837
Analysis specification	Pre-specified
Analysis type	non-inferiority[88]
Parameter estimate	Seroresponse difference
Point estimate	-18.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.13
upper limit	-12.1

Notes:

[88] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: GMT of SARS-CoV-2 nAb Against the B.1.351 Variant and the Original

Wuhan-Hu-1 Strain by Booster Cohort:- AZD1222:AZD1222	
End point title	GMT of SARS-CoV-2 nAb Against the B.1.351 Variant and the Original Wuhan-Hu-1 Strain by Booster Cohort:- AZD1222:AZD1222

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of log-transformed titre, where 'n' was the number of participants with titre information.Booster Cohort:- AZD1222:AZD1222 with response against B.1.351 variant is comparator group and Booster Cohort:- AZD1222:AZD1222 with response against the original Wuhan-Hu-1 strain is reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

End point values	Booster Cohort:- AZD1222:AZD1222 (Comparator)	Booster Cohort:- AZD1222:AZD1222 (Reference)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	329	329		
Units: 1/dilution				
geometric mean (confidence interval 95%)	185.70 (169.32 to 203.66)	246.45 (227.39 to 267.12)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD1222 (Comparator) v Booster Cohort:- AZD1222:AZD1222 (Reference)
Number of subjects included in analysis	658
Analysis specification	Pre-specified
Analysis type	non-inferiority[89]
Parameter estimate	GMT ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.85

Notes:

[89] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD1222 and Primary Vaccination Cohort:- AZD1222 (4)

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD1222 and Primary Vaccination Cohort:- AZD1222 (4)[90]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- AZD1222:AZD1222 is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against B.1.351 Variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[90] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Booster Cohort:- AZD1222:AZD1222		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	329		
Units: Percentage of participants				
number (confidence interval 95%)	51.45 (46.03 to 56.85)	65.96 (60.56 to 71.07)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD1222 v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	673
Analysis specification	Pre-specified
Analysis type	non-inferiority[91]
Parameter estimate	Seroresponse difference
Point estimate	14.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.07
upper limit	21.71

Notes:

[91] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD1222 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- AZD1222:AZD1222 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control[92]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- AZD1222:AZD1222 with response against B.1.351 variant is the comparator group and AZD1222 in Historical Control with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[92] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- AZD1222:AZD1222	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	329	508		
Units: Percentage of participants				
number (confidence interval 95%)	65.96 (60.56 to 71.07)	84.06 (80.58 to 87.13)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD1222 v Historical Control
Number of subjects included in analysis	837
Analysis specification	Pre-specified
Analysis type	non-inferiority[93]
Parameter estimate	Seroresponse difference
Point estimate	-18.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.13
upper limit	-12.1

Notes:

[93] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant and the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD2816

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant and the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD2816

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- AZD1222:AZD2816 with response against B.1.351 variant is the comparator group and Booster Cohort:- AZD1222:AZD2816 with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

End point values	Booster Cohort:- AZD1222:AZD2816 (Comparator)	Booster Cohort:- AZD1222:AZD2816 (Reference)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	320	320		
Units: Percentage of participants				
number (confidence interval 95%)	82.81 (78.22 to 86.78)	65.94 (60.46 to 71.12)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD2816 (Comparator) v Booster Cohort:- AZD1222:AZD2816 (Reference)

Number of subjects included in analysis	640
Analysis specification	Pre-specified
Analysis type	non-inferiority[94]
Parameter estimate	Seroresponse difference
Point estimate	16.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.15
upper limit	23.4

Notes:

[94] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant and the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD1222

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant and the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- AZD1222:AZD1222

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- AZD1222:AZD1222 with response against B.1.351 variant is the comparator group and Booster Cohort:- AZD1222:AZD1222 with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

End point values	Booster Cohort:- AZD1222:AZD1222 (Comparator)	Booster Cohort:- AZD1222:AZD1222 (Reference)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	329	329		
Units: Percentage of participants				
number (confidence interval 95%)	65.96 (60.56 to 71.07)	65.96 (60.56 to 71.07)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- AZD1222:AZD1222 (Comparator) v Booster Cohort:- AZD1222:AZD1222 (Reference)

Number of subjects included in analysis	658
Analysis specification	Pre-specified
Analysis type	non-inferiority[95]
Parameter estimate	Seroresponse difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.21
upper limit	7.21

Notes:

[95] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD1222 and Primary Vaccination Cohort:- AZD1222 (4)

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD1222 and Primary Vaccination Cohort:- AZD1222 (4)[96]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- mRNA:AZD1222 is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Primary Vaccination Cohort: 28 days after the second dose (Day 57)

Notes:

[96] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Booster Cohort:- mRNA:AZD1222		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	348	280		
Units: 1/dilution				
geometric mean (confidence interval 95%)	360.43 (324.90 to 399.84)	718.90 (670.46 to 770.84)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:	
The analyses were derived using ANCOVA.	
Comparison groups	Booster Cohort:- mRNA:AZD1222 v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	628
Analysis specification	Pre-specified
Analysis type	non-inferiority[97]
Parameter estimate	GMT ratio
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.75
upper limit	2.28

Notes:

[97] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD1222 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD1222 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control[98]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- mRNA:AZD1222 with response against B.1.351 variant is the comparator group and AZD1222 in Historical Control with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[98] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- mRNA:AZD1222	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	280	508		
Units: 1/dilution				
geometric mean (confidence interval 95%)	718.90 (670.46 to 770.84)	242.80 (224.82 to 262.23)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD1222 v Historical Control
Number of subjects included in analysis	788
Analysis specification	Pre-specified
Analysis type	non-inferiority[99]
Parameter estimate	GMT ratio
Point estimate	2.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.64
upper limit	3.32

Notes:

[99] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD1222 and AZD1222 in Historical Control

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD1222 and AZD1222 in Historical Control[100]

End point description:

Severe acute respiratory syndrome-coronavirus-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- mRNA:AZD1222 is the comparator group and AZD1222 in Historical Control is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[100] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- mRNA:AZD1222	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	280	508		
Units: Percentage of participants				
number (confidence interval 95%)	42.86 (36.99 to 48.88)	84.06 (80.58 to 87.13)		

Statistical analyses

Statistical analysis title	Seroresponse Difference
Statistical analysis description:	
The analyses were derived using ANCOVA.	
Comparison groups	Booster Cohort:- mRNA:AZD1222 v Historical Control
Number of subjects included in analysis	788
Analysis specification	Pre-specified
Analysis type	non-inferiority[101]
Parameter estimate	Seroresponse difference
Point estimate	-41.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-47.57
upper limit	-34.41

Notes:

[101] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: GMT of SARS-CoV-2 nAb Against the B.1.351 Variant and the Original Wuhan-Hu-1 Strain by Booster Cohort:- mRNA:AZD1222

End point title	GMT of SARS-CoV-2 nAb Against the B.1.351 Variant and the Original Wuhan-Hu-1 Strain by Booster Cohort:- mRNA:AZD1222

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- mRNA:AZD1222 with response against B.1.351 variant is the comparator group and Booster Cohort:- mRNA:AZD1222 with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

End point values	Booster Cohort:- mRNA:AZD1222 (Comparator)	Booster Cohort:- mRNA:AZD1222 (Reference)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	280	280		
Units: 1/dilution				
geometric mean (confidence interval 95%)	718.90 (670.46 to 770.84)	841.96 (790.34 to 896.96)		

Statistical analyses

Statistical analysis title	GMT Ratio
Statistical analysis description:	
The analyses were derived using ANCOVA.	
Comparison groups	Booster Cohort:- mRNA:AZD1222 (Comparator) v Booster Cohort:- mRNA:AZD1222 (Reference)
Number of subjects included in analysis	560
Analysis specification	Pre-specified
Analysis type	non-inferiority[102]
Parameter estimate	GMT ratio
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	0.94

Notes:

[102] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against the B.1.351 Variant and the Original Wuhan-Hu-1 Strain by Booster Cohort:- mRNA:AZD2816

End point title	GMT of SARS-CoV-2 nAb Against the B.1.351 Variant and the Original Wuhan-Hu-1 Strain by Booster Cohort:- mRNA:AZD2816

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Booster Cohort:- mRNA:AZD2816 with response against B.1.351 variant is the comparator group and Booster Cohort:- mRNA:AZD2816 with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

End point values	Booster Cohort:- mRNA:AZD2816 (Comparator)	Booster Cohort:- mRNA:AZD2816 (Reference)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	280	280		
Units: 1/dilution				
geometric mean (confidence interval 95%)	1587.58 (1463.98 to 1721.61)	1052.73 (974.55 to 1137.19)		

Statistical analyses

Statistical analysis title	GMT Ratio
Statistical analysis description:	
The analyses were derived using ANCOVA.	
Comparison groups	Booster Cohort:- mRNA:AZD2816 (Comparator) v Booster Cohort:- mRNA:AZD2816 (Reference)
Number of subjects included in analysis	560
Analysis specification	Pre-specified
Analysis type	non-inferiority[103]
Parameter estimate	GMT ratio
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.35
upper limit	1.69

Notes:

[103] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD1222 and Primary Vaccination Cohort:- AZD1222 (4)

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD1222 and Primary Vaccination Cohort:- AZD1222 (4)[104]

End point description:

Severe acute respiratory syndrome-coronavirus-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- mRNA:AZD1222 is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against B.1.351 Variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[104] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Booster Cohort:- mRNA:AZD1222		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	280		
Units: Percentage of participants				
number (confidence interval 95%)	51.45 (46.03 to 56.85)	57.50 (51.48 to 63.36)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD1222 v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	non-inferiority[105]
Parameter estimate	Seroresponse difference
Point estimate	6.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.81
upper limit	13.77

Notes:

[105] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant and the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD2816

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant and the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD2816

End point description:

Severe acute respiratory syndrome-coronavirus-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- mRNA:AZD2816 with response against B.1.351 variant is the comparator group and Booster Cohort:- mRNA:AZD2816 with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of

subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

End point values	Booster Cohort:- mRNA:AZD2816 (Comparator)	Booster Cohort:- mRNA:AZD2816 (Reference)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	277	277		
Units: Percentage of participants				
number (confidence interval 95%)	80.51 (75.34 to 85.00)	49.82 (43.78 to 55.86)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD2816 (Comparator) v Booster Cohort:- mRNA:AZD2816 (Reference)
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	non-inferiority[106]
Parameter estimate	Seroresponse difference
Point estimate	30.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.94
upper limit	37.9

Notes:

[106] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD1222 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Booster Cohort:- mRNA:AZD1222 and the Original Wuhan-Hu-1 Strain Elicited by AZD1222 in Historical Control[107]

End point description:

Severe acute respiratory syndrome-coronavirus-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- mRNA:AZD1222 with response against B.1.351 variant is the comparator group and AZD1222 in Historical Control with response against the original Wuhan-Hu-1 strain is the reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum

titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohort: 28 days after booster dose (Day 29) and Historical Control: 28 days after the second dose (Day 57)

Notes:

[107] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Booster Cohort:- mRNA:AZD1222	Historical Control		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	280	508		
Units: Percentage of participants				
number (confidence interval 95%)	57.50 (51.48 to 63.36)	84.06 (80.58 to 87.13)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD1222 v Historical Control
Number of subjects included in analysis	788
Analysis specification	Pre-specified
Analysis type	non-inferiority[108]
Parameter estimate	Seroresponse difference
Point estimate	-26.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.1
upper limit	-19.94

Notes:

[108] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant and the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD1222

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 nAb Against B.1.351 Variant and the Original Wuhan-Hu-1 Strain Elicited by Booster Cohort:- mRNA:AZD1222

End point description:

Severe acute respiratory syndrome-coronavirus-2 nAb were measured by pseudoneutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Booster Cohort:- mRNA:AZD1222 with response against B.1.351 variant is the comparator group and Booster Cohort:- mRNA:AZD1222 with response against the original Wuhan-Hu-1 strain is the reference group.

Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after second dose (Day 57)

End point values	Booster Cohort:- mRNA:AZD1222 (Comparator)	Booster Cohort:- mRNA:AZD1222 (Reference)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	280	280		
Units: Percentage of participants				
number (confidence interval 95%)	57.50 (51.48 to 63.36)	42.86 (36.99 to 48.88)		

Statistical analyses

Statistical analysis title	Seroresponse Difference

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Booster Cohort:- mRNA:AZD1222 (Comparator) v Booster Cohort:- mRNA:AZD1222 (Reference)
Number of subjects included in analysis	560
Analysis specification	Pre-specified
Analysis type	non-inferiority[109]
Parameter estimate	Seroresponse difference
Point estimate	14.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.36
upper limit	22.64

Notes:

[109] - Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI rate difference in seroresponse between the comparator group and reference group was > or =-10%.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4) on Day 29

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4) on Day 29[110]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Primary Vaccination Cohort:- AZD2816 (4) is the comparator group and Primary Vaccination Cohort:- AZD1222

(4) is the reference group, both compared for response against B.1.351 variant. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after first dose (Day 29)

Notes:

[110] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	361	357		
Units: 1/dilution				
geometric mean (confidence interval 95%)	233.65 (226.02 to 241.54)	398.60 (381.99 to 415.95)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	718
Analysis specification	Pre-specified
Analysis type	non-inferiority[111]
Parameter estimate	GMT ratio
Point estimate	1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.62
upper limit	1.8

Notes:

[111] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD2816 (4) and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 (4) on Day 29

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD2816 (4) and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 (4) on Day 29[112]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of the mean of log-transformed titre, where 'n' was the number of participants with titre information. Primary Vaccination Cohort:- AZD2816 (4) with response against B.1.351 variant is comparator group and Primary Vaccination Cohort:- AZD1222 (4) with response against the original Wuhan-Hu-1 strain is reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after first dose (Day 29)

Notes:

[112] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	361	357		
Units: 1/dilution				
geometric mean (confidence interval 95%)	433.42 (398.43 to 471.48)	364.20 (330.75 to 401.04)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using analysis of covariance (ANCOVA).

Comparison groups	Primary Vaccination Cohort:- AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	718
Analysis specification	Pre-specified
Analysis type	non-inferiority[113]
Parameter estimate	GMT ratio
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	0.96

Notes:

[113] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary

Vaccination Cohort:- AZD1222 + AZD2816 (4) and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 (4) on Day 29

End point title	GMT of SARS-CoV-2 nAb Against B.1.351 Variant Elicited by Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) and the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD1222 (4) on Day 29[114]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. GMT was calculated as antilogarithm of Σ(log base 2 transformed titre/n), i.e. as anti-logarithm transformation of mean of log-transformed titre, where 'n' was number of participants with titre information. Primary Vaccination Cohort:-AZD1222+AZD2816(4) with response against B.1.351 variant is comparator group and Primary Vaccination Cohort:-AZD1222(4) with response against the original Wuhan-Hu-1 strain is reference group. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after first dose (Day 29)

Notes:

[114] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	361	357		
Units: 1/dilution				
geometric mean (confidence interval 95%)	525.20 (481.75 to 572.58)	261.55 (240.05 to 284.97)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	718
Analysis specification	Pre-specified
Analysis type	non-inferiority[115]
Parameter estimate	GMT ratio
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	0.56

Notes:

[115] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4) on Day 29

End point title	GMT of SARS-CoV-2 nAb Against the Original Wuhan-Hu-1 Strain Elicited by Primary Vaccination Cohort:- AZD2816 (4) and Primary Vaccination Cohort:- AZD1222 (4) on Day 29[116]

End point description:

The SARS-CoV-2 nAb were measured by pseudoneutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Primary Vaccination Cohort:- AZD2816 (4) is the comparator group and Primary Vaccination Cohort:- AZD1222 (4) is the reference group, both compared for response against the original Wuhan-Hu-1 strain. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

28 days after first dose (Day 29)

Notes:

[116] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	361	357		
Units: 1/dilution				
geometric mean (confidence interval 95%)	471.69 (420.91 to 528.59)	177.02 (160.25 to 195.53)		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

The analyses were derived using ANCOVA.

Comparison groups	Primary Vaccination Cohort:- AZD2816 (4) v Primary Vaccination Cohort:- AZD1222 (4)
Number of subjects included in analysis	718
Analysis specification	Pre-specified
Analysis type	non-inferiority[117]
Parameter estimate	GMT ratio
Point estimate	0.38

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	0.44

Notes:

[117] - Noninferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMT ratio of the comparator group and reference group was > 0.67.

Secondary: GMT of ChAdOx1 nAb in Primary Vaccination Cohorts and Following a Booster Dose of AZD2816

End point title	GMT of ChAdOx1 nAb in Primary Vaccination Cohorts and Following a Booster Dose of AZD2816[118]

End point description:

Chimpanzee adenovirus Ox1 (ChAdOx1) vector nAb were measured by neutralisation assay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohorts: 28 days after booster dose (Day 29) and Primary Vaccination Cohorts: 28 days after the second dose (Day 57 for 4-week dosing interval cohorts and Day 113 for 12-week dosing interval cohort)

Notes:

[118] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)	Primary Vaccination Cohort:- AZD2816 (12)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	232	225	217	7
Units: 1/dilution				
geometric mean (confidence interval 95%)	2369.38 (2165.69 to 2592.23)	1640.99 (1510.43 to 1782.83)	1656.53 (1529.80 to 1793.75)	2082.82 (787.88 to 5506.10)

End point values	Booster Cohort:- AZD1222:AZD2816	Booster Cohort:- mRNA:AZD2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	320	277		
Units: 1/dilution				
geometric mean (confidence interval 95%)	3830.85 (3574.28 to 4105.83)	811.44 (721.11 to 913.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Seroresponse of ChAdOx1 nAb in Primary Vaccination Cohorts and Following a Booster Dose of AZD2816

End point title	Percentage of Participants With Seroresponse of ChAdOx1 nAb in Primary Vaccination Cohorts and Following a Booster Dose of AZD2816[119]

End point description:

Chimpanzee adenovirus Ox1 vector nAb were measured by neutralisation assay. Seroresponse was defined as >= 4-fold increase in the GMT of nAb from baseline. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohorts: 28 days after booster dose (Day 29) and Primary Vaccination Cohorts: 28 days after the second dose (Day 57 for 4-week dosing interval cohorts and Day 113 for 12-week dosing interval cohort)

Notes:

[119] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)	Primary Vaccination Cohort:- AZD2816 (12)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	227	224	209	7
Units: Percentage of participants				
number (confidence interval 95%)	89.43 (84.68 to 93.11)	93.30 (89.20 to 96.20)	91.39 (86.73 to 94.82)	85.71 (42.13 to 99.64)

End point values	Booster Cohort:- AZD1222:AZD2816	Booster Cohort:- mRNA:AZD2816		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	319	275		
Units: Percentage of participants				
number (confidence interval 95%)	62.07 (56.50 to 67.42)	87.64 (83.15 to 91.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMT of SARS-CoV-2 Spike Protein Binding Antibodies in Primary Vaccination Cohorts and Booster Cohorts

End point title	GMT of SARS-CoV-2 Spike Protein Binding Antibodies in Primary Vaccination Cohorts and Booster Cohorts

End point description:

The SARS-CoV-2 spike (S)-protein binding antibodies were measured by multiplexed immunoassay. The GMT was calculated as the antilogarithm of Σ(log base 2 transformed titre/n), i.e. as the anti-logarithm transformation of the mean of the log-transformed titre, where 'n' was the number of participants with titre information. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohorts: 28 days after booster dose (Day 29) and Primary Vaccination Cohorts: 28 days after the second dose (Day 57 for 4-week dosing interval cohorts and Day 113 for 12-week dosing interval cohort)

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)	Primary Vaccination Cohort:- AZD2816 (12)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	347	341	333	157
Units: 1/dilution				
geometric mean (confidence interval 95%)				
B.1.351	28618.30 (25758.25 to 31795.92)	29325.20 (26677.38 to 32235.81)	23119.62 (20524.01 to 26043.50)	43047.62 (37018.88 to 50058.17)
Wuhan-Hu-1	59332.38 (53222.73 to 66143.39)	21570.78 (19701.94 to 23616.89)	38145.52 (33713.61 to 43160.03)	25672.89 (21953.82 to 30021.99)

End point values	Booster Cohort:- AZD1222:AZD1222	Booster Cohort:- AZD1222:AZD2816	Booster Cohort:- mRNA:AZD1222	Booster Cohort:- mRNA:AZD2816

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	329	320	279	279
Units: 1/dilution				
geometric mean (confidence interval 95%)				
B.1.351	14382.37 (13365.31 to 15476.82)	16561.93 (15630.53 to 17548.83)	45587.11 (42653.03 to 48723.02)	65705.69 (62446.19 to 69135.33)
Wuhan-Hu-1	34214.45 (31691.34 to 36938.43)	29254.7 (27650.20 to 30952.30)	106061.18 (98649.55 to 114029.66)	113358.29 (107769.93 to 119236.43)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Seroresponse of SARS-CoV-2 Spike Protein Binding Antibodies in Primary Vaccination Cohorts and Booster Cohorts

End point title	Percentage of Participants With Seroresponse of SARS-CoV-2 Spike Protein Binding Antibodies in Primary Vaccination Cohorts and Booster Cohorts

End point description:

The SARS-CoV-2 S-protein binding antibodies were measured by multiplexed immunoassay. Seroresponse was defined as >= 4-fold increase in the GMT of S-protein binding antibodies from baseline. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohorts: 28 days after booster dose (Day 29) and Primary Vaccination Cohorts: 28 days after the second dose (Day 57 for 4-week dosing interval cohorts and Day 113 for 12-week dosing interval cohort)

End point values	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)	Primary Vaccination Cohort:- AZD2816 (12)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	345	341	333	156
Units: Percentage of participants				
number (confidence interval 95%)				
B.1.351	97.10 (94.73 to 98.60)	97.36 (95.05 to 98.79)	93.99 (90.88 to 96.29)	98.08 (94.48 to 99.60)
Wuhan-Hu-1	97.68 (95.48 to 98.99)	95.01 (92.14 to 97.07)	94.29 (91.23 to 96.53)	96.15 (91.82 to 98.58)

End point values	Booster	Booster	Booster	Booster

	Cohort:-AZD1222:AZD1222	Cohort:-AZD1222:AZD2816	Cohort:-mRNA:AZD1222	Cohort:-mRNA:AZD2816
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	329	320	279	278
Units: Percentage of participants				
number (confidence interval 95%)				
B.1.351	70.82 (65.58 to 75.68)	75.94 (70.87 to 80.52)	30.47 (25.12 to 36.23)	51.08 (45.04 to 57.10)
Wuhan-Hu-1	67.78 (62.44 to 72.80)	64.69 (59.18 to 69.92)	36.56 (30.90 to 42.51)	41.01 (35.17 to 47.04)

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation Between ChAdOx1 nAb and SARS-CoV-2 nAb Titres

End point title	Correlation Between ChAdOx1 nAb and SARS-CoV-2 nAb Titres

End point description:

The SARS-CoV-2 nAb and ChAdOx1 vector nAb were measured by pseudoneutralisation assay. Correlations were based on log2 titre values and assessed by using Spearman rank correlation for all cohorts except Primary Vaccination Cohort:-AZD2816(12) for which Pearson correlation was used. Correlation coefficient is reported in values from +1 to -1 (+1=perfect association, 0=no association, and -1=perfect negative association). The closer the correlation coefficient is to zero, weaker the association. Seronegative immunogenicity analysis set: all participants who received at least 1 dose of study treatment, had baseline and post-dose antibody measurements, at least 1 post-dose quantifiable serum titre, and no protocol deviations judged to have potential to interfere with the antibody response, were analysed according to treatment actually received, and were seronegative at baseline. The number of subjects analyzed denotes those participants who were evaluable at the specified time frame.

End point type	Secondary

End point timeframe:

Booster Cohorts: 28 days after booster dose (Day 29) and Primary Vaccination Cohorts: 28 days after the second dose (Day 57 for 4-week dosing interval cohorts and Day 113 for 12-week dosing interval cohort)

End point values	Primary Vaccination Cohort:-AZD1222 (4)	Primary Vaccination Cohort:-AZD2816 (4)	Primary Vaccination Cohort:-AZD1222 + AZD2816 (4)	Primary Vaccination Cohort:-AZD2816 (12)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	232	225	217	7
Units: Correlation coefficient				
number (confidence interval 95%)				
B.1.351	-0.1656 (-0.29 to -0.04)	-0.0536 (-0.18 to 0.08)	-0.0783 (-0.21 to 0.06)	0.0253 (-0.74 to 0.76)
Wuhan-Hu-1	-0.1263 (-0.25 to 0.00)	0.0006 (-0.13 to 0.13)	-0.0162 (-0.15 to 0.12)	-0.1460 (-0.81 to 0.69)

End point values	Booster Cohort:-AZD1222:AZD1222	Booster Cohort:-AZD1222:AZD2816	Booster Cohort:-mRNA:AZD1222	Booster Cohort:-mRNA:AZD2816
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	327	320	275	277
Units: Correlation coefficient				
number (confidence interval 95%)				
B.1.351	0.2061 (0.10 to 0.31)	0.2297 (0.12 to 33)	0.0225 (-0.10 to 0.14)	-0.0591 (-0.18 to 0.06)
Wuhan-Hu-1	0.1288 (0.02 to 0.23)	0.1583 (0.05 to 0.26)	0.0005 (-0.12 to 0.12)	-0.0534 (-0.17 to 0.06)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During the 6 months follow-up period after vaccination (vaccines administered on Days 1 and 29 or Day 85 [only for primary vaccination cohorts])

Adverse event reporting additional description:

Safety analysis set included all participants who received at least 1 dose of study treatment and were analysed according to the treatment actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Primary Vaccination Cohort:- AZD1222 (4)

Reporting group description:

Previously unvaccinated participants received IM AZD1222 5*10^10 vp on Days 1 and 29 (4-week dosing interval).

Reporting group title	Primary Vaccination Cohort:- AZD2816 (4)

Reporting group description:

Previously unvaccinated participants received IM AZD2816 5*10^10 vp on Days 1 and 29 (4-week dosing interval).

Reporting group title	Booster Cohort:- AZD1222:AZD1222

Reporting group description:

Participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD1222 5*10^10 vp on Day 1.

Reporting group title	Booster Cohort:- AZD1222:AZD2816

Reporting group description:

Participants, who previously received 2 doses of AZD1222 vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.

Reporting group title	Booster Cohort:- mRNA:AZD1222

Reporting group description:

Participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD1222 5*10^10 vp on Day 1.

Reporting group title	Booster Cohort:- mRNA:AZD2816

Reporting group description:

Participants, who previously received 2 doses of approved mRNA based vaccine according to the authorized dose and dosing regimen, with second dose administered at least 90 days prior to study treatment, received booster dose of IM AZD2816 5*10^10 vp on Day 1.

Reporting group title	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)

Reporting group description:

Previously unvaccinated participants received IM AZD1222 5*10^10 vp on Day 1 and IM AZD2816 5*10^10 vp on Day 29 (4-week dosing interval).

Reporting group title	Primary Vaccination Cohort:- AZD2816 (12)

Reporting group description:

Previously unvaccinated participants received IM AZD2816 5*10^10 vp on Days 1 and 85 (12-week dosing interval).

Serious adverse events	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)	Booster Cohort:- AZD1222:AZD1222
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 409 (0.73%)	3 / 413 (0.73%)	6 / 373 (1.61%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma1			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	1 / 373 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			

subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	1 / 373 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 409 (0.24%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 409 (0.00%)	1 / 413 (0.24%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 409 (0.24%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute coronary syndrome			
subjects affected / exposed	0 / 409 (0.00%)	1 / 413 (0.24%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Bell's palsy			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	1 / 373 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic neuropathy			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	1 / 373 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglossal nerve paralysis			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	1 / 373 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 409 (0.00%)	1 / 413 (0.24%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Small intestinal obstruction			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	1 / 373 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	1 / 373 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Chronic kidney disease			

subjects affected / exposed	0 / 409 (0.00%)	1 / 413 (0.24%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 409 (0.00%)	1 / 413 (0.24%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph node tuberculosis			
subjects affected / exposed	1 / 409 (0.24%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubo-ovarian abscess			
subjects affected / exposed	0 / 409 (0.00%)	0 / 413 (0.00%)	0 / 373 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Booster Cohort:-	Booster Cohort:-	Booster Cohort:-

	AZD1222:AZD2816	mRNA:AZD1222	mRNA:AZD2816
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 375 (2.13%)	3 / 322 (0.93%)	5 / 323 (1.55%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 375 (0.00%)	1 / 322 (0.31%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	1 / 375 (0.27%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			
subjects affected / exposed	1 / 375 (0.27%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Rectal adenocarcinoma1			
subjects affected / exposed	0 / 375 (0.00%)	1 / 322 (0.31%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 375 (0.27%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			

subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute coronary syndrome			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	1 / 323 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	1 / 323 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	1 / 323 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Bell's palsy			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	1 / 375 (0.27%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic neuropathy			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglossal nerve paralysis			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 375 (0.27%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Small intestinal obstruction			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			
subjects affected / exposed	1 / 375 (0.27%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 375 (0.27%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	1 / 323 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	1 / 323 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Chronic kidney disease			

subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	1 / 323 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph node tuberculosis			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 375 (0.27%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 375 (0.00%)	0 / 322 (0.00%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubo-ovarian abscess			
subjects affected / exposed	0 / 375 (0.00%)	1 / 322 (0.31%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Primary Vaccination	Primary Vaccination	

	Cohort:- AZD1222 + AZD2816 (4)	Cohort:- AZD2816 (12)	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 411 (1.22%)	2 / 208 (0.96%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma1			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			

subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 411 (0.24%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			

subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Bell's palsy			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglossal nerve paralysis			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 411 (0.24%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Small intestinal obstruction			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 411 (0.24%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 411 (0.24%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Chronic kidney disease			

subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	1 / 411 (0.24%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph node tuberculosis			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	0 / 411 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 411 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubo-ovarian abscess			
subjects affected / exposed	0 / 411 (0.00%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Primary Vaccination Cohort:- AZD1222 (4)	Primary Vaccination Cohort:- AZD2816 (4)	Booster Cohort:- AZD1222:AZD1222
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 409 (7.82%)	42 / 413 (10.17%)	39 / 373 (10.46%)
Infections and infestations			
COVID-19			
subjects affected / exposed	32 / 409 (7.82%)	42 / 413 (10.17%)	39 / 373 (10.46%)
occurrences (all)	32	42	39

Non-serious adverse events	Booster Cohort:- AZD1222:AZD2816	Booster Cohort:- mRNA:AZD1222	Booster Cohort:- mRNA:AZD2816
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 375 (9.87%)	25 / 322 (7.76%)	27 / 323 (8.36%)
Infections and infestations			
COVID-19			
subjects affected / exposed	37 / 375 (9.87%)	25 / 322 (7.76%)	27 / 323 (8.36%)
occurrences (all)	37	26	27

Non-serious adverse events	Primary Vaccination Cohort:- AZD1222 + AZD2816 (4)	Primary Vaccination Cohort:- AZD2816 (12)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 411 (10.22%)	30 / 208 (14.42%)	
Infections and infestations			
COVID-19			
subjects affected / exposed	42 / 411 (10.22%)	30 / 208 (14.42%)	
occurrences (all)	42	30	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 June 2021	Addition of 2 treatment arms: 1) AZD1222 as a single booster vaccination in participants previously vaccinated with an mRNA Coronavirus disease 2019 vaccine and 2) heterologous vaccination with AZD1222 plus AZD2816 in previously unvaccinated participants. Further definition of analysis sets. Addition of thrombotic events with thrombocytopenia as a discontinuation criteria.
29 July 2021	Added an additional interim analysis to evaluate immunogenicity in a subset of AZD1222 previously vaccinated subjects boosted with AZD1222 or AZD2816. Revised Objectives/Endpoints from descriptive to comparative, with ranking of primary, key secondary, other secondary, and exploratory objectives. Added non-inferiority margins to primary analysis and added additional participants to maintain power.
11 October 2021	Removed the age cap regarding the previously unvaccinated cohort. Revised the primary and key secondary noninferiority analyses of the previously vaccinated cohort to include historical controls, and include the statistical approach to be used.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Since different assays were used between strains and also within same strains between this study and historical control study D8110C00001, spike protein binding antibody results were summarised descriptively; no comparative analyses were conducted.

Notes: