Clinical trial results:
A Phase 3, Randomized, Observer-Blind Study to Evaluate the Safety, Tolerability, and Immunogenicity of Multiple Production LOTS and Dose Levels of The Vaccine Candidate BNT162b2 Against COVID-19 in Healthy Participants 12 Through 50Years of Age and the Safety, Tolerability, and Immunogenicity of BNT162b2 RNA-Based COVID-19 Vaccine Candidates as a Booster Dose in Healthy Participants 18 Through 50Years of Age

Summary

EudraCT number	2021-005903-11
Trial protocol	Outside EU/EEA
Global end of trial date	22 July 2021

Results information

Result version number	v2 (current)
This version publication date	07 January 2023
First version publication date	06 February 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	C4591017

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04713553
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BioNTech SE
Sponsor organisation address	An der Goldgrube 12, Mainz, Germany, 55131
Public contact	BioNTech clinical trials patient information, BioNTech SE, +49 6131 90840, patients@biontech.de
Scientific contact	BioNTech clinical trials patient information, BioNTech SE, +49 6131 90840, patients@biontech.de

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1) To demonstrate that the immune responses induced by BNT162b2 are similar across the 3 US lots (Arms 1, 2, and 3) in subjects without evidence of SARS CoV-2 infection during the study. 2) To demonstrate that the immune response induced by the EU lot (Arm 4) of BNT162b2 is similar to the pooled US lots (Arms 1, 2, and 3) in subjects without evidence of SARS-CoV-2 infection during the study. 3) To demonstrate the non-inferiority of the immune response to BNT162b2 in subjects receiving 20 microgram (mcg) compared to subjects receiving the standard 30 mcg dose (prepared from the same manufacturing lot) without evidence of SARS-CoV-2 infection during the study. 4) To evaluate the safety of BNT162b2 when administered on a 2-dose schedule in healthy subjects 12 through 50 years of age.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 February 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	United States: 1573
Worldwide total number of subjects	1573
EEA total number of subjects	0

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	445
Adults (18-64 years)	1128
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in two parts: primary study and booster study.

Pre-assignment

Screening details:

Total number of subjects enrolled in study and assigned to study intervention were 1574, however, only 1573 subjects received study intervention (1 subject was excluded for not meeting inclusion criteria).

Period 1

Period 1 title	Primary Study (2 Months)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	BNT162b2 30 mcg: US Lot 1

Arm description:

Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 1) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Arm type	Experimental
Investigational medicinal product name	BNT162b2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received BNT162b2 30 mcg single dose vaccine at Visit 1 and 2 separated by 21 days.

Arm title	BNT162b2 30 mcg: US Lot 2

Arm description:

Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 2) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Arm type	Experimental
Investigational medicinal product name	BNT162b2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received BNT162b2 30 mcg single dose vaccine at Visit 1 and 2 separated by 21 days.

Arm title	BNT162b2 30 mcg: US Lot 3

Arm description:

Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 3) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Arm type	Experimental

Investigational medicinal product name	BNT162b2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received BNT162b2 30 mcg single dose vaccine at Visit 1 and 2 separated by 21 days.

Arm title	BNT162b2 30 mcg: EU Lot

Arm description:

Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (EU Lot) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Arm type	Experimental
Investigational medicinal product name	BNT162b2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received BNT162b2 30 mcg single dose vaccine at Visit 1 and 2 separated by 21 days.

Arm title	BNT162b2 20 mcg: US Lot 1

Arm description:

Subjects were randomised in primary study to receive 20 mcg intramuscular dose of BNT162b2 vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Arm type	Experimental
Investigational medicinal product name	BNT162b2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received BNT162b2 20 mcg single dose vaccine at Visit 1 and 2 separated by 21 days.

Number of subjects in period 1	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: US Lot 3
Started	351	352	346
Completed	347	346	344
Not completed	4	6	2
Consent withdrawn by subject	2	3	-
Not specified	1	2	-
Lost to follow-up	1	1	2
Withdrawal by parent/guardian	-	-	-

Number of subjects in period 1	BNT162b2 30 mcg: EU Lot	BNT162b2 20 mcg: US Lot 1
Started	173	351
Completed	171	349
Not completed	2	2

Consent withdrawn by subject	-	1
Not specified	-	1
Lost to follow-up	1	-
Withdrawal by parent/guardian	1	-

Period 2

Period 2 title	Booster Study (1 Month)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	BNT162b2 30 mcg: Booster Dose

Arm description:

Subjects who received 2 doses of 30 mcg BNT162b2 vaccine in primary study from US Lot 1 were randomised to booster study to receive a single 30 mcg intramuscular dose of BNT162b2 vaccine at 3 months after second dose in the primary study. Subjects were followed up for safety for up to 28-35 days after vaccination.

Arm type	Experimental
Investigational medicinal product name	BNT162b2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received BNT162b2 30 mcg single dose vaccine at Visit 4.

Arm title	BNT162b2.B.1.351 30 mcg: Booster Dose

Arm description:

Subjects who received 2 doses of 30 mcg BNT162b2 vaccine in primary study from US Lot 1, 2 or 3 were randomised to booster study to receive a single 30 mcg intramuscular dose of BNT162b2.B.1.351 vaccine at 3 months after second dose in the primary study. Subjects were followed up for safety for up to 28-35 days after vaccination.

Arm type	Experimental
Investigational medicinal product name	BNT162b2.B.1.351
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received BNT162b2.B.1.351 30 mcg single dose vaccine at Visit 4.

Number of subjects in period 2	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose
Started	31	31
Completed	31	31

Baseline characteristics

Reporting groups	
Reporting group title	BNT162b2 30 mcg: US Lot 1
Reporting group description:	
Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 1) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.	
Reporting group title	BNT162b2 30 mcg: US Lot 2
Reporting group description:	
Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 2) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.	
Reporting group title	BNT162b2 30 mcg: US Lot 3
Reporting group description:	
Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 3) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.	
Reporting group title	BNT162b2 30 mcg: EU Lot
Reporting group description:	
Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (EU Lot) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.	
Reporting group title	BNT162b2 20 mcg: US Lot 1
Reporting group description:	
Subjects were randomised in primary study to receive 20 mcg intramuscular dose of BNT162b2 vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.	

Reporting group values	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: US Lot 3
Number of subjects	351	352	346
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)	99	96	101
Adults (18-64 years)	252	256	245
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	28.0	27.8	27.5
standard deviation	± 11.66	± 11.76	± 11.54
Sex: Female, Male Units: Subjects			
Female	177	176	159
Male	174	176	187

Race Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	36	48	40
Native Hawaiian or Other Pacific Islander	1	1	1
Black or African American	21	16	15
White	286	280	283
More than one race	6	5	5
Unknown or Not Reported	1	1	1
Ethnicity Units: Subjects			
Hispanic or Latino	44	32	55
Not Hispanic or Latino	306	319	291
Unknown or Not Reported	1	1	0

Reporting group values	BNT162b2 30 mcg: EU Lot	BNT162b2 20 mcg: US Lot 1	Total
Number of subjects	173	351	1573
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)	48	101	445
Adults (18-64 years)	125	250	1128
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	27.7	27.5	
standard deviation	± 11.40	± 11.71	-
Sex: Female, Male Units: Subjects			
Female	83	163	758
Male	90	188	815
Race Units: Subjects			
American Indian or Alaska Native	0	3	5
Asian	24	44	192
Native Hawaiian or Other Pacific Islander	0	2	5
Black or African American	2	14	68
White	142	283	1274
More than one race	4	5	25
Unknown or Not Reported	1	0	4
Ethnicity Units: Subjects			
Hispanic or Latino	22	42	195

Not Hispanic or Latino	151	309	1376
Unknown or Not Reported	0	0	2

End points

End points reporting groups

Reporting group title	BNT162b2 30 mcg: US Lot 1

Reporting group description:

Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 1) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Reporting group title	BNT162b2 30 mcg: US Lot 2

Reporting group description:

Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 2) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Reporting group title	BNT162b2 30 mcg: US Lot 3

Reporting group description:

Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 3) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Reporting group title	BNT162b2 30 mcg: EU Lot

Reporting group description:

Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (EU Lot) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Reporting group title	BNT162b2 20 mcg: US Lot 1

Reporting group description:

Subjects were randomised in primary study to receive 20 mcg intramuscular dose of BNT162b2 vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Reporting group title	BNT162b2 30 mcg: Booster Dose

Reporting group description:

Subjects who received 2 doses of 30 mcg BNT162b2 vaccine in primary study from US Lot 1 were randomised to booster study to receive a single 30 mcg intramuscular dose of BNT162b2 vaccine at 3 months after second dose in the primary study. Subjects were followed up for safety for up to 28-35 days after vaccination.

Reporting group title	BNT162b2.B.1.351 30 mcg: Booster Dose

Reporting group description:

Subjects who received 2 doses of 30 mcg BNT162b2 vaccine in primary study from US Lot 1, 2 or 3 were randomised to booster study to receive a single 30 mcg intramuscular dose of BNT162b2.B.1.351 vaccine at 3 months after second dose in the primary study. Subjects were followed up for safety for up to 28-35 days after vaccination.

Subject analysis set title	Pooled US Lots
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 1 + US Lot 2 + US Lot 3) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Subject analysis set title	BNT162b2; Arm 3 (US Lot 3)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 3) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Primary: Geometric Mean Ratios (GMRs) of Full-Length S-Binding Immunoglobulin G (IgG) Concentrations Between Individual US Lots 1, 2, and 3 at 1 Month After Dose 2: Primary Study

End point title	Geometric Mean Ratios (GMRs) of Full-Length S-Binding Immunoglobulin G (IgG) Concentrations Between Individual US Lots 1, 2, and 3 at 1 Month After Dose 2: Primary Study[1]

End point description:

Geometric mean concentration (GMC) of full-length S-binding IgG level for individual US lots (US lots 1, 2, and 3) was determined and reported in the descriptive section. Assay results below the lower limit of quantitation (LLOQ) were set to 0.5*LLOQ. GMRs were reported in the statistical analysis section and was calculated as ratio of GMCs of individual US Lots BNT162b2 30 mcg: US Lot 1, BNT162b2 30 mcg: US Lot 2 and BNT162b2 30 mcg: US Lot 3. Evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, with Dose 2 received within predefined window, had at least 1 valid immunogenicity result from blood sample collected within an appropriate window at 1 month after Dose 2, were negative for both SARS-CoV-2 test (RT-PCR and N-blinding antibody) during study and had no other protocol deviations determined by clinician. Here, "N"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Month after Dose 2

Notes:

[1] - 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: Statistical Analysis was not planned for this endpoint

End point values	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: US Lot 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	324	311	310	
Units: Unit per milliliter				
geometric mean (confidence interval 95%)	6299.5 (5835.4 to 6800.5)	6231.9 (5763.7 to 6738.2)	6774.8 (6264.9 to 7326.1)	

Statistical analyses

Statistical analysis title	US Lot 1 vs US Lot 2

Statistical analysis description:

GMRs and corresponding 2-sided 95% CIs were calculated by exponentiating difference in LS means and corresponding CIs based on analysis of logarithmically transformed assay results using a linear regression model with terms of age and vaccine group.

Comparison groups	BNT162b2 30 mcg: US Lot 2 v BNT162b2 30 mcg: US Lot 1
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	equivalence[2]
Parameter estimate	Geometric mean ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.13

Notes:

[2] - Equivalence was to be achieved if the 2-sided 95% confidence interval (CI) for GMR falls within the interval (0.67, 1.5).

Statistical analysis title	US Lot 2 vs US Lot 3

Statistical analysis description:

GMRs and corresponding 2-sided 95% CIs were calculated by exponentiating difference in LS means and corresponding CIs based on analysis of logarithmically transformed assay results using a linear regression model with terms of age and vaccine group.

Comparison groups	BNT162b2 30 mcg: US Lot 2 v BNT162b2 30 mcg: US Lot 3
Number of subjects included in analysis	621
Analysis specification	Pre-specified
Analysis type	equivalence[3]
Parameter estimate	Geometric mean ratio
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.03

Notes:

[3] - Equivalence was to be achieved if the 2-sided 95% CI for GMR falls within the interval (0.67, 1.5).

Statistical analysis title	US Lot 1 vs US Lot 3

Statistical analysis description:

GMRs and corresponding 2-sided 95% CIs were calculated by exponentiating difference in LS means and corresponding CIs based on analysis of logarithmically transformed assay results using a linear regression model with terms of age and vaccine group.

Comparison groups	BNT162b2 30 mcg: US Lot 1 v BNT162b2 30 mcg: US Lot 3
Number of subjects included in analysis	634
Analysis specification	Pre-specified
Analysis type	equivalence[4]
Parameter estimate	Geometric mean ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.04

Notes:

[4] - Equivalence was to be achieved if the 2-sided 95% CI for GMR falls within the interval (0.67, 1.5).

Primary: Geometric Mean Ratios (GMRs) of Full-Length S-Binding IgG Concentrations Between EU Lot and Pooled US Lots at 1 Month After Dose 2: Primary Study

End point title	Geometric Mean Ratios (GMRs) of Full-Length S-Binding IgG Concentrations Between EU Lot and Pooled US Lots at 1 Month After Dose 2: Primary Study[5]

End point description:

GMC of full-length S-binding IgG level for EU lot and pooled US lots (BNT162b2 30 mcg: US Lot 1, BNT162b2 30 mcg: US Lot 2 and BNT162b2 30 mcg: US Lot 3 reporting arm) were determined and reported in the descriptive section. Assay results below the LLOQ were set to 0.5*LLOQ. GMRs were reported in the statistical analysis section and was calculated as ratios of GMCs of BNT162b2 30 mcg: EU Lot and pooled US Lots (BNT162b2 30 mcg: US Lot 1, BNT162b2 30 mcg: US Lot 2 and BNT162b2 30 mcg: US Lot 3 reporting arm). Evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, with Dose 2 received within predefined window, had at least 1 valid immunogenicity result from blood sample collected within an appropriate window at 1 month after Dose 2, were negative for both SARS-CoV-2 test (RT-PCR and N-blinding antibody) during study and had no other protocol deviations determined by clinician. Here, "N"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Month after Dose 2

Notes:

[5] - 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: Statistical Analysis was not planned for this endpoint

End point values	BNT162b2 30 mcg: EU Lot	Pooled US Lots		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	160	945		
Units: Unit per milliliter				
geometric mean (confidence interval 95%)	6098.6 (5474.7 to 6793.7)	6428.8 (6149.5 to 6720.7)		

Statistical analyses

Statistical analysis title	EU Lot vs Pooled US Lots

Statistical analysis description:

GMRs and corresponding 2-sided 95% CIs were calculated by exponentiating difference in LS means and corresponding CIs based on analysis of logarithmically transformed assay results using a linear regression model with terms of age and vaccine group.

Comparison groups	BNT162b2 30 mcg: EU Lot v Pooled US Lots
Number of subjects included in analysis	1105
Analysis specification	Pre-specified
Analysis type	equivalence[6]
Parameter estimate	Geometric mean ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.07

Notes:

[6] - Equivalence was to be achieved if the 2-sided 95% CI for GMR falls within the interval (0.67, 1.5).

Primary: Geometric Mean Ratios (GMRs) of SARS-CoV-2 Neutralizing Titers Between 20-microgram Dose and 30-microgram Dose at 1 Month After Dose 2: Primary Study

End point title	Geometric Mean Ratios (GMRs) of SARS-CoV-2 Neutralizing Titers Between 20-microgram Dose and 30-microgram Dose at 1 Month After Dose 2: Primary Study[7]

End point description:

Geometric mean titer for SARS-CoV-2 neutralizing titers for 20 mcg dose and 30 mcg dose of US Lot 1 was determined and reported in descriptive section. GMTs and 2-sided 95% CIs were calculated by exponentiating LS mean of titers and corresponding CIs based on linear regression model. Assay results below LLOQ were set to 0.5*LLOQ. GMRs were reported in the statistical analysis section and were calculated as the ratio of geometric mean titer of the 20-mcg dose (US Lot 1) to the geometric mean titer of the 30 mcg dose (US Lot 1). Evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, with Dose 2 received within predefined window, had at least 1 valid immunogenicity result from blood sample collected within an appropriate window at 1 month after Dose 2, were negative for both SARS-CoV-2 test (RT-PCR and N-blinding antibody) during study and had no other protocol deviations determined by clinician. Here, "N"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Month after Dose 2

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: Statistical Analysis was not planned for this endpoint

End point values	BNT162b2 30 mcg: US Lot 1	BNT162b2 20 mcg: US Lot 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	318	324		
Units: Titer				
geometric mean (confidence interval 95%)	906.3 (847.8 to 968.9)	976.6 (914.1 to 1043.4)		

Statistical analyses

Statistical analysis title	30 mcg vs 20 mcg

Statistical analysis description:

GMRs and corresponding 2-sided 95% CIs were calculated by exponentiating difference in LS means and corresponding CIs based on analysis of logarithmically transformed assay results using a linear regression model with terms of age and vaccine group.

Comparison groups	BNT162b2 30 mcg: US Lot 1 v BNT162b2 20 mcg: US Lot 1
Number of subjects included in analysis	642
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.02

Notes:

[8] - Noninferiority of the 20-µg dose to the corresponding 30-µg dose was said to be achieved if the lower limit of the 2-sided 95% CI for the GMR is >0.67.

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 1: Primary Study

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 1: Primary Study[9]

End point description:

Local reactions were collected by the subject using an electronic diary. Local reactions included redness, swelling, and pain at injection site after Dose 1. Redness, swelling, and pain at injection site after Dose 1 were reported. Safety population included all randomised subjects who received at least 1 dose of the study intervention. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after Dose 1

Notes:

[9] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: US Lot 3	BNT162b2 30 mcg: EU Lot
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	351	352	345	173
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness	1.1 (0.3 to 2.9)	2.0 (0.8 to 4.1)	2.9 (1.4 to 5.3)	2.3 (0.6 to 5.8)
Swelling	2.0 (0.8 to 4.1)	3.7 (2.0 to 6.2)	3.8 (2.0 to 6.4)	2.9 (0.9 to 6.6)
Pain at injection site	82.9 (78.6 to 86.7)	79.3 (74.6 to 83.4)	84.6 (80.4 to 88.3)	86.1 (80.1 to 90.9)

End point values	BNT162b2 20 mcg: US Lot 1	Pooled US Lots		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	351	1048		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness	2.0 (0.8 to 4.1)	2.0 (1.2 to 3.0)		
Swelling	3.4 (1.8 to 5.9)	3.1 (2.2 to 4.4)		
Pain at injection site	78.1 (73.4 to 82.3)	82.3 (79.8 to 84.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 2: Primary Study

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 2: Primary Study[10]

End point description:

Local reactions were collected by the subject using an electronic diary. Local reactions included redness, swelling, and pain at injection site after Dose 2. Redness, swelling, and pain at injection site after Dose 2 were reported. Safety population included all randomised subjects who received at least 1 dose of the study intervention. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after Dose 2

Notes:

[10] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: US Lot 3	BNT162b2 30 mcg: EU Lot
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	349	350	343	172
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness	3.7 (2.0 to 6.3)	4.0 (2.2 to 6.6)	4.4 (2.5 to 7.1)	2.9 (1.0 to 6.7)
Swelling	4.9 (2.9 to 7.7)	6.0 (3.8 to 9.0)	4.7 (2.7 to 7.5)	3.5 (1.3 to 7.4)
Pain at injection site	80.2 (75.7 to 84.3)	77.7 (73.0 to 82.0)	83.1 (78.7 to 86.9)	77.3 (70.3 to 83.4)

End point values	BNT162b2 20 mcg: US Lot 1	Pooled US Lots		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	348	1042		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness	3.2 (1.6 to 5.6)	4.0 (2.9 to 5.4)		
Swelling	3.7 (2.0 to 6.3)	5.2 (3.9 to 6.7)		
Pain at injection site	79.6 (75.0 to 83.7)	80.3 (77.8 to 82.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After any Dose: Primary Study

End point title	Percentage of Subjects With Local Reactions Within 7 Days After any Dose: Primary Study[11][12]

End point description:

Local reactions were collected by the subject using an electronic diary. Local reactions included redness, swelling, and pain at injection site after each vaccination. Redness, swelling, and pain at injection site after any dose were reported. Safety population included all randomised subjects who received at least 1 dose of the study intervention. 1 subject randomised to US Lot 1 was administered US Lot 1 for Dose 1 and US Lot 3 for Dose 2, therefore, the subject was included in both reporting groups (US Lot 1 and US Lot 3).

End point type	Primary

End point timeframe:

Within 7 days after any dose

Notes:

[11] - 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 planned for this endpoint

[12] - 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: Statistical Analysis was not planned for this endpoint

End point values	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: EU Lot	BNT162b2 20 mcg: US Lot 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	351	352	173	351
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness	4.6 (2.6 to 7.3)	5.4 (3.3 to 8.3)	4.6 (2.0 to 8.9)	4.6 (2.6 to 7.3)
Swelling	6.0 (3.7 to 9.0)	8.8 (6.1 to 12.3)	4.6 (2.0 to 8.9)	6.3 (4.0 to 9.3)
Pain at injection site	90.9 (87.4 to 93.7)	85.8 (81.7 to 89.3)	91.3 (86.1 to 95.1)	89.5 (85.8 to 92.5)

End point values	Pooled US Lots	BNT162b2; Arm 3 (US Lot 3)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1049	347		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness	5.5 (4.2 to 7.1)	6.6 (4.2 to 9.8)		
Swelling	7.3 (5.8 to 9.1)	7.2 (4.7 to 10.5)		
Pain at injection site	89.2 (87.2 to 91.0)	91.1 (87.6 to 93.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 3: Booster Study

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 3: Booster Study[13]

End point description:

Local reactions were collected by the subject using an electronic diary. Local reactions included redness, swelling, and pain at injection site after Dose 3. Redness, swelling, and pain at injection site after Dose 3 were reported. Safety population included all randomised subjects who received dose 3 of the study intervention.

End point type	Primary

End point timeframe:

Within 7 days after Dose 3

Notes:

[13] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness	9.7 (2.0 to 25.8)	3.2 (0.1 to 16.7)		
Swelling	6.5 (0.8 to 21.4)	6.5 (0.8 to 21.4)		
Pain at injection site	90.3 (74.2 to 98.0)	93.5 (78.6 to 99.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 1: Primary Study

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 1: Primary Study[14]

End point description:

Systemic events were reported using an electronic diary. Fever was defined as temperature >=38.0 degree Celsius (C) and categorised as >=38.0 to 38.4 C; >38.4 to 38.9 C; >38.9 to 40.0 C; >40.0 C. Systemic events including fever, fatigue, headache, chills, new or worsened muscle pain, new or worsened joint pain, vomiting, diarrhea, and use of antipyretic/analgesic medication after Dose 1 were reported. Safety population included all randomised subjects who received at least 1 dose of the study intervention. Here, "Overall Number of Subjects Analysed" = subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after Dose 1

Notes:

[14] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: US Lot 3	BNT162b2 30 mcg: EU Lot
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	351	352	345	173
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38.0 C	0.3 (0.0 to 1.6)	0 (0.0 to 1.0)	2.0 (0.8 to 4.1)	1.2 (0.1 to 4.1)
Fever >=38.0 C to 38.4 C	0.3 (0.0 to 1.6)	0 (0.0 to 1.0)	1.2 (0.3 to 2.9)	0.6 (0.0 to 3.2)
Fever >38.4 C to 38.9 C	0 (0.0 to 1.0)	0 (0.0 to 1.0)	0.6 (0.1 to 2.1)	0.6 (0.0 to 3.2)
Fever >38.9 C to 40.0 C	0 (0.0 to 1.0)	0 (0.0 to 1.0)	0.3 (0.0 to 1.6)	0 (0.0 to 2.1)
Fever >40.0 C	0 (0.0 to 1.0)	0 (0.0 to 1.0)	1 (0.0 to 1.1)	0 (0.0 to 2.1)
Fatigue	53.3 (47.9 to 58.6)	45.5 (40.2 to 50.8)	50.7 (45.3 to 56.1)	49.1 (41.5 to 56.8)
Headache	36.2 (31.1 to 41.5)	32.7 (27.8 to 37.8)	33.3 (28.4 to 38.6)	38.7 (31.4 to 46.4)
Chills	8.5 (5.8 to 12.0)	7.7 (5.1 to 11.0)	10.1 (7.2 to 13.8)	8.1 (4.5 to 13.2)

Vomiting	0.6 (0.1 to 2.0)	0.6 (0.1 to 2.0)	1.2 (0.3 to 2.9)	0.6 (0.0 to 3.2)
Diarrhea	9.7 (6.8 to 13.3)	8.0 (5.4 to 11.3)	7.8 (5.2 to 11.2)	9.2 (5.4 to 14.6)
New/worsened muscle pain	14.5 (11.0 to 18.7)	13.1 (9.7 to 17.0)	16.5 (12.8 to 20.9)	17.3 (12.0 to 23.8)
New/worsened joint pain	6.8 (4.4 to 10.0)	6.5 (4.2 to 9.6)	7.0 (4.5 to 10.2)	7.5 (4.1 to 12.5)
Use of antipyretic/analgesic medication	16.8 (13.0 to 21.1)	14.5 (11.0 to 18.6)	18.8 (14.9 to 23.4)	22.0 (16.0 to 28.9)

End point values	BNT162b2 20 mcg: US Lot 1	Pooled US Lots		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	351	1048		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38.0 C	0 (0.0 to 1.0)	0.8 (0.3 to 1.5)		
Fever >=38.0 C to 38.4 C	0 (0.0 to 1.0)	0.5 (0.2 to 1.1)		
Fever >38.4 C to 38.9 C	0 (0.0 to 1.0)	0.2 (0.0 to 0.7)		
Fever >38.9 C to 40.0 C	0 (0.0 to 1.0)	0.1 (0.0 to 0.5)		
Fever >40.0 C	0 (0.0 to 1.0)	0 (0.0 to 0.4)		
Fatigue	49.0 (43.7 to 54.4)	49.8 (46.7 to 52.9)		
Headache	35.6 (30.6 to 40.9)	34.1 (31.2 to 37.0)		
Chills	6.8 (4.4 to 10.0)	8.8 (7.1 to 10.7)		
Vomiting	0.9 (0.2 to 2.5)	0.8 (0.3 to 1.5)		
Diarrhea	10.0 (7.0 to 13.6)	8.5 (6.9 to 10.3)		
New/worsened muscle pain	16.2 (12.5 to 20.5)	14.7 (12.6 to 17.0)		
New/worsened joint pain	6.6 (4.2 to 9.7)	6.8 (5.3 to 8.5)		
Use of antipyretic/analgesic medication	18.2 (14.3 to 22.7)	16.7 (14.5 to 19.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 2: Primary Study

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 2: Primary Study[15]

End point description:

Systemic events were reported using an electronic diary. Fever was defined as temperature >=38.0 C and categorised as >=38.0 to 38.4 C; >38.4 to 38.9 C; >38.9 to 40.0 C; >40.0 C. Systemic events including fever, fatigue, headache, chills, new or worsened muscle pain, new or worsened joint pain, vomiting, diarrhea, and use of antipyretic/analgesic medication after Dose 2 were reported. Safety population included all randomised subjects who received at least 1 dose of the study intervention. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after Dose 2

Notes:

[15] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: US Lot 3	BNT162b2 30 mcg: EU Lot
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	349	350	343	172
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38.0 C	7.2 (4.7 to 10.4)	6.3 (4.0 to 9.4)	6.7 (4.3 to 9.9)	8.7 (5.0 to 14.0)
Fever >=38.0 C to 38.4 C	4.6 (2.6 to 7.3)	3.4 (1.8 to 5.9)	3.2 (1.6 to 5.7)	6.4 (3.2 to 11.2)
Fever >38.4 C to 38.9 C	2.0 (0.8 to 4.1)	2.0 (0.8 to 4.1)	2.3 (1.0 to 4.5)	1.2 (0.1 to 4.1)
Fever >38.9 C to 40.0 C	0.6 (0.1 to 2.1)	0.9 (0.2 to 2.5)	0.9 (0.2 to 2.5)	1.2 (0.1 to 4.1)
Fever >40.0 C	0 (0.0 to 1.1)	0 (0.0 to 1.0)	0.3 (0.0 to 1.6)	0 (0.0 to 2.1)
Fatigue	69.9 (64.8 to 74.7)	66.6 (61.4 to 71.5)	71.4 (66.3 to 76.2)	69.8 (62.3 to 76.5)
Headache	57.0 (51.6 to 62.3)	56.6 (51.2 to 61.8)	56.9 (51.4 to 62.2)	56.4 (48.6 to 63.9)
Chills	28.1 (23.4 to 33.1)	31.1 (26.3 to 36.3)	33.8 (28.8 to 39.1)	28.5 (21.9 to 35.9)
Vomiting	2.3 (1.0 to 4.5)	1.4 (0.5 to 3.3)	2.3 (1.0 to 4.5)	1.7 (0.4 to 5.0)
Diarrhea	8.3 (5.6 to 11.7)	9.1 (6.3 to 12.7)	7.9 (5.3 to 11.2)	9.3 (5.4 to 14.7)
New/worsened muscle pain	32.7 (27.8 to 37.9)	38.6 (33.4 to 43.9)	35.6 (30.5 to 40.9)	36.0 (28.9 to 43.7)
New/worsened joint pain	19.2 (15.2 to 23.7)	24.6 (20.2 to 29.4)	19.2 (15.2 to 23.8)	19.2 (13.6 to 25.9)
Use of antipyretic/analgesic medication	35.2 (30.2 to 40.5)	41.1 (35.9 to 46.5)	40.8 (35.6 to 46.2)	41.9 (34.4 to 49.6)

End point values	BNT162b2 20 mcg: US Lot 1	Pooled US Lots		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	348	1042		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38.0 C	5.7 (3.5 to 8.7)	6.7 (5.3 to 8.4)		
Fever >=38.0 C to 38.4 C	4.3 (2.4 to 7.0)	3.7 (2.7 to 5.1)		
Fever >38.4 C to 38.9 C	1.4 (0.5 to 3.3)	2.1 (1.3 to 3.2)		
Fever >38.9 C to 40.0 C	0 (0.0 to 1.1)	0.8 (0.3 to 1.5)		
Fever >40.0 C	0 (0.0 to 2.1)	0.1 (0.0 to 0.5)		
Fatigue	66.7 (61.4 to 71.6)	69.3 (66.4 to 72.1)		
Headache	50.6 (45.2 to 55.9)	56.8 (53.7 to 59.8)		
Chills	23.6 (19.2 to 28.4)	31.0 (28.2 to 33.9)		
Vomiting	1.4 (0.5 to 3.3)	2.0 (1.3 to 3.1)		

Diarrhea	6.9 (4.5 to 10.1)	8.4 (6.8 to 10.3)		
New/worsened muscle pain	35.6 (30.6 to 40.9)	35.6 (32.7 to 38.6)		
New/worsened joint pain	19.5 (15.5 to 24.1)	21.0 (18.6 to 23.6)		
Use of antipyretic/analgesic medication	37.9 (32.8 to 43.3)	39.1 (36.1 to 42.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After any Dose: Primary Study

End point title	Percentage of Subjects With Systemic Events Within 7 Days After any Dose: Primary Study[16][17]

End point description:

Systemic events were reported using an electronic diary. Fever was defined as temperature >=38.0 C and categorised as >=38.0 to 38.4 C; >38.4 to 38.9 C; >38.9 to 40.0 C; >40.0 C. Systemic events including fever, fatigue, headache, chills, new or worsened muscle pain, new or worsened joint pain, vomiting, diarrhea, and use of antipyretic/analgesic medication after any dose were reported. Safety population included all randomised subjects who received at least 1 dose of the study intervention. 1 subject randomised to US Lot 1 was administered US Lot 1 for Dose 1 and US Lot 3 for Dose 2, therefore, the subject was included in both reporting groups (US Lot 1 and US Lot 3).

End point type	Primary

End point timeframe:

Within 7 days after any dose

Notes:

[16] - 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 planned for this endpoint

[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: Statistical Analysis was not planned for this endpoint

End point values	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: EU Lot	BNT162b2 20 mcg: US Lot 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	351	352	173	351
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38.0 C	7.4 (4.9 to 10.7)	6.3 (4.0 to 9.3)	9.2 (5.4 to 14.6)	5.7 (3.5 to 8.7)
Fever >=38.0 C to 38.4 C	4.8 (2.8 to 7.6)	3.4 (1.8 to 5.9)	6.4 (3.2 to 11.1)	4.3 (2.4 to 7.0)
Fever >38.4 C to 38.9 C	2.0 (0.8 to 4.1)	2.0 (0.8 to 4.1)	1.7 (0.4 to 5.0)	1.4 (0.5 to 3.3)
Fever >38.9 C to 40.0 C	0.6 (0.1 to 2.0)	0.9 (0.2 to 2.5)	1.2 (0.1 to 4.1)	0 (0.0 to 1.0)
Fever >40.0 C	0 (0.0 to 1.0)	0 (0.0 to 1.0)	0 (0.0 to 2.1)	0 (0.0 to 1.0)
Fatigue	78.6 (74.0 to 82.8)	73.6 (68.6 to 78.1)	76.9 (69.9 to 82.9)	75.5 (70.7 to 79.9)
Headache	66.7 (61.5 to 71.6)	65.1 (59.8 to 70.0)	68.8 (61.3 to 75.6)	63.8 (58.5 to 68.9)
Chills	32.8 (27.9 to 37.9)	34.1 (29.1 to 39.3)	32.4 (25.5 to 39.9)	26.2 (21.7 to 31.1)

Vomiting	2.8 (1.4 to 5.2)	2.0 (0.8 to 4.1)	2.3 (0.6 to 5.8)	2.3 (1.0 to 4.4)
Diarrhea	16.2 (12.5 to 20.5)	14.2 (10.7 to 18.3)	15.0 (10.1 to 21.2)	15.4 (11.8 to 19.6)
New/worsened muscle pain	38.7 (33.6 to 44.1)	43.5 (38.2 to 48.8)	43.9 (36.4 to 51.7)	40.5 (35.3 to 45.8)
New/worsened joint pain	23.4 (19.0 to 28.1)	27.3 (22.7 to 32.2)	24.3 (18.1 to 31.4)	22.2 (18.0 to 26.9)
Use of antipyretic/analgesic medication medication	41.9 (36.7 to 47.2)	43.8 (38.5 to 49.1)	51.4 (43.7 to 59.1)	43.6 (38.3 to 49.0)

End point values	Pooled US Lots	BNT162b2; Arm 3 (US Lot 3)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1049	347		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38.0 C	7.3 (5.8 to 9.1)	8.4 (5.7 to 11.8)		
Fever >=38.0 C to 38.4 C	4.1 (3.0 to 5.5)	4.0 (2.2 to 6.7)		
Fever >38.4 C to 38.9 C	2.3 (1.5 to 3.4)	2.9 (1.4 to 5.2)		
Fever >38.9 C to 40.0 C	0.9 (0.4 to 1.6)	1.2 (0.3 to 2.9)		
Fever >40.0 C	0.1 (0.0 to 0.5)	0.3 (0.0 to 1.6)		
Fatigue	77.8 (75.1 to 80.3)	81.0 (76.4 to 85.0)		
Headache	65.4 (62.4 to 68.3)	64.3 (59.0 to 69.3)		
Chills	34.7 (31.8 to 37.7)	37.2 (32.1 to 42.5)		
Vomiting	2.8 (1.9 to 3.9)	3.5 (1.8 to 6.0)		
Diarrhea	14.8 (12.7 to 17.1)	13.8 (10.4 to 17.9)		
New/worsened muscle pain	41.8 (38.8 to 44.9)	43.2 (37.9 to 48.6)		
New/worsened joint pain	24.9 (22.3 to 27.6)	23.9 (19.5 to 28.8)		
Use of antipyretic/analgesic medication medication	44.0 (41.0 to 47.1)	46.4 (41.1 to 51.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 3: Booster Study

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 3: Booster Study[18]

End point description:

Systemic events were reported using an electronic diary. Fever was defined as temperature >=38.0 C and categorised as >=38.0 to 38.4 C; >38.4 to 38.9 C; >38.9 to 40.0 C; >40.0 C. Systemic events including fever, fatigue, headache, chills, new or worsened muscle pain, new or worsened joint pain, vomiting, diarrhea, and use of antipyretic/analgesic medication after Dose 3 were reported. Safety population included all randomised subjects who received dose 3 of the study intervention.

End point type	Primary

End point timeframe:

Within 7 days after Dose 3

Notes:

[18] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38.0 C	3.2 (0.1 to 16.7)	6.5 (0.8 to 21.4)		
Fever >=38.0 C to 38.4 C	0 (0.0 to 11.2)	6.5 (0.8 to 21.4)		
Fever >38.4 C to 38.9 C	3.2 (0.1 to 16.7)	0 (0.0 to 11.2)		
Fever >38.9 C to 40.0 C	0 (0.0 to 11.2)	0 (0.0 to 11.2)		
Fever >40.0 C	0 (0.0 to 11.2)	0 (0.0 to 11.2)		
Fatigue	67.7 (48.6 to 83.3)	83.9 (66.3 to 94.5)		
Headache	41.9 (24.5 to 60.9)	58.1 (39.1 to 75.5)		
Chills	25.8 (11.9 to 44.6)	19.4 (7.5 to 37.5)		
Vomiting	3.2 (0.1 to 16.7)	0 (0.0 to 11.2)		
Diarrhea	16.1 (5.5 to 33.7)	6.5 (0.8 to 21.4)		
New/worsened muscle pain	41.9 (24.5 to 60.9)	19.4 (7.5 to 37.5)		
New/worsened joint pain	12.9 (3.6 to 29.8)	12.9 (3.6 to 29.8)		
Use of antipyretic/analgesic medication	32.3 (16.7 to 51.4)	35.5 (19.2 to 54.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs) From Dose 1 to 1 Month After Dose 2: Primary Study

End point title	Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs) From Dose 1 to 1 Month After Dose 2: Primary Study[19]

End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly or that was considered to be an important medical event. Safety population included all randomised subjects who received at least 1 dose of the study intervention.

End point type	Primary

End point timeframe:

Day 1 of Dose 1 up to 1 Month after Dose 2 (for a maximum of 2 months)

Notes:

[19] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: US Lot 3	BNT162b2 30 mcg: EU Lot
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	351	352	346	173
Units: Percentage of subjects				
number (not applicable)				
AEs, n=351,352,346,173,351,1049	5.4	6.0	5.2	10.4
SAEs, n=351,352,346,173,351,1049	0	0	0.3	0.6

End point values	BNT162b2 20 mcg: US Lot 1	Pooled US Lots		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	351	1049		
Units: Percentage of subjects				
number (not applicable)				
AEs, n=351,352,346,173,351,1049	6.8	5.5		
SAEs, n=351,352,346,173,351,1049	0	0.1		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs) From Dose 3 to 1 Month After Dose 3: Booster Study

End point title	Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs) From Dose 3 to 1 Month After Dose 3: Booster Study[20]

End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly or that was considered to be an important medical event. Safety population included all randomised subjects who received dose 3 of the study intervention.

End point type	Primary

End point timeframe:

From Dose 3 to 1 Month after Dose 3 (for a maximum of 35 days)

Notes:

[20] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: Percentage of subjects				
number (not applicable)				
AEs, n=31, 31	6.5	3.2		
SAEs, n=31, 31	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of SARS-CoV-2 Reference-strain at Baseline: Booster Study

End point title	Geometric Mean Titers (GMTs) of SARS-CoV-2 Reference-strain at Baseline: Booster Study[21]

End point description:

GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline (prior to Dose 1 of Primary study)

Notes:

[21] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: Titer				
geometric mean (confidence interval 95%)	20.5 (20.5 to 20.5)	20.5 (20.5 to 20.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of SARS-CoV-2 Reference-strain 1 Month After Dose 2: Booster Study

End point title	Geometric Mean Titers (GMTs) of SARS-CoV-2 Reference-strain

	1 Month After Dose 2: Booster Study[22]

End point description:

GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Month after Dose 2 of primary study

Notes:

[22] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: Titer				
geometric mean (confidence interval 95%)	971.4 (750.5 to 1257.4)	749.0 (575.2 to 975.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of SARS-CoV-2 Reference-strain Before Dose 3: Booster Study

End point title	Geometric Mean Titers (GMTs) of SARS-CoV-2 Reference-strain Before Dose 3: Booster Study[23]

End point description:

GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Before Dose 3

Notes:

[23] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Titer				
geometric mean (confidence interval 95%)	263.5 (186.9 to 371.3)	224.2 (176.4 to 285.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of SARS-CoV-2 Reference-strain 1 Week After Dose 3: Booster Study

End point title	Geometric Mean Titers (GMTs) of SARS-CoV-2 Reference-strain 1 Week After Dose 3: Booster Study[24]

End point description:

GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Week after Dose 3

Notes:

[24] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Titer				
geometric mean (confidence interval 95%)	2159.3 (1568.4 to 2972.8)	1283.4 (939.4 to 1753.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of SARS-CoV-2 Reference-strain 1 Month After Dose 3: Booster Study

End point title	Geometric Mean Titers (GMTs) of SARS-CoV-2 Reference-strain 1 Month After Dose 3: Booster Study[25]

End point description:

GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Month after Dose 3

Notes:

[25] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Titer				
geometric mean (confidence interval 95%)	2035.5 (1502.2 to 2758.1)	943.3 (699.1 to 1272.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of SARS-CoV-2 B.1.351-strain at Baseline: Booster Study

End point title	Geometric Mean Titers (GMTs) of SARS-CoV-2 B.1.351-strain at Baseline: Booster Study[26]

End point description:

GMTs and 2-sided 95% CIs were planned to be calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Data for this endpoint was not analysed as the immunogenicity samples were not tested for SARS-CoV-2 B.1.351-strain at Baseline as the South African strain was no longer of clinical interest and required responses have been well understood from other studies.

End point type	Primary

End point timeframe:

Baseline (prior to Dose 1 of Primary study)

Notes:

[26] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[27]	0[28]		
Units: Titer				
geometric mean (confidence interval 95%)	(to)	(to)		

Notes:

[27] - Data was not analysed per Sponsor discretion.

[28] - Data was not analysed per Sponsor discretion.

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of SARS-CoV-2 B.1.351-strain 1 Month After Dose 2: Booster Study

End point title	Geometric Mean Titers (GMTs) of SARS-CoV-2 B.1.351-strain 1 Month After Dose 2: Booster Study[29]

End point description:

GMTs and 2-sided 95% CIs were planned to be calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Data for this endpoint was not analysed as the immunogenicity samples were not tested for SARS-CoV-2 B.1.351-strain at 1 month after dose 2 as the South African strain was no longer of clinical interest and required responses have been well understood from other studies.

End point type	Primary

End point timeframe:

1 Month after Dose 2 of primary study

Notes:

[29] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[30]	0[31]		
Units: Titer				
geometric mean (confidence interval 95%)	(to)	(to)		

Notes:

[30] - Data was not analysed per Sponsor discretion.

[31] - Data was not analysed per Sponsor discretion.

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of SARS-CoV-2 B.1.351-strain 1 Week After Dose 3: Booster Study

End point title	Geometric Mean Titers (GMTs) of SARS-CoV-2 B.1.351-strain 1 Week After Dose 3: Booster Study[32]

End point description:

GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 ×

LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Week after Dose 3

Notes:

[32] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Titer				
geometric mean (confidence interval 95%)	1614.1 (1172.8 to 2221.6)	1729.8 (1160.0 to 2579.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of SARS-CoV-2 B.1.351-strain Before Dose 3: Booster Study

End point title	Geometric Mean Titers (GMTs) of SARS-CoV-2 B.1.351-strain Before Dose 3: Booster Study[33]

End point description:

GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Before Dose 3

Notes:

[33] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Titer				
geometric mean (confidence interval 95%)	103.0 (75.4 to 140.8)	94.0 (67.5 to 130.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of SARS-CoV-2 B.1.351-strain 1 Month After Dose 3: Booster Study

End point title	Geometric Mean Titers (GMTs) of SARS-CoV-2 B.1.351-strain 1 Month After Dose 3: Booster Study[34]

End point description:

GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Month after Dose 3

Notes:

[34] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Titer				
geometric mean (confidence interval 95%)	1358.4 (968.5 to 1905.1)	1411.1 (950.1 to 2095.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Concentrations (GMCs) of Full-length S-binding IgG Levels at Baseline: Booster Study

End point title	Geometric Mean Concentrations (GMCs) of Full-length S-binding IgG Levels at Baseline: Booster Study[35]

End point description:

GMCs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline (prior to Dose 1 of Primary study)

Notes:

[35] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Unit per milliliter				
geometric mean (confidence interval 95%)	3.4 (2.0 to 5.7)	3.4 (2.3 to 5.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Concentrations (GMCs) of Full-length S-binding IgG Levels 1 Month After Dose 2: Booster Study

End point title	Geometric Mean Concentrations (GMCs) of Full-length S-binding IgG Levels 1 Month After Dose 2: Booster Study[36]

End point description:

GMCs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Month after Dose 2 of primary study

Notes:

[36] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Unit per milliliter				
geometric mean (confidence interval 95%)	6529.1 (5212.9 to 8177.6)	3796.9 (1899.8 to 7588.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Concentrations (GMCs) of Full-length S-binding IgG Levels Before Dose 3: Booster Study

End point title	Geometric Mean Concentrations (GMCs) of Full-length S-binding IgG Levels Before Dose 3: Booster Study[37]

End point description:

GMCs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Before Dose 3

Notes:

[37] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Unit per milliliter				
geometric mean (confidence interval 95%)	1834.5 (1458.5 to 2307.5)	1851.6 (1441.9 to 2377.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Concentrations (GMCs) of Full-length S-binding IgG Levels 1 Week After Dose 3: Booster Study

End point title	Geometric Mean Concentrations (GMCs) of Full-length S-

	binding IgG Levels 1 Week After Dose 3: Booster Study[38]

End point description:

GMCs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Week after Dose 3

Notes:

[38] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Unit per milliliter				
geometric mean (confidence interval 95%)	10756.9 (8478.9 to 13647.0)	10412.3 (7733.0 to 14020.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Concentrations (GMCs) of Full-length S-binding IgG Levels 1 Month After Dose 3: Booster Study

End point title	Geometric Mean Concentrations (GMCs) of Full-length S-binding IgG Levels 1 Month After Dose 3: Booster Study[39]

End point description:

GMCs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Month after Dose 3

Notes:

[39] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Unit per milliliter				
geometric mean (confidence interval 95%)	7983.0 (6266.0 to 10170.6)	6676.9 (5242.6 to 8503.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rises (GMFRs) in Full-length S-binding IgG Levels From 1 Month After Dose 2 to 1 Week After Dose 3: Booster Study

End point title	Geometric Mean Fold Rises (GMFRs) in Full-length S-binding IgG Levels From 1 Month After Dose 2 to 1 Week After Dose 3: Booster Study[40]

End point description:

GMFRs were defined as ratios of the geometric mean concentration of IgG at 1 week after Dose 3 to the geometric mean concentration of IgG at 1 month after dose 2. GMFRs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

From 1 Month after Dose 2 to 1 Week after Dose 3

Notes:

[40] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Fold rise				
geometric mean (confidence interval 95%)	1.6 (1.3 to 2.0)	2.7 (1.3 to 5.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rises (GMFRs) in Full-length S-binding IgG Levels From 1 Month After Dose 2 to 1 Month After Dose 3: Booster Study

End point title	Geometric Mean Fold Rises (GMFRs) in Full-length S-binding IgG Levels From 1 Month After Dose 2 to 1 Month After Dose 3: Booster Study[41]

End point description:

GMFRs were defined as ratios of the geometric mean concentration of IgG at 1 month after Dose 3 to the geometric mean concentration of IgG at 1 month after dose 2. GMFRs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

From 1 Month after Dose 2 to 1 Month after Dose 3

Notes:

[41] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Fold rise				
geometric mean (confidence interval 95%)	1.2 (1.0 to 1.5)	1.8 (0.9 to 3.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rises (GMFRs) in Full-length S-binding IgG Levels Before Dose 3 to 1 Week After Dose 3: Booster Study

End point title	Geometric Mean Fold Rises (GMFRs) in Full-length S-binding IgG Levels Before Dose 3 to 1 Week After Dose 3: Booster Study[42]

End point description:

GMFRs were defined as ratios of the geometric mean concentration of IgG at 1 week after Dose 3 to the geometric mean concentration of IgG before dose 3. GMFRs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Before Dose 3 to 1 Week after Dose 3

Notes:

[42] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Fold rise				
geometric mean (confidence interval 95%)	5.9 (4.9 to 7.0)	5.6 (4.4 to 7.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rises (GMFRs) in Full-length S-binding IgG Levels Before Dose 3 to 1 Month After Dose 3: Booster Study

End point title	Geometric Mean Fold Rises (GMFRs) in Full-length S-binding IgG Levels Before Dose 3 to 1 Month After Dose 3: Booster Study[43]

End point description:

GMFRs were defined as ratios of the geometric mean concentration of IgG at 1 month after Dose 3 to the geometric mean concentration of IgG before dose 3. GMFRs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Before Dose 3 to 1 Month after Dose 3

Notes:

[43] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Fold rise				
geometric mean (confidence interval 95%)	4.4 (3.7 to 5.2)	3.6 (2.9 to 4.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 Reference-strain From 1 Month After Dose 2 to 1 Week After Dose 3: Booster Study

End point title	Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 Reference-

	strain From 1 Month After Dose 2 to 1 Week After Dose 3: Booster Study[44]

End point description:

GMFRs were defined as ratios of the geometric mean titers of SARS-CoV-2 reference-strain at 1 week after Dose 3 to the geometric mean titers of SARS-CoV-2 reference-strain at 1 month after dose 2. GMFRs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

From 1 Month after Dose 2 to 1 Week after Dose 3

Notes:

[44] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Fold rise				
geometric mean (confidence interval 95%)	2.2 (1.6 to 3.0)	1.7 (1.3 to 2.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 Reference-strain From 1 Month After Dose 2 to 1 Month After Dose 3: Booster Study

End point title	Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 Reference-strain From 1 Month After Dose 2 to 1 Month After Dose 3: Booster Study[45]

End point description:

GMFRs were defined as ratios of the geometric mean titers of SARS-CoV-2 reference-strain at 1 month after Dose 3 to the geometric mean titers of SARS-CoV-2 reference-strain at 1 month after dose 2. GMFRs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

From 1 Month after Dose 2 to 1 Month after Dose 3

Notes:

[45] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Fold rise				
geometric mean (confidence interval 95%)	2.1 (1.6 to 2.7)	1.2 (0.9 to 1.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 Reference-strain Before Dose 3 to 1 Month After Dose 3: Booster Study

End point title	Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 Reference-strain Before Dose 3 to 1 Month After Dose 3: Booster Study[46]

End point description:

GMFRs were defined as ratios of the geometric mean titers of SARS-CoV-2 reference-strain at 1 month after Dose 3 to the geometric mean titers of SARS-CoV-2 reference-strain before dose 3. GMFRs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Before Dose 3 to 1 Month after Dose 3

Notes:

[46] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Fold rise				
geometric mean (confidence interval 95%)	7.7 (5.6 to 10.7)	4.2 (3.2 to 5.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 Reference-strain Before Dose 3 to 1 Week After Dose 3: Booster Study

End point title	Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 Reference-

	strain Before Dose 3 to 1 Week After Dose 3: Booster Study[47]

End point description:

GMFRs were defined as ratios of the geometric mean titers of SARS-CoV-2 reference-strain at 1 week after Dose 3 to the geometric mean titers of SARS-CoV-2 reference-strain before dose 3. GMFRs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Before Dose 3 to 1 Week after Dose 3

Notes:

[47] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Fold rise				
geometric mean (confidence interval 95%)	8.2 (5.3 to 12.7)	5.7 (4.5 to 7.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 B.1.351-strain From 1 Month After Dose 2 to 1 Week After Dose 3: Booster Study

End point title	Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 B.1.351-strain From 1 Month After Dose 2 to 1 Week After Dose 3: Booster Study[48]

End point description:

GMFRs were defined as ratios of the geometric mean titers of SARS-CoV-2 B.1.351-strain at 1 month after Dose 3 to the geometric mean titers of SARS-CoV-2 B.1.351-strain at 1 month after dose 2. GMFRs were planned to be calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Data for this endpoint was not analysed as the immunogenicity samples were not tested for SARS-CoV-2 B.1.351-strain at 1 month after dose 2 as the South African strain was no longer of clinical interest and required responses have been well understood from other studies.

End point type	Primary

End point timeframe:

From 1 Month after Dose 2 to 1 Week after Dose 3

Notes:

[48] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[49]	0[50]		
Units: Fold rise				
geometric mean (confidence interval 95%)	(to)	(to)		

Notes:

[49] - Data was not analysed per Sponsor discretion.

[50] - Data was not analysed per Sponsor discretion.

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 B.1.351-strain From 1 Month After Dose 2 to 1 Month After Dose 3: Booster Study

End point title	Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 B.1.351-strain From 1 Month After Dose 2 to 1 Month After Dose 3: Booster Study[51]

End point description:

GMFRs were defined as ratios of the geometric mean titers of SARS-CoV-2 B.1.351-strain at 1 month after Dose 3 to the geometric mean titers of SARS-CoV-2 B.1.351-strain at 1 month after dose 2. GMFRs were planned to be calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Data for this endpoint was not analysed as the immunogenicity samples were not tested for SARS-CoV-2 B.1.351-strain at 1 month after dose 2 as the South African strain was no longer of clinical interest and required responses have been well understood from other studies.

End point type	Primary

End point timeframe:

From 1 Month after Dose 2 to 1 Month after Dose 3

Notes:

[51] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[52]	0[53]		
Units: Fold rise				
geometric mean (confidence interval 95%)	(to)	(to)		

Notes:

[52] - Data was not analysed per Sponsor discretion.

[53] - Data was not analysed per Sponsor discretion.

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 B.1.351-strain Before Dose 3 to 1 Week After Dose 3: Booster Study

End point title	Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 B.1.351-strain Before Dose 3 to 1 Week After Dose 3: Booster Study[54]

End point description:

GMFRs were defined as ratios of the geometric mean titers of SARS-CoV-2 B.1.351-strain at 1 week after Dose 3 to the geometric mean titers of SARS-CoV-2 B.1.351-strain before dose 3. GMFRs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analyzed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Before Dose 3 to 1 Week after Dose 3

Notes:

[54] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Fold rise				
geometric mean (confidence interval 95%)	15.7 (11.2 to 22.0)	18.4 (13.8 to 24.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 B.1.351-strain Before Dose 3 to 1 Month After Dose 3: Booster Study

End point title	Geometric Mean Fold Rise (GMFRs) in SARS-CoV-2 B.1.351-strain Before Dose 3 to 1 Month After Dose 3: Booster Study[55]

End point description:

GMFRs were defined as ratios of the geometric mean titers of SARS-CoV-2 B.1.351-strain at 1 month after Dose 3 to the geometric mean titers of SARS-CoV-2 B.1.351-strain before dose 3. GMFRs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analyzed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Before Dose 3 to 1 Month after Dose 3

Notes:

[55] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Fold rise				
geometric mean (confidence interval 95%)	13.2 (9.6 to 18.1)	15.0 (11.3 to 19.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Seroresponse to Reference Strain at 1 Month After Dose 2: Booster Study

End point title	Percentage of Subjects With Seroresponse to Reference Strain at 1 Month After Dose 2: Booster Study[56]

End point description:

Seroresponse was defined as greater than equal to (>=) 4-fold increase from baseline (before Dose 1 in primary study) to the specified time point. If the baseline measurement was below LLOQ, a post vaccination measurement of >=4*LLOQ was considered a seroresponse. Exact 2-sided 95% CI was based on the Clopper and Pearson method. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Month after Dose 2

Notes:

[56] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: Percentage of subjects				
number (confidence interval 95%)	100 (87.2 to 100.0)	100 (86.3 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Seroresponse to Reference Strain Before Dose 3: Booster Study

End point title	Percentage of Subjects With Seroresponse to Reference Strain Before Dose 3: Booster Study[57]

End point description:

Seroresponse was defined as >=4-fold increase from baseline (before Dose 1 in primary study) to the specified time point. If the baseline measurement was below LLOQ, a post vaccination measurement of >=4*LLOQ was considered a seroresponse. Exact 2-sided 95% CI was based on the Clopper and Pearson method. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Before Dose 3

Notes:

[57] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: Percentage of subjects				
number (confidence interval 95%)	92.6 (75.7 to 99.1)	92.0 (74.0 to 99.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Seroresponse to Reference Strain 1 Week After Dose 3: Booster Study

End point title	Percentage of Subjects With Seroresponse to Reference Strain 1 Week After Dose 3: Booster Study[58]

End point description:

Seroresponse was defined as >=4-fold increase from baseline (before Dose 1 in primary study) to the specified time point. If the baseline measurement was below LLOQ, a post vaccination measurement of >=4*LLOQ was considered a seroresponse. Exact 2-sided 95% CI was based on the Clopper and Pearson method. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Week after Dose 3

Notes:

[58] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: Percentage of subjects				
number (confidence interval 95%)	100 (87.2 to 100.0)	100 (86.3 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Seroresponse to Reference Strain 1 Month After Dose 3: Booster Study

End point title	Percentage of Subjects With Seroresponse to Reference Strain 1 Month After Dose 3: Booster Study[59]

End point description:

Seroresponse was defined as >=4-fold increase from baseline (before Dose 1 in primary study) to the specified time point. If the baseline measurement was below LLOQ, a post vaccination measurement of >=4*LLOQ was considered a seroresponse. Exact 2-sided 95% CI was based on the Clopper and Pearson method. Booster evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, Dose 2 – primary study, Dose 3 – booster study within predefined window, had at least 1 valid immunogenicity result from blood sample collected within appropriate window at 1 month after Dose 3, were negative for both SARS-CoV-2 test at Dose 1,1-month post Dose 2, 3, and had no other protocol deviations determined by clinician. Here, "Overall Number of Subjects Analysed"= subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 Month after Dose 3

Notes:

[59] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: Percentage of subjects				
number (confidence interval 95%)	100 (87.2 to 100.0)	100 (86.3 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Seroresponse to B.1.351 Variant Strain at 1 Month After Dose 2: Booster Study

End point title	Percentage of Subjects With Seroresponse to B.1.351 Variant Strain at 1 Month After Dose 2: Booster Study[60]

End point description:

Seroresponse was defined as >=4-fold increase from baseline (before Dose 1 in primary study) to the specified time point. Data for this endpoint was not analysed as the immunogenicity samples were not tested for SARS-CoV-2 B.1.351-strain at Baseline and 1 month after dose 2 as the South African strain was no longer of clinical interest and required responses have been well understood from other studies.

End point type	Primary

End point timeframe:

1 Month after Dose 2

Notes:

[60] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[61]	0[62]		
Units: Percentage of subjects				
number (confidence interval 95%)	(to)	(to)		

Notes:

[61] - Data was not analysed per Sponsor discretion.

[62] - Data was not analysed per Sponsor discretion.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Seroresponse to B.1.351 Variant Strain Before Dose 3: Booster Study

End point title	Percentage of Subjects With Seroresponse to B.1.351 Variant Strain Before Dose 3: Booster Study[63]

End point description:

Seroresponse was defined as >=4-fold increase from baseline (before Dose 1 in primary study) to the specified time point. Data for this endpoint was not analysed as the immunogenicity samples were not tested for SARS-CoV-2 B.1.351-strain at Baseline as the South African strain was no longer of clinical interest and required responses have been well understood from other studies.

End point type	Primary

End point timeframe:

Before Dose 3

Notes:

[63] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[64]	0[65]		
Units: Percentage of subjects				
number (confidence interval 95%)	(to)	(to)		

Notes:

[64] - Data was not analysed per Sponsor discretion.

[65] - Data was not analysed per Sponsor discretion.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Seroresponse to B.1.351 Variant Strain 1 Week After Dose 3: Booster Study

End point title	Percentage of Subjects With Seroresponse to B.1.351 Variant Strain 1 Week After Dose 3: Booster Study[66]

End point description:

Seroresponse was defined as >=4-fold increase from baseline (before Dose 1 in primary study) to the specified time point. Data for this endpoint was not analysed as the immunogenicity samples were not tested for SARS-CoV-2 B.1.351-strain at Baseline as the South African strain was no longer of clinical interest and required responses have been well understood from other studies.

End point type	Primary

End point timeframe:

1 Week after Dose 3

Notes:

[66] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[67]	0[68]		
Units: Percentage of subjects				
number (confidence interval 95%)	(to)	(to)		

Notes:

[67] - Data was not analysed per Sponsor discretion.

[68] - Data was not analysed per Sponsor discretion.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Seroresponse to B.1.351 Variant Strain 1 Month After Dose 3: Booster Study

End point title	Percentage of Subjects With Seroresponse to B.1.351 Variant Strain 1 Month After Dose 3: Booster Study[69]

End point description:

Seroresponse was defined as >=4-fold increase from baseline (before Dose 1 in primary study) to the specified time point. Data for this endpoint was not analysed as the immunogenicity samples were not tested for SARS-CoV-2 B.1.351-strain at Baseline as the South African strain was no longer of clinical interest and required responses have been well understood from other studies.

End point type	Primary

End point timeframe:

1 Month after Dose 3

Notes:

[69] - 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 planned for this endpoint

End point values	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[70]	0[71]		
Units: Percentage of subjects				
number (confidence interval 95%)	(to)	(to)		

Notes:

[70] - Data was not analysed per Sponsor discretion.

[71] - Data was not analysed per Sponsor discretion.

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentrations (GMCs) of Full-Length S-Binding IgG Levels at Baseline and 1 Month After Dose 2 for 30 mcg Dose of BNT162b2: Primary Study

End point title	Geometric Mean Concentrations (GMCs) of Full-Length S-Binding IgG Levels at Baseline and 1 Month After Dose 2 for 30 mcg Dose of BNT162b2: Primary Study[72]

End point description:

GMCs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5* LLOQ. Evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, with Dose 2 received within predefined window, had at least 1 valid immunogenicity result from blood sample collected within an appropriate window at 1 month after Dose 2, were negative for both SARS-CoV-2 test (RT-PCR and N-blinding antibody) during study and had no other protocol deviations determined by clinician. Here, "N"= subjects evaluable for this endpoint and n=subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline (before Dose 1), 1 Month after Dose 2

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: Statistical Analysis was not planned for this endpoint

End point values	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: US Lot 3	BNT162b2 30 mcg: EU Lot
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	324	311	310	160
Units: Units per milliliter				
geometric mean (confidence interval 95%)				
Baseline, n=323,311,310,160,944	3.1 (2.7 to 3.5)	2.6 (2.3 to 3.0)	2.6 (2.2 to 3.0)	2.6 (2.1 to 3.2)
1 Month After Dose 2,n=324,311,310,160,945	6269.8 (5717.7 to 6875.2)	6222.3 (5721.5 to 6766.9)	6818.9 (6280.9 to 7403.1)	6098.9 (5446.0 to 6830.1)

End point values	Pooled US Lots			
Subject group type	Subject analysis set			
Number of subjects analysed	945			

Units: Units per milliliter				
geometric mean (confidence interval 95%)				
Baseline, n=323,311,310,160,944 1 Month After Dose 2,n=324,311,310,160,945	2.8 (2.5 to 3.0) 6428.7 (6116.6 to 6756.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Fold Rises (GMFRs) in Full-Length S-Binding IgG Levels From Baseline to 1 Month After Dose 2 for 30 mcg Dose of BNT162b2: Primary Study

End point title	Geometric Mean Fold Rises (GMFRs) in Full-Length S-Binding IgG Levels From Baseline to 1 Month After Dose 2 for 30 mcg Dose of BNT162b2: Primary Study[73]

End point description:

GMFRs were defined as ratios of the geometric mean concentration of IgG at 1 month after Dose 2 to the geometric mean concentration of IgG at Baseline. GMFRs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5*LLOQ. Evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, with Dose 2 received within predefined window, had at least 1 valid immunogenicity result from blood sample collected within an appropriate window at 1 month after Dose 2, were negative for both SARS-CoV-2 test (RT-PCR and N-blinding antibody) during study and had no other protocol deviations determined by clinician. Here, "N"= subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Baseline (before Dose 1) up to 1 Month after Dose 2

Notes:

[73] - 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: Statistical Analysis was not planned for this endpoint

End point values	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: US Lot 3	BNT162b2 30 mcg: EU Lot
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	323	311	310	160
Units: Fold rise				
geometric mean (confidence interval 95%)	2036.6 (1744.5 to 2377.7)	2367.1 (2028.6 to 2762.2)	2645.2 (2271.2 to 3080.8)	2373.8 (1901.2 to 2963.9)

End point values	Pooled US Lots			
Subject group type	Subject analysis set			
Number of subjects analysed	944			
Units: Fold rise				
geometric mean (confidence interval 95%)	2331.9 (2133.7 to 2548.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMT) of SARS-CoV-2 Neutralizing Titers at Baseline and 1 Month After Dose 2 for 20 mcg and 30 mcg dose of BNT162b2 from US Lot 1: Primary Study

End point title	Geometric Mean Titers (GMT) of SARS-CoV-2 Neutralizing Titers at Baseline and 1 Month After Dose 2 for 20 mcg and 30 mcg dose of BNT162b2 from US Lot 1: Primary Study[74]

End point description:

GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5* LLOQ. Evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, with Dose 2 received within predefined window, had at least 1 valid immunogenicity result from blood sample collected within an appropriate window at 1 month after Dose 2, were negative for both SARS-CoV-2 test (RT-PCR and N-blinding antibody) during study and had no other protocol deviations determined by clinician. Here, "N"= subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (before Dose 1), 1 Month after Dose 2

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: Statistical Analysis was not planned for this endpoint

End point values	BNT162b2 30 mcg: US Lot 1	BNT162b2 20 mcg: US Lot 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	324	318		
Units: Titer				
geometric mean (confidence interval 95%)				
Baseline	20.5 (20.5 to 20.5)	20.5 (20.5 to 20.5)		
1 Month after Dose 2	969.6 (905.7 to 1038.0)	913.0 (843.4 to 988.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Fold Rises (GMFRs) in SARS-CoV-2 Neutralizing Titers From Baseline to 1 Month After Dose 2 for 20 mcg and 30 mcg dose of BNT162b2 from US Lot 1: Primary Study

End point title	Geometric Mean Fold Rises (GMFRs) in SARS-CoV-2 Neutralizing Titers From Baseline to 1 Month After Dose 2 for

	20 mcg and 30 mcg dose of BNT162b2 from US Lot 1: Primary Study[75]

End point description:

GMFRs were defined as ratios of the geometric mean titers of SARS-CoV-2 at 1 month after Dose 2 to the geometric mean titers of SARS-CoV-2 at Baseline. GMFRs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5* LLOQ. Evaluable immunogenicity population: Subjects who received 2 doses of vaccine in primary study, with Dose 2 received within predefined window, had at least 1 valid immunogenicity result from blood sample collected within an appropriate window at 1 month after Dose 2, were negative for both SARS-CoV-2 test (RT-PCR and N-blinding antibody) during study and had no other protocol deviations determined by clinician. Here, "N"= subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Baseline (before Dose 1) up to 1 Month after Dose 2

Notes:

[75] - 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: Statistical Analysis was not planned for this endpoint

End point values	BNT162b2 30 mcg: US Lot 1	BNT162b2 20 mcg: US Lot 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	324	318		
Units: Fold rise				
geometric mean (confidence interval 95%)	47.3 (44.2 to 50.6)	44.5 (41.1 to 48.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs-For primary study: From Dose 1 to 1 Month after Dose 2 (up to a maximum of 2 months); For booster study: From Dose 3 to 1 Month after Dose 3 (up to a maximum of 35 days); Local reactions/systemic events: Within 7 days after each dose

Adverse event reporting additional description:

Safety population set. AEs included events collected in e-diary (systematic assessment) and events collected on CRF at each visit (non-systematic assessment).1 subject randomised to US Lot 1 was administered US Lot 1 for Dose 1 & US Lot 3 for Dose 2, therefore, subject was included in both reporting groups (US Lot 1&US Lot 3) for non-SAEs.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	BNT162b2 30 mcg: US Lot 1

Reporting group description:

Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 1) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Reporting group title	BNT162b2 30 mcg: US Lot 2

Reporting group description:

Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 2) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Reporting group title	BNT162b2 30 mcg: EU Lot

Reporting group description:

Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (EU Lot) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Reporting group title	BNT162b2 20 mcg: US Lot 1

Reporting group description:

Subjects were randomised in primary study to receive 20 mcg intramuscular dose of BNT162b2 vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Reporting group title	BNT162b2 30 mcg: Booster Dose

Reporting group description:

Subjects who received 2 doses of 30 mcg BNT162b2 vaccine in primary study from US Lot 1 were randomised to booster study to receive a single 30 mcg intramuscular dose of BNT162b2 vaccine at 3 months after second dose in the primary study. Subjects were followed up for safety for up to 28-35 days after vaccination.

Reporting group title	BNT162b2.B.1.351 30 mcg: Booster Dose

Reporting group description:

Subjects who received 2 doses of 30 mcg BNT162b2 vaccine in primary study from US Lot 1, 2 or 3 were randomised to booster study to receive a single 30 mcg intramuscular dose of BNT162b2.B.1.351 vaccine at 3 months after second dose in the primary study. Subjects were followed up for safety for up to 28-35 days after vaccination.

Reporting group title	BNT162b2; Arm 3 (US Lot 3)

Reporting group description:

Subjects were randomised in primary study to receive 30 mcg intramuscular dose of BNT162b2 (US Lot 3) vaccine as 2-dose schedule separated by 21 days. Subjects were followed up for safety for up to 28-35 days after second dose of vaccine, for a maximum of 2 months.

Serious adverse events	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: EU Lot
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 351 (0.00%)	0 / 352 (0.00%)	1 / 173 (0.58%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Migrainosus			
subjects affected / exposed	0 / 351 (0.00%)	0 / 352 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 351 (0.00%)	0 / 352 (0.00%)	0 / 173 (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	BNT162b2 20 mcg: US Lot 1	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 351 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Migrainosus			
subjects affected / exposed	0 / 351 (0.00%)	0 / 31 (0.00%)	0 / 31 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 351 (0.00%)	0 / 31 (0.00%)	0 / 31 (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	BNT162b2; Arm 3 (US Lot 3)		

Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 347 (0.29%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Migrainosus			
subjects affected / exposed	0 / 347 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	BNT162b2 30 mcg: US Lot 1	BNT162b2 30 mcg: US Lot 2	BNT162b2 30 mcg: EU Lot
Total subjects affected by non-serious adverse events			
subjects affected / exposed	341 / 351 (97.15%)	336 / 352 (95.45%)	165 / 173 (95.38%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign abdominal neoplasm			
subjects affected / exposed	0 / 351 (0.00%)	0 / 352 (0.00%)	0 / 173 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	234 / 351 (66.67%)	229 / 352 (65.06%)	119 / 173 (68.79%)
occurrences (all)	234	229	119
Syncope			
subjects affected / exposed	0 / 351 (0.00%)	0 / 352 (0.00%)	2 / 173 (1.16%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Chills			
alternative assessment type: Systematic			

subjects affected / exposed	115 / 351 (32.76%)	120 / 352 (34.09%)	56 / 173 (32.37%)
occurrences (all)	115	120	56
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	276 / 351 (78.63%)	259 / 352 (73.58%)	133 / 173 (76.88%)
occurrences (all)	276	259	133
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 351 (4.56%)	19 / 352 (5.40%)	8 / 173 (4.62%)
occurrences (all)	16	19	8
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	319 / 351 (90.88%)	302 / 352 (85.80%)	158 / 173 (91.33%)
occurrences (all)	319	302	158
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 351 (5.98%)	31 / 352 (8.81%)	8 / 173 (4.62%)
occurrences (all)	21	31	8
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	26 / 351 (7.41%)	22 / 352 (6.25%)	16 / 173 (9.25%)
occurrences (all)	26	22	16
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 351 (0.00%)	0 / 352 (0.00%)	0 / 173 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	57 / 351 (16.24%)	50 / 352 (14.20%)	26 / 173 (15.03%)
occurrences (all)	57	50	26
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 351 (2.85%)	7 / 352 (1.99%)	4 / 173 (2.31%)
occurrences (all)	10	7	4

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 351 (0.00%)	1 / 352 (0.28%)	3 / 173 (1.73%)
occurrences (all)	0	1	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	82 / 351 (23.36%)	96 / 352 (27.27%)	42 / 173 (24.28%)
occurrences (all)	82	96	42
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	136 / 351 (38.75%)	153 / 352 (43.47%)	76 / 173 (43.93%)
occurrences (all)	136	153	76
Neck pain			
subjects affected / exposed	0 / 351 (0.00%)	0 / 352 (0.00%)	0 / 173 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	BNT162b2 20 mcg: US Lot 1	BNT162b2 30 mcg: Booster Dose	BNT162b2.B.1.351 30 mcg: Booster Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	342 / 351 (97.44%)	30 / 31 (96.77%)	31 / 31 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign abdominal neoplasm			
subjects affected / exposed	0 / 351 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	224 / 351 (63.82%)	13 / 31 (41.94%)	18 / 31 (58.06%)
occurrences (all)	224	13	18
Syncope			
subjects affected / exposed	0 / 351 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chills			
alternative assessment type: Systematic			

subjects affected / exposed	92 / 351 (26.21%)	8 / 31 (25.81%)	6 / 31 (19.35%)
occurrences (all)	92	8	6
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	265 / 351 (75.50%)	21 / 31 (67.74%)	26 / 31 (83.87%)
occurrences (all)	265	21	26
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 351 (4.56%)	3 / 31 (9.68%)	1 / 31 (3.23%)
occurrences (all)	16	3	1
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	314 / 351 (89.46%)	28 / 31 (90.32%)	29 / 31 (93.55%)
occurrences (all)	314	28	29
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 351 (6.27%)	2 / 31 (6.45%)	2 / 31 (6.45%)
occurrences (all)	22	2	2
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	20 / 351 (5.70%)	1 / 31 (3.23%)	2 / 31 (6.45%)
occurrences (all)	20	1	2
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 351 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	54 / 351 (15.38%)	5 / 31 (16.13%)	2 / 31 (6.45%)
occurrences (all)	54	5	2
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 351 (2.28%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	8	1	0

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 351 (0.57%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	78 / 351 (22.22%)	4 / 31 (12.90%)	4 / 31 (12.90%)
occurrences (all)	78	4	4
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	142 / 351 (40.46%)	13 / 31 (41.94%)	6 / 31 (19.35%)
occurrences (all)	142	13	6
Neck pain			
subjects affected / exposed	0 / 351 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1

Non-serious adverse events	BNT162b2; Arm 3 (US Lot 3)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	335 / 347 (96.54%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign abdominal neoplasm			
subjects affected / exposed	0 / 347 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	223 / 347 (64.27%)		
occurrences (all)	223		
Syncope			
subjects affected / exposed	0 / 347 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chills			
alternative assessment type: Systematic			

subjects affected / exposed	129 / 347 (37.18%)		
occurrences (all)	129		
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	281 / 347 (80.98%)		
occurrences (all)	281		
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 347 (6.63%)		
occurrences (all)	23		
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	316 / 347 (91.07%)		
occurrences (all)	316		
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	25 / 347 (7.20%)		
occurrences (all)	25		
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	29 / 347 (8.36%)		
occurrences (all)	29		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 347 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	48 / 347 (13.83%)		
occurrences (all)	48		
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 347 (3.46%)		
occurrences (all)	12		

Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 1 / 347 (0.29%) 1		
Musculoskeletal and connective tissue disorders Arthralgia alternative assessment type: Systematic subjects affected / exposed occurrences (all) Myalgia alternative assessment type: Systematic subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all)	 83 / 347 (23.92%) 83 150 / 347 (43.23%) 150 0 / 347 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 May 2021	A booster study was added in which an additional dose of either BNT162b2 or BNT162b2.B.1.351 (beta variant of concern) was given to a subset of 60 subjects 18 through 50 yrs of age, 3 months after Dose 2, for assessment of safety and immunogenicity.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported