Clinical trial results:
A Phase 2/3 Protocol to Investigate the Safety, Tolerability, and Immunogenicity of BNT162b2 RNA - Based Vaccine Candidates for SARS-Cov-2 New Variants in Healthy Individuals

Summary

EudraCT number	2024-000361-24
Trial protocol	Outside EU/EEA
Global end of trial date	

Results information

Result version number	v1
This version publication date	20 December 2024
First version publication date	20 December 2024

Trial information

Trial identification

Sponsor protocol code	C4591054

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05997290
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	Interim
Date of interim/final analysis	25 April 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 March 2024
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

SSA: Describe the safety & tolerability profile of BNT162b2 (Omi XBB.1.5) 30 micrograms (mcg) in messenger ribonucleic acid (mRNA) coronavirus disease 2019 (COVID-19) vaccine-experienced participants >=12 years of age & describe immune response to BNT162b2 (Omi XBB.1.5) 30 mcg & to bivalent BNT162b2 (WT/Omi BA.4/BA.5) 30 mcg in mRNA COVID-19 vaccine–experienced participants =>12 years of age. SSB: Describe the safety & tolerability profile of BNT162b2 (Omi XBB.1.5) 30 mcg given as a single dose to COVID-19 vaccine-naïve participants who were previously SARS-CoV-2 exposed, >=12 years of age & demonstrate the noninferiority with respect to level of neutralizing titer & with respect to seroresponse rate of the anti-XBB.1.5 immune response elicited by BNT162b2 (Omi XBB.1.5) 30 mcg given as a single dose to COVID-19 vaccine–naïve participants, who were previously SARS-CoV-2 exposed, >=12 years of age compared to BNT162b2 (Omi XBB.1.5) 30 mcg given to vaccine-experienced participants in SSA.

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 trials participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 August 2023
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: 723
Worldwide total number of subjects	723
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 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	39

Adults (18-64 years)	517
From 65 to 84 years	165
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

SSA: A total of 417 participants were screened in sub-study A out of which 412 were vaccinated. SSB: A total of 311 participants were screened and vaccinated in sub-study B.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	SSA: Group 1: 12-17 years

Arm description:

Participants aged 12 to 17 years who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via intramuscular (IM) route on Day 1 of this study.

Arm type	Experimental
Investigational medicinal product name	BNT162b2 (Omi XBB.1.5)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a single dose of 30 mcg BNT162b2 (Omi XBB.1.5) administered intramuscularly.

Arm title	SSA: Group 2: 18-55 years

Arm description:

Participants aged 18 to 55 years who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.

Arm type	Experimental
Investigational medicinal product name	BNT162b2 (Omi XBB.1.5)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a single dose of 30 mcg BNT162b2 (Omi XBB.1.5) administered intramuscularly.

Arm title	SSA: Group 3: >55 years

Arm description:

Participants aged greater than (>) 55 years who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.

Arm type	Experimental

Investigational medicinal product name	BNT162b2 (Omi XBB.1.5)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a single dose of 30 mcg BNT162b2 (Omi XBB.1.5) administered intramuscularly.

Arm title	SSB: Group 1: 12-17 years

Arm description:

Participants aged 12-17 years who were previously exposed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.

Arm type	Experimental
Investigational medicinal product name	BNT162b2 (Omi XBB.1.5)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a single dose of 30 mcg BNT162b2 (Omi XBB.1.5) administered intramuscularly.

Arm title	SSB: Group 2: 18-55 years

Arm description:

Participants aged 18-55 years who were previously exposed to SARS-CoV-2 and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.

Arm type	Experimental
Investigational medicinal product name	BNT162b2 (Omi XBB.1.5)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a single dose of 30 mcg BNT162b2 (Omi XBB.1.5) administered intramuscularly.

Arm title	SSB: Group 3: >55 years

Arm description:

Participants aged >55 years who were previously exposed to SARS-CoV-2 and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this

Arm type	Experimental
Investigational medicinal product name	BNT162b2 (Omi XBB.1.5)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a single dose of 30 mcg BNT162b2 (Omi XBB.1.5) administered intramuscularly.

Number of subjects in period 1	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years
Started	30	174	208
Safety Population	30	174	208
Evaluable Immunogenicity Population	27 [1]	167 [2]	188 [3]
Completed	29	172	203
Not completed	1	2	5
Consent withdrawn by subject	1	-	2
Death	-	-	1
Lost to follow-up	-	2	-
Protocol deviation	-	-	2

Number of subjects in period 1	SSB: Group 1: 12-17 years	SSB: Group 2: 18-55 years	SSB: Group 3: >55 years
Started	9	253	49
Safety Population	9	253	49
Evaluable Immunogenicity Population	9	243	47
Completed	9	225	44
Not completed	0	28	5
Consent withdrawn by subject	-	6	1
Death	-	-	-
Lost to follow-up	-	22	4
Protocol deviation	-	-	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Evaluable immunogenicity population included all eligible assigned participants who received the study intervention to which they were assigned, had at least 1 valid and determinate immunogenicity result from the blood sample collected within 28 to 42 days after the study vaccination, and had no other important protocol deviations as determined by the clinician.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Evaluable immunogenicity population included all eligible assigned participants who received the study intervention to which they were assigned, had at least 1 valid and determinate immunogenicity result from the blood sample collected within 28 to 42 days after the study vaccination, and had no other important protocol deviations as determined by the clinician.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Evaluable immunogenicity population included all eligible assigned participants who received the study intervention to which they were assigned, had at least 1 valid and determinate immunogenicity result from the blood sample collected within 28 to 42 days after the study vaccination, and had no other important protocol deviations as determined by the clinician.

Baseline characteristics

Reporting groups	
Reporting group title	SSA: Group 1: 12-17 years
Reporting group description:	
Participants aged 12 to 17 years who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via intramuscular (IM) route on Day 1 of this study.	
Reporting group title	SSA: Group 2: 18-55 years
Reporting group description:	
Participants aged 18 to 55 years who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.	
Reporting group title	SSA: Group 3: >55 years
Reporting group description:	
Participants aged greater than (>) 55 years who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.	
Reporting group title	SSB: Group 1: 12-17 years
Reporting group description:	
Participants aged 12-17 years who were previously exposed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.	
Reporting group title	SSB: Group 2: 18-55 years
Reporting group description:	
Participants aged 18-55 years who were previously exposed to SARS-CoV-2 and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.	
Reporting group title	SSB: Group 3: >55 years
Reporting group description:	
Participants aged >55 years who were previously exposed to SARS-CoV-2 and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this	

Reporting group values	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years
Number of subjects	30	174	208
Age Categorical Units: Participants			
Adolescents (12-17 years)	30	0	0
Adults (18-64 years)	0	174	63
From 65-84 years	0	0	143
85 years and over	0	0	2
Age Continuous Units: years			
arithmetic mean	14.0	40.4	68.6
standard deviation	± 1.74	± 9.82	± 6.74
Gender Categorical Units: Participants			
Female	19	100	123
Male	11	74	85

Race Units: Subjects			
White	26	135	164
Black or African American	3	23	27
American Indian or Alaska Native	0	0	1
Asian	1	11	10
Native Hawaiian or other Pacific Islander	0	0	2
Multiracial	0	5	3
Unknown	0	0	1
Ethnicity Units: Subjects			
Hispanic/Latino	6	35	34
Non-Hispanic/non-Latino	24	138	173
Not reported	0	1	1

Reporting group values	SSB: Group 1: 12-17 years	SSB: Group 2: 18-55 years	SSB: Group 3: >55 years
Number of subjects	9	253	49
Age Categorical Units: Participants			
Adolescents (12-17 years)	9	0	0
Adults (18-64 years)	0	253	27
From 65-84 years	0	0	22
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	14.6	34.5	64.0
standard deviation	± 1.67	± 10.43	± 6.35
Gender Categorical Units: Participants			
Female	5	138	23
Male	4	115	26
Race Units: Subjects			
White	2	162	30
Black or African American	7	87	16
American Indian or Alaska Native	0	0	1
Asian	0	4	2
Native Hawaiian or other Pacific Islander	0	0	0
Multiracial	0	0	0
Unknown	0	0	0
Ethnicity Units: Subjects			
Hispanic/Latino	3	136	19
Non-Hispanic/non-Latino	6	117	30
Not reported	0	0	0

Reporting group values	Total		
Number of subjects	723		

Age Categorical Units: Participants			
Adolescents (12-17 years)	39		
Adults (18-64 years)	517		
From 65-84 years	165		
85 years and over	2		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical Units: Participants			
Female	408		
Male	315		
Race Units: Subjects			
White	519		
Black or African American	163		
American Indian or Alaska Native	2		
Asian	28		
Native Hawaiian or other Pacific Islander	2		
Multiracial	8		
Unknown	1		
Ethnicity Units: Subjects			
Hispanic/Latino	233		
Non-Hispanic/non-Latino	488		
Not reported	2		

End points

End points reporting groups

Reporting group title	SSA: Group 1: 12-17 years

Reporting group description:

Participants aged 12 to 17 years who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via intramuscular (IM) route on Day 1 of this study.

Reporting group title	SSA: Group 2: 18-55 years

Reporting group description:

Participants aged 18 to 55 years who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.

Reporting group title	SSA: Group 3: >55 years

Reporting group description:

Participants aged greater than (>) 55 years who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.

Reporting group title	SSB: Group 1: 12-17 years

Reporting group description:

Participants aged 12-17 years who were previously exposed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.

Reporting group title	SSB: Group 2: 18-55 years

Reporting group description:

Participants aged 18-55 years who were previously exposed to SARS-CoV-2 and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.

Reporting group title	SSB: Group 3: >55 years

Reporting group description:

Participants aged >55 years who were previously exposed to SARS-CoV-2 and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this

Subject analysis set title	SSA Total Study Participants: C4591054
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study. This analysis set is created for safety analysis.

Subject analysis set title	SSA Historical Control: C4591044 BNT162b2 12-17 years
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged 12 to 17 years from study C4591044 (NCT05472038) Cohort 2/Cohort 3 who received bivalent BNT162b2 (WT/Omi BA.4/BA.5) 30 mcg as a fourth dose were used as historical control for immunogenicity. This analysis set is created for immunogenicity analysis.

Subject analysis set title	SSA Historical Control: C4591044 BNT162b2 18-55 years
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged 18 to 55 years from study C4591044 (NCT05472038) Cohort 2/Cohort 3 who received bivalent BNT162b2 (WT/Omi BA.4/BA.5) 30 mcg as a fourth dose were used as historical control for immunogenicity. This analysis set is created for immunogenicity analysis.

Subject analysis set title	SSA Historical Control: C4591044 BNT162b2 >55 years
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged >55 years from study C4591044 (NCT05472038) Cohort 2/Cohort 3 who received bivalent BNT162b2 (WT/Omi BA.4/BA.5) 30 mcg as a fourth dose were used as historical control for immunogenicity. This analysis set is created for immunogenicity analysis.

Subject analysis set title	SSA Total Study Participants: C4591054
Subject analysis set type	Per protocol

Subject analysis set description:

Participants who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study. This analysis set is created for immunogenicity analysis.

Subject analysis set title	SSA Total Historical Control: C4591044 BNT162b2
Subject analysis set type	Per protocol

Subject analysis set description:

Participants from study C4591044 (NCT05472038) Cohort 2/Cohort 3 who received bivalent BNT162b2 (WT/Omi BA.4/BA.5) 30 mcg as a fourth dose were used as historical control for immunogenicity. This analysis set is created for immunogenicity analysis.

Subject analysis set title	SSB Total Study Participants
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants aged >=12 years who were previously exposed to SARS-CoV-2 and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 in SSB. This analysis set is created for safety analysis.

Subject analysis set title	SSB: Vaccine-Naïve Substudy B
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged >=12 years who were previously exposed to SARS-CoV-2 and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 in SSB. This analysis set is created for immunogenicity analysis.

Subject analysis set title	SSB Control: Vaccine-Experienced Substudy A
Subject analysis set type	Per protocol

Subject analysis set description:

Participants who received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 in SSA were included. This analysis set is created for immunogenicity analysis.

Primary: Percentage of Participants With Local Reactions Within 7 Days After Vaccination: SSA

End point title	Percentage of Participants With Local Reactions Within 7 Days After Vaccination: SSA[1][2]

End point description:

Local reactions: pain at injection site, redness and swelling recorded by participants in an electronic diary (e-diary) or as adverse events (AEs) in the case report form (CRF). Redness & swelling measured & recorded in measuring device units (mdu)(range:1 to 21),1mdu=0.5 cm &were graded as mild (greater than[>] 2.0 to 5.0 cm),moderate(>5.0 to 10.0 cm),severe(>10.0 cm)&Grade 4(necrosis [swelling]&necrosis or exfoliative dermatitis[redness]).Pain at injection site graded as mild(did not interfere with activity),moderate(interfered with activity),severe(prevented daily activity)&Grade(G)4(emergency room [ER]visit or hospitalisation for severe pain at injection site).G4 LR classified by investigator or medically qualified person.Exact 2-sided confidence interval(CI)based on Clopper and Pearson method. Safety population: all participants who received study intervention.Number of Participants Analysed=Participants evaluable.

End point type	Primary

End point timeframe:

Day 1 to Day 7 after vaccination

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the

baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years	SSA Total Study Participants: C4591054
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	30	174	206	410
Units: Percentage of Participants				
number (confidence interval 95%)				
Redness: Any	10.0 (2.1 to 26.5)	4.0 (1.6 to 8.1)	5.8 (3.0 to 10.0)	5.4 (3.4 to 8.0)
Redness: Mild	6.7 (0.8 to 22.1)	3.4 (1.3 to 7.4)	3.9 (1.7 to 7.5)	3.9 (2.2 to 6.3)
Redness: Moderate	3.3 (0.1 to 17.2)	0.6 (0.0 to 3.2)	1.9 (0.5 to 4.9)	1.5 (0.5 to 3.2)
Redness: Severe	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
Redness: Grade 4	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
Swelling: Any	16.7 (5.6 to 34.7)	7.5 (4.0 to 12.4)	5.8 (3.0 to 10.0)	7.3 (5.0 to 10.3)
Swelling: Mild	13.3 (3.8 to 30.7)	5.7 (2.8 to 10.3)	3.9 (1.7 to 7.5)	5.4 (3.4 to 8.0)
Swelling: Moderate	3.3 (0.1 to 17.2)	1.7 (0.4 to 5.0)	1.9 (0.5 to 4.9)	2.0 (0.8 to 3.8)
Swelling: Severe	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
Swelling: Grade 4	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
Pain at the injection site: Any	80.0 (61.4 to 92.3)	75.9 (68.8 to 82.0)	52.4 (45.4 to 59.4)	64.4 (59.5 to 69.0)
Pain at the injection site: Mild	50.0 (31.3 to 68.7)	59.8 (52.1 to 67.1)	46.6 (39.6 to 53.7)	52.4 (47.5 to 57.4)
Pain at the injection site: Moderate	30.0 (14.7 to 49.4)	16.1 (11.0 to 22.4)	5.8 (3.0 to 10.0)	12.0 (9.0 to 15.5)
Pain at the injection site: Severe	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
Pain at the injection site: Grade 4	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Systemic Events Within 7 Days After Vaccination: SSA

End point title	Percentage of Participants With Systemic Events Within 7 Days After Vaccination: SSA[3][4]

End point description:

Systemic events were recorded by participants in an e-diary or as AEs in the CRF. Fever: defined as oral temperature >=38 degree Celsius (deg C) and categorised as >= 38.0-38.4 deg C, >38.4-38.9 deg C, >38.9-40.0 deg C and >40.0 deg C. Fatigue, headache, chills, new or worsened muscle pain and joint pain: mild (didn't interfere with activity), moderate (some interference with activity), severe (prevented daily routine activity). Vomiting: mild: 1-2 times in 24 hours (h), moderate: >2 times in 24h, severe: required intravenous (IV) hydration. Diarrhoea: mild: 2-3 loose stools in 24h, moderate: 4-5 loose stools in 24h, severe: 6 or more loose stools in 24h. Grade 4 for all events except fever: ER visit/hospitalization. Grade 4 events were classified by investigator or medically qualified person. Exact 2-sided CI was based on Clopper and Pearson method. Safety population: All participants who received the study intervention. Number of Participants Analysed= Participants evaluable.

End point type	Primary

End point timeframe:

Day 1 to Day 7 after vaccination

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years	SSA Total Study Participants: C4591054
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	30	174	206	410
Units: Percentage of participants				
number (confidence interval 95%)				
Fever: Any	16.7 (5.6 to 34.7)	4.0 (1.6 to 8.1)	3.9 (1.7 to 7.5)	4.9 (3.0 to 7.4)
Fever: >=38.0 degree C to 38.4 degree C	10.0 (2.1 to 26.5)	3.4 (1.3 to 7.4)	2.4 (0.8 to 5.6)	3.4 (1.9 to 5.7)
Fever: >38.4 degree C to 38.9 degree C	3.3 (0.1 to 17.2)	0.6 (0.0 to 3.2)	1.0 (0.1 to 3.5)	1.0 (0.3 to 2.5)
Fever: >38.9 degree C to 40.0 degree C	3.3 (0.1 to 17.2)	0 (0.0 to 2.1)	0.5 (0.0 to 2.7)	0.5 (0.1 to 1.8)
Fever: >40.0 degree C	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
Fatigue: Any	56.7 (37.4 to 74.5)	56.9 (49.2 to 64.4)	35.4 (28.9 to 42.4)	46.1 (41.2 to 51.1)
Fatigue: Mild	30.0 (14.7 to 49.4)	31.6 (24.8 to 39.1)	18.4 (13.4 to 24.4)	24.9 (20.8 to 29.4)
Fatigue: Moderate	26.7 (12.3 to 45.9)	24.1 (18.0 to 31.2)	17.0 (12.1 to 22.8)	20.7 (16.9 to 25.0)
Fatigue: Severe	0 (0.0 to 11.6)	1.1 (0.1 to 4.1)	0 (0.0 to 1.8)	0.5 (0.1 to 1.8)
Fatigue: Grade 4	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
Headache: Any	36.7 (19.9 to 56.1)	43.7 (36.2 to 51.4)	26.2 (20.3 to 32.8)	34.4 (29.8 to 39.2)
Headache: Mild	30.0 (14.7 to 49.4)	31.0 (24.3 to 38.5)	20.4 (15.1 to 26.5)	25.6 (21.5 to 30.1)
Headache: Moderate	6.7 (0.8 to 22.1)	12.6 (8.1 to 18.5)	5.8 (3.0 to 10.0)	8.8 (6.2 to 11.9)
Headache: Severe	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
Headache: Grade 4	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
Chills: Any	20.0 (7.7 to 38.6)	9.2 (5.3 to 14.5)	9.2 (5.6 to 14.0)	10.0 (7.3 to 13.3)
Chills: Mild	10.0 (2.1 to 26.5)	6.9 (3.6 to 11.7)	6.3 (3.4 to 10.5)	6.8 (4.6 to 9.7)
Chills: Moderate	10.0 (2.1 to 26.5)	2.3 (0.6 to 5.8)	2.9 (1.1 to 6.2)	3.2 (1.7 to 5.4)
Chills: Severe	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
Chills: Grade 4	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
Vomiting: Any	0 (0.0 to 11.6)	2.3 (0.6 to 5.8)	0 (0.0 to 1.8)	1.0 (0.3 to 2.5)
Vomiting: Mild	0 (0.0 to 11.6)	2.3 (0.6 to 5.8)	0 (0.0 to 1.8)	1.0 (0.3 to 2.5)
Vomiting: Moderate	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
Vomiting: Severe	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
Vomiting: Grade 4	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)

Diarrhea: Any	0 (0.0 to 11.6)	13.2 (8.6 to 19.2)	8.7 (5.3 to 13.5)	10.0 (7.3 to 13.3)
Diarrhea: Mild	0 (0.0 to 11.6)	11.5 (7.2 to 17.2)	7.3 (4.1 to 11.7)	8.5 (6.0 to 11.7)
Diarrhea: Moderate	0 (0.0 to 11.6)	1.1 (0.1 to 4.1)	1.5 (0.3 to 4.2)	1.2 (0.4 to 2.8)
Diarrhea: Severe	0 (0.0 to 11.6)	0.6 (0.0 to 3.2)	0 (0.0 to 1.8)	0.2 (0.0 to 1.4)
Diarrhea: Grade 4	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
New or worsened muscle pain: Any	23.3 (9.9 to 42.3)	21.8 (15.9 to 28.7)	12.1 (8.0 to 17.4)	17.1 (13.6 to 21.1)
New or worsened muscle pain: Mild	3.3 (0.1 to 17.2)	12.1 (7.6 to 17.9)	5.3 (2.7 to 9.4)	8.0 (5.6 to 11.1)
New or worsened muscle pain: Moderate	20.0 (7.7 to 38.6)	9.8 (5.8 to 15.2)	6.8 (3.8 to 11.1)	9.0 (6.4 to 12.2)
New or worsened muscle pain: Severe	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
New or worsened muscle pain: Grade 4	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
New or worsened joint pain: Any	16.7 (5.6 to 34.7)	14.4 (9.5 to 20.5)	7.8 (4.5 to 12.3)	11.2 (8.3 to 14.7)
New or worsened joint pain: Mild	6.7 (0.8 to 22.1)	8.6 (4.9 to 13.8)	5.3 (2.7 to 9.4)	6.8 (4.6 to 9.7)
New or worsened joint pain: Moderate	10.0 (2.1 to 26.5)	5.7 (2.8 to 10.3)	2.4 (0.8 to 5.6)	4.4 (2.6 to 6.8)
New or worsened joint pain: Severe	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)
New or worsened joint pain: Grade 4	0 (0.0 to 11.6)	0 (0.0 to 2.1)	0 (0.0 to 1.8)	0 (0.0 to 0.9)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Adverse Events (AEs) From Vaccination Through 1 Month After Vaccination: SSA

End point title	Percentage of Participants With Adverse Events (AEs) From Vaccination Through 1 Month After Vaccination: SSA[5][6]

End point description:

An AE was defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Percentage of participants reporting AEs from study vaccination on Day 1 up to 1 month after the study vaccination were reported in this endpoint. Exact 2-sided CI was based on Clopper and Pearson method. Only AEs collected by non-systematic assessment (i.e., excluding local reactions and systemic events) were reported in this endpoint. Safety population included all participants who received the study intervention.

End point type	Primary

End point timeframe:

From vaccination on Day 1 up to 1 month after vaccination

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years	SSA Total Study Participants: C4591054
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	30	174	208	412
Units: Percentage of participants				
number (confidence interval 95%)	16.7 (5.6 to 34.7)	7.5 (4.0 to 12.4)	8.2 (4.8 to 12.8)	8.5 (6.0 to 11.6)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Serious Adverse Events (SAEs) From Vaccination Through 6 Months After the Study Vaccination: SSA

End point title	Percentage of Participants With Serious Adverse Events (SAEs) From Vaccination Through 6 Months After the Study Vaccination: SSA[7][8]

End point description:

An SAE was defined as any untoward medical occurrence at any dose that resulted in any of the following outcomes: death; life-threatening; required inpatient hospitalization or prolongation of existing hospitalization; persistent or significant disability/incapacity; congenital anomaly/birth defect; suspected transmission via a Pfizer product of an infectious agent, pathogenic or non-pathogenic; or considered as an important medical event. Percentage of participants reporting SAEs from study vaccination on Day 1 up to 6 months after the study vaccination were reported in this endpoint. Exact 2-sided CI was based on Clopper and Pearson method. Safety population included all participants who received the study intervention.

End point type	Primary

End point timeframe:

From vaccination on Day 1 up to 6 months after vaccination

Notes:

[7] - 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: Only descriptive data was planned for this endpoint.

[8] - 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: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years	SSA Total Study Participants: C4591054
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	30	174	208	412
Units: Percentage of Participants				
number (confidence interval 95%)	3.3 (0.1 to 17.2)	0 (0.0 to 2.1)	1.9 (0.5 to 4.9)	1.2 (0.4 to 2.8)

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMT) of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Omi XBB.1.5-Neutralizing Titers at 1 Month After Vaccination: SSA and Historical Control of the Bivalent BNT162b2 (WT/Omi BA.4/BA.5) Group from Study C4591044

End point title	Geometric Mean Titers (GMT) of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Omi XBB.1.5-Neutralizing Titers at 1 Month After Vaccination: SSA and Historical Control of the Bivalent BNT162b2 (WT/Omi BA.4/BA.5) Group from Study C4591044[9][10]

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 lower limit of quantitation (LLOQ) were set to 0.5*LLOQ. Evaluable immunogenicity population included all eligible assigned participants who received the study intervention to which they were assigned, had at least 1 valid and determinate immunogenicity result from the blood sample collected within 28 to 42 days after the study vaccination, and had no other important protocol deviations as determined by the clinician. Here, Number of Participants Analysed signifies number of participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

At 1 month after vaccination

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: Only descriptive data was planned for this endpoint.

[10] - 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: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years	SSA Historical Control: C4591044 BNT162b2 12-17 years
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	27	166	185	15
Units: Titer				
geometric mean (confidence interval 95%)	3632.1 (2043.8 to 6454.7)	2503.6 (2003.0 to 3129.3)	2606.8 (2065.5 to 3289.9)	837.1 (459.5 to 1524.9)

End point values	SSA Historical Control: C4591044 BNT162b2 18-55 years	SSA Historical Control: C4591044 BNT162b2 >55 years	SSA Total Study Participants: C4591054	SSA Total Historical Control: C4591044 BNT162b2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	85	100	378	200
Units: Titer				
geometric mean (confidence interval 95%)	615.5 (459.0 to 825.2)	560.4 (430.0 to 730.2)	2622.3 (2246.6 to 3060.9)	601.0 (499.5 to 723.1)

Statistical analyses

No statistical analyses for this end point

Primary: GMT of SARS-CoV-2 Omi BA.4/BA.5-Neutralizing Titers at 1 Month After Vaccination: SSA and Historical Control of the Bivalent BNT162b2 (WT/Omi BA.4/BA.5) Group from Study C4591044

End point title	GMT of SARS-CoV-2 Omi BA.4/BA.5-Neutralizing Titers at 1 Month After Vaccination: SSA and Historical Control of the Bivalent BNT162b2 (WT/Omi BA.4/BA.5) Group from Study C4591044[11][12]

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 included all eligible assigned participants who received the study intervention to which they were assigned, had at least 1 valid and determinate immunogenicity result from the blood sample collected within 28 to 42 days after the study vaccination, and had no other important protocol deviations as determined by the clinician. Here, Number of Participants Analysed signifies number of participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

At 1 month after vaccination

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: Only descriptive data was 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: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years	SSA Historical Control: C4591044 BNT162b2 12-17 years
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	26	167	187	15
Units: Titer				
geometric mean (confidence interval 95%)	7903.6 (4961.5 to 12590.4)	4831.8 (4044.5 to 5772.3)	5046.1 (4123.3 to 6175.3)	6376.3 (3568.4 to 11393.8)

End point values	SSA Historical Control: C4591044 BNT162b2 18-55 years	SSA Historical Control: C4591044 BNT162b2 >55 years	SSA Total Study Participants: C4591054	SSA Total Historical Control: C4591044 BNT162b2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	85	100	380	200
Units: Titer				
geometric mean (confidence interval 95%)	3868.2 (2974.8 to 5029.9)	4122.7 (3261.2 to 5211.6)	5105.1 (4483.4 to 5813.0)	4146.0 (3512.6 to 4893.5)

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rise (GMFR) of SARS-CoV-2 Omi XBB.1.5-Neutralizing Titers From Before Vaccination to 1 Month After Vaccination: SSA and Historical Control of the Bivalent BNT162b2 (WT/Omi BA.4/BA.5) Group from Study C4591044

End point title	Geometric Mean Fold Rise (GMFR) of SARS-CoV-2 Omi XBB.1.5-Neutralizing Titers From Before Vaccination to 1 Month After Vaccination: SSA and Historical Control of the Bivalent BNT162b2 (WT/Omi BA.4/BA.5) Group from Study C4591044[13][14]

End point description:

GMFR and 2-sided 95% CI 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 included all eligible assigned participants who received the study intervention to which they were assigned, had at least 1 valid and determinate immunogenicity result from the blood sample collected within 28 to 42 days after the study vaccination, and had no other important protocol deviations as determined by the clinician. Here, Number of Participants Analysed signifies number of participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

From before vaccination on Day 1 up to 1 month after vaccination

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: Only descriptive data was planned for this endpoint.

[14] - 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: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years	SSA Historical Control: C4591044 BNT162b2 12-17 years
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	27	165	184	15
Units: Fold rise				
geometric mean (confidence interval 95%)	11.8 (6.3 to 22.2)	10.7 (8.7 to 13.1)	13.5 (10.7 to 17.1)	7.1 (3.9 to 12.8)

End point values	SSA Historical Control: C4591044 BNT162b2 18-55 years	SSA Historical Control: C4591044 BNT162b2 >55 years	SSA Total Study Participants: C4591054	SSA Total Historical Control: C4591044 BNT162b2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	82	100	376	197
Units: Fold rise				
geometric mean (confidence interval 95%)	6.1 (4.5 to 8.3)	5.2 (4.1 to 6.5)	12.1 (10.4 to 14.0)	5.7 (4.8 to 6.8)

Statistical analyses

No statistical analyses for this end point

Primary: GMFR of SARS-CoV-2 Omi BA.4/BA.5-Neutralizing Titers From Before Vaccination to 1 Month After Vaccination: SSA and Historical Control of the Bivalent BNT162b2 (WT/Omi BA.4/BA.5) Group from Study C4591044

End point title	GMFR of SARS-CoV-2 Omi BA.4/BA.5-Neutralizing Titers From Before Vaccination to 1 Month After Vaccination: SSA and Historical Control of the Bivalent BNT162b2 (WT/Omi BA.4/BA.5) Group from Study C4591044[15][16]

End point description:

GMFR and 2-sided 95% CI 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 included all eligible assigned participants who received the study intervention to which they were assigned, had at least 1 valid and determinate immunogenicity result from the blood sample collected within 28 to 42 days after the study vaccination, and had no other important protocol deviations as determined by the clinician. Here, Number of Participants Analysed signifies number of participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

From before vaccination on Day 1 up to 1 month after vaccination

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: Only descriptive data was planned for this endpoint.

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years	SSA Historical Control: C4591044 BNT162b2 12-17 years
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	26	167	186	15
Units: Fold rise				
geometric mean (confidence interval 95%)	3.5 (2.2 to 5.8)	4.3 (3.7 to 5.0)	5.1 (4.3 to 6.2)	5.7 (3.4 to 9.4)

End point values	SSA Historical Control: C4591044 BNT162b2 18-55 years	SSA Historical Control: C4591044 BNT162b2 >55 years	SSA Total Study Participants: C4591054	SSA Total Historical Control: C4591044 BNT162b2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	85	100	379	200
Units: Fold rise				
geometric mean (confidence interval 95%)	6.2 (4.6 to 8.4)	7.4 (5.7 to 9.6)	4.6 (4.1 to 5.2)	6.8 (5.6 to 8.1)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Seroresponse to SARS-CoV-2 Omi XBB.1.5-Neutralizing Titers at 1 Month After Vaccination: SSA and Historical Control of the Bivalent BNT162b2 (WT/Omi BA.4/BA.5) Group from Study C4591044

End point title	Percentage of Participants With Seroresponse to SARS-CoV-2 Omi XBB.1.5-Neutralizing Titers at 1 Month After Vaccination: SSA and Historical Control of the Bivalent BNT162b2 (WT/Omi BA.4/BA.5) Group from Study C4591044[17][18]

End point description:

Seroresponse was defined as achieving >= 4-fold rise from baseline (before the study vaccination). If the baseline measurement was below the LLOQ, the postvaccination assay result of >= 4* LLOQ was considered a seroresponse. Exact 2-sided CI was based on the Clopper and Pearson method. Evaluable immunogenicity population included all eligible assigned participants who received the study intervention to which they were assigned, had at least 1 valid and determinate immunogenicity result from the blood sample collected within 28 to 42 days after the study vaccination, and had no other important protocol deviations as determined by the clinician. Here, Number of Participants Analysed signifies number of participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

At 1 month after vaccination

Notes:

[17] - 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: Only descriptive data was planned for this endpoint.

[18] - 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: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years	SSA Historical Control: C4591044 BNT162b2 12-17 years
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	27	165	184	15
Units: Percentage of Participants				
number (confidence interval 95%)	74.1 (53.7 to 88.9)	76.4 (69.1 to 82.6)	71.7 (64.6 to 78.1)	66.7 (38.4 to 88.2)

End point values	SSA Historical Control: C4591044 BNT162b2 18-55 years	SSA Historical Control: C4591044 BNT162b2 >55 years	SSA Total Study Participants: C4591054	SSA Total Historical Control: C4591044 BNT162b2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	82	100	376	197
Units: Percentage of Participants				
number (confidence interval 95%)	52.4 (41.1 to 63.6)	51.0 (40.8 to 61.1)	73.9 (69.2 to 78.3)	52.8 (45.6 to 59.9)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Seroresponse to SARS-CoV-2 Omi BA.4/BA.5-Neutralizing Titers at 1 Month After Vaccination: SSA and Historical Control of the Bivalent BNT162b2 (WT/Omi BA.4/BA.5) Group from Study C4591044

End point title	Percentage of Participants With Seroresponse to SARS-CoV-2 Omi BA.4/BA.5-Neutralizing Titers at 1 Month After Vaccination: SSA and Historical Control of the Bivalent BNT162b2 (WT/Omi BA.4/BA.5) Group from Study C4591044[19][20]

End point description:

Seroresponse was defined as achieving >= 4-fold rise from baseline (before the study vaccination). If the baseline measurement was below the LLOQ, the postvaccination assay result of >= 4* LLOQ was considered a seroresponse. Exact 2-sided CI was based on the Clopper and Pearson method. Evaluable immunogenicity population included all eligible assigned participants who received the study intervention to which they were assigned, had at least 1 valid and determinate immunogenicity result from the blood sample collected within 28 to 42 days after the study vaccination, and had no other important protocol deviations as determined by the clinician. Here, Number of Participants Analysed signifies number of participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

At 1 month after vaccination

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: Only descriptive data was planned for this endpoint.

[20] - 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: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years	SSA Historical Control: C4591044 BNT162b2 12-17 years
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	26	167	186	15
Units: Percentage of participants				
number (confidence interval 95%)	46.2 (26.6 to 66.6)	43.7 (36.1 to 51.6)	52.7 (45.3 to 60.0)	73.3 (44.9 to 92.2)

End point values	SSA Historical Control: C4591044 BNT162b2 18-55 years	SSA Historical Control: C4591044 BNT162b2 >55 years	SSA Total Study Participants: C4591054	SSA Total Historical Control: C4591044 BNT162b2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	85	100	379	200
Units: Percentage of participants				
number (confidence interval 95%)	58.8 (47.6 to 69.4)	65.0 (54.8 to 74.3)	48.3 (43.2 to 53.4)	63.0 (55.9 to 69.7)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Local Reactions Within 7 Days After Vaccination: SSB

End point title	Percentage of Participants With Local Reactions Within 7 Days After Vaccination: SSB[21][22]

End point description:

Local reactions: pain at injection site, redness and swelling recorded by participants in an e-diary or as AEs in the CRF. Redness & swelling measured & recorded in mdu (range:1 to 21), 1 mdu= 0.5 cm & were graded as mild (>2.0 to 5.0 cm), moderate (>5.0 to 10.0 cm), severe (>10.0 cm) & Grade 4 (necrosis [swelling] & necrosis or exfoliative dermatitis [redness]). Pain at injection site graded as mild (did not interfere with activity), moderate (interfered with activity), severe (prevented daily activity) & G4 (ER visit or hospitalisation for severe pain at injection site). G4 LR classified by investigator or medically qualified person. Exact 2-sided CI based on Clopper and Pearson method. Safety population: all participants who received study intervention. Number of Participants Analysed= Participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

Day 1 to Day 7 after vaccination

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: Only descriptive data was planned for this endpoint.

[22] - 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: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSB: Group 1: 12-17 years	SSB: Group 2: 18-55 years	SSB: Group 3: >55 years	SSB Total Study Participants
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	9	250	49	308
Units: Percentage of Participants				
number (confidence interval 95%)				
Redness: Any	0 (0.0 to 33.6)	8.8 (5.6 to 13.0)	2.0 (0.1 to 10.9)	7.5 (4.8 to 11.0)
Redness: Mild	0 (0.0 to 33.6)	5.6 (3.1 to 9.2)	2.0 (0.1 to 10.9)	4.9 (2.8 to 7.9)
Redness: Moderate	0 (0.0 to 33.6)	2.8 (1.1 to 5.7)	0 (0.0 to 7.3)	2.3 (0.9 to 4.6)
Redness: Severe	0 (0.0 to 33.6)	0.4 (0.0 to 2.2)	0 (0.0 to 7.3)	0.3 (0.0 to 1.8)
Redness: Grade 4	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
Swelling: Any	11.1 (0.3 to 48.2)	12.0 (8.2 to 16.7)	10.2 (3.4 to 22.2)	11.7 (8.3 to 15.8)
Swelling: Mild	11.1 (0.3 to 48.2)	6.8 (4.0 to 10.7)	8.2 (2.3 to 19.6)	7.1 (4.5 to 10.6)
Swelling: Moderate	0 (0.0 to 33.6)	5.2 (2.8 to 8.7)	2.0 (0.1 to 10.9)	4.5 (2.5 to 7.5)
Swelling: Severe	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)

Swelling: Grade 4	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
Pain at the injection site: Any	44.4 (13.7 to 78.8)	58.0 (51.6 to 64.2)	36.7 (23.4 to 51.7)	54.2 (48.5 to 59.9)
Pain at the injection site: Mild	44.4 (13.7 to 78.8)	36.4 (30.4 to 42.7)	32.7 (19.9 to 47.5)	36.0 (30.7 to 41.7)
Pain at the injection site: Moderate	0 (0.0 to 33.6)	21.2 (16.3 to 26.8)	4.1 (0.5 to 14.0)	17.9 (13.7 to 22.6)
Pain at the injection site: Severe	0 (0.0 to 33.6)	0.4 (0.0 to 2.2)	0 (0.0 to 7.3)	0.3 (0.0 to 1.8)
Pain at the injection site: Grade 4	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Systemic Events Within 7 Days After Vaccination: SSB

End point title	Percentage of Participants With Systemic Events Within 7 Days After Vaccination: SSB[23][24]

End point description:

Systemic events were recorded by participants in an e-diary or as AEs in the CRF. Fever: defined as oral temperature >=38 deg C and categorised as >= 38.0-38.4 deg C, >38.4-38.9 deg C, >38.9-40.0 deg C and >40.0 deg C. Fatigue, headache, chills, new or worsened muscle pain and joint pain: mild (didn't interfere with activity), moderate (some interference with activity), severe (prevented daily routine activity). Vomiting: mild: 1-2 times in 24h, moderate: >2 times in 24h, severe: required IV hydration. Diarrhoea: mild: 2-3 loose stools in 24h, moderate: 4-5 loose stools in 24h, severe: 6 or more loose stools in 24h. Grade 4 for all events except fever: ER visit/hospitalization. Grade 4 events were classified by investigator or medically qualified person. Exact 2-sided CI was based on Clopper and Pearson method. Safety population: All participants who received the study intervention. Number of Participants Analysed= Participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

Day 1 to Day 7 after vaccination

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: Only descriptive data was planned for this endpoint.

[24] - 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: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSB: Group 1: 12-17 years	SSB: Group 2: 18-55 years	SSB: Group 3: >55 years	SSB Total Study Participants
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	9	250	49	308
Units: Percentage of participants				
number (confidence interval 95%)				
Fever: Any	11.1 (0.3 to 48.2)	2.4 (0.9 to 5.2)	6.1 (1.3 to 16.9)	3.2 (1.6 to 5.9)
Fever: >=38.0 degree C to 38.4 degree C	0 (0.0 to 33.6)	0.8 (0.1 to 2.9)	4.1 (0.5 to 14.0)	1.3 (0.4 to 3.3)
Fever: >38.4 degree C to 38.9 degree C	11.1 (0.3 to 48.2)	1.2 (0.2 to 3.5)	0 (0.0 to 7.3)	1.3 (0.4 to 3.3)
Fever: >38.9 degree C to 40.0 degree C	0 (0.0 to 33.6)	0.4 (0.0 to 2.2)	2.0 (0.1 to 10.9)	0.6 (0.1 to 2.3)

Fever: >40.0 degree C	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
Fatigue: Any	11.1 (0.3 to 48.2)	34.8 (28.9 to 41.1)	24.5 (13.3 to 38.9)	32.5 (27.3 to 38.0)
Fatigue: Mild	0 (0.0 to 33.6)	13.6 (9.6 to 18.5)	8.2 (2.3 to 19.6)	12.3 (8.9 to 16.5)
Fatigue: Moderate	11.1 (0.3 to 48.2)	21.2 (16.3 to 26.8)	16.3 (7.3 to 29.7)	20.1 (15.8 to 25.0)
Fatigue: Severe	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
Fatigue: Grade 4	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
Headache: Any	11.1 (0.3 to 48.2)	30.8 (25.1 to 36.9)	16.3 (7.3 to 29.7)	27.9 (23.0 to 33.3)
Headache: Mild	11.1 (0.3 to 48.2)	12.0 (8.2 to 16.7)	12.2 (4.6 to 24.8)	12.0 (8.6 to 16.2)
Headache: Moderate	0 (0.0 to 33.6)	18.0 (13.4 to 23.3)	4.1 (0.5 to 14.0)	15.3 (11.4 to 19.8)
Headache: Severe	0 (0.0 to 33.6)	0.8 (0.1 to 2.9)	0 (0.0 to 7.3)	0.6 (0.1 to 2.3)
Headache: Grade 4	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
Chills: Any	11.1 (0.3 to 48.2)	12.0 (8.2 to 16.7)	10.2 (3.4 to 22.2)	11.7 (8.3 to 15.8)
Chills: Mild	11.1 (0.3 to 48.2)	7.2 (4.3 to 11.1)	4.1 (0.5 to 14.0)	6.8 (4.3 to 10.2)
Chills: Moderate	0 (0.0 to 33.6)	4.8 (2.5 to 8.2)	6.1 (1.3 to 16.9)	4.9 (2.8 to 7.9)
Chills: Severe	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
Chills: Grade 4	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
Vomiting: Any	0 (0.0 to 33.6)	4.8 (2.5 to 8.2)	2.0 (0.1 to 10.9)	4.2 (2.3 to 7.1)
Vomiting: Mild	0 (0.0 to 33.6)	2.4 (0.9 to 5.2)	2.0 (0.1 to 10.9)	2.3 (0.9 to 4.6)
Vomiting: Moderate	0 (0.0 to 33.6)	2.4 (0.9 to 5.2)	0 (0.0 to 7.3)	1.9 (0.7 to 4.2)
Vomiting: Severe	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
Vomiting: Grade 4	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
Diarrhoea: Any	11.1 (0.3 to 48.2)	16.8 (12.4 to 22.0)	8.2 (2.3 to 19.6)	15.3 (11.4 to 19.8)
Diarrhoea: Mild	11.1 (0.3 to 48.2)	10.0 (6.6 to 14.4)	6.1 (1.3 to 16.9)	9.4 (6.4 to 13.2)
Diarrhoea: Moderate	0 (0.0 to 33.6)	6.4 (3.7 to 10.2)	2.0 (0.1 to 10.9)	5.5 (3.2 to 8.7)
Diarrhoea: Severe	0 (0.0 to 33.6)	0.4 (0.0 to 2.2)	0 (0.0 to 7.3)	0.3 (0.0 to 1.8)
Diarrhoea: Grade 4	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
New or worsened muscle pain: Any	11.1 (0.3 to 48.2)	18.0 (13.4 to 23.3)	18.4 (8.8 to 32.0)	17.9 (13.7 to 22.6)
New or worsened muscle pain: Mild	11.1 (0.3 to 48.2)	8.0 (5.0 to 12.1)	10.2 (3.4 to 22.2)	8.4 (5.6 to 12.1)
New or worsened muscle pain: Moderate	0 (0.0 to 33.6)	10.0 (6.6 to 14.4)	8.2 (2.3 to 19.6)	9.4 (6.4 to 13.2)
New or worsened muscle pain: Severe	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
New or worsened muscle pain: Grade 4	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
New or worsened joint pain: Any	11.1 (0.3 to 48.2)	12.8 (8.9 to 17.6)	12.2 (4.6 to 24.8)	12.7 (9.2 to 16.9)
New or worsened joint pain: Mild	11.1 (0.3 to 48.2)	6.4 (3.7 to 10.2)	6.1 (1.3 to 16.9)	6.5 (4.0 to 9.9)
New or worsened joint pain: Moderate	0 (0.0 to 33.6)	6.4 (3.7 to 10.2)	6.1 (1.3 to 16.9)	6.2 (3.8 to 9.5)
New or worsened joint pain: Severe	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)
New or worsened joint pain: Grade 4	0 (0.0 to 33.6)	0 (0.0 to 1.5)	0 (0.0 to 7.3)	0 (0.0 to 1.2)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With AEs From Vaccination Through 1 Month After Vaccination: SSB

End point title	Percentage of Participants With AEs From Vaccination Through 1 Month After Vaccination: SSB[25][26]

End point description:

An AE was defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Percentage of participants reporting AEs from study vaccination on Day 1 up to 1 month after the study vaccination were reported in this endpoint. Exact 2-sided CI was based on Clopper and Pearson method. Only AEs collected by non-systematic assessment (i.e., excluding local reactions and systemic events) were reported in this endpoint. Safety population included all participants who received the study intervention.

End point type	Primary

End point timeframe:

From vaccination on Day 1 up to 1 month after vaccination

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: Only descriptive data was planned for this endpoint.

[26] - 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: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSB: Group 1: 12-17 years	SSB: Group 2: 18-55 years	SSB: Group 3: >55 years	SSB Total Study Participants
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	9	253	49	311
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0.0 to 33.6)	2.4 (0.9 to 5.1)	2.0 (0.1 to 10.9)	2.3 (0.9 to 4.6)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With SAEs From Vaccination Through 6 Months After the Study Vaccination: SSB

End point title	Percentage of Participants With SAEs From Vaccination Through 6 Months After the Study Vaccination: SSB[27][28]

End point description:

An SAE was defined as any untoward medical occurrence at any dose that resulted in any of the following outcomes: death; life-threatening; required inpatient hospitalization or prolongation of existing

hospitalization; persistent or significant disability/incapacity; congenital anomaly/birth defect; suspected transmission via a Pfizer product of an infectious agent, pathogenic or non-pathogenic; or considered as an important medical event. Percentage of participants reporting SAEs from study vaccination on Day 1 up to 6 months after the study vaccination were reported in this endpoint. Exact 2-sided CI was based on Clopper and Pearson method. Safety population included all participants who received the study intervention.

End point type	Primary

End point timeframe:

From vaccination on Day 1 up to 6 months after vaccination

Notes:

[27] - 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: Only descriptive data was planned for this endpoint.

[28] - 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: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	SSB: Group 1: 12-17 years	SSB: Group 2: 18-55 years	SSB: Group 3: >55 years	SSB Total Study Participants
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	9	253	49	311
Units: Percentage of participants				
number (confidence interval 95%)	0 (0.0 to 33.6)	0.8 (0.1 to 2.8)	2.0 (0.1 to 10.9)	1.0 (0.2 to 2.8)

Statistical analyses

No statistical analyses for this end point

Primary: Difference in Percentages of Participants With Seroresponse to the XBB.1.5 Strain 1 Month After BNT162b2 (Omi XBB.1.5): COVID-19 Vaccine-Naïve Participants in SSB Versus Vaccine-Experienced Participants in SSA

End point title	Difference in Percentages of Participants With Seroresponse to the XBB.1.5 Strain 1 Month After BNT162b2 (Omi XBB.1.5): COVID-19 Vaccine-Naïve Participants in SSB Versus Vaccine-Experienced Participants in SSA

End point description:

Seroresponse was defined as achieving >= 4-fold rise from baseline. If the baseline measurement was below the LLOQ, the postvaccination assay result of >= 4* LLOQ was considered a seroresponse. Percentage of participants with seroresponse is reported in descriptive section and percentage difference in statistical analysis section. Evaluable immunogenicity population included all eligible assigned participants who received the study intervention to which they were assigned, had at least 1 valid and determinate immunogenicity result from the blood sample collected within 28 to 42 days after the study vaccination, and had no other important protocol deviations as determined by the clinician. Here, Number of Participants Analysed signifies number of participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

At 1 month after vaccination

End point values	SSB: Vaccine-Naïve Substudy B	SSB Control: Vaccine-Experienced Substudy A		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	298	295		
Units: Percentage of participants				
number (confidence interval 95%)	84.9 (80.3 to 88.8)	73.9 (68.5 to 78.8)		

Statistical analyses

Statistical analysis title	Vaccine-Naïve SSB vs Vaccine-Experienced SSA

Statistical analysis description:

2-Sided CI, based on the Miettinen and Nurminen method stratified by baseline neutralizing titer category (< median, >= median) and age group (< median, >= median). Noninferiority based on seroresponse was declared if the lower limit of the 2-sided 95% CI for the difference in percentages was greater than -10%.

Comparison groups	SSB: Vaccine-Naïve Substudy B v SSB Control: Vaccine-Experienced Substudy A
Number of subjects included in analysis	593
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Percentage Difference
Point estimate	7.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.34
upper limit	13.28

Primary: Geometric Mean Ratio (GMR) of the SARS-CoV-2 XBB.1.5-Neutralizing Titers 1 Month After BNT162b2 (Omi XBB.1.5): COVID-19 Vaccine-Naïve Participants in SSB Versus Vaccine-Experienced Participants in SSA

End point title	Geometric Mean Ratio (GMR) of the SARS-CoV-2 XBB.1.5-Neutralizing Titers 1 Month After BNT162b2 (Omi XBB.1.5): COVID-19 Vaccine-Naïve Participants in SSB Versus Vaccine-Experienced Participants in SSA

End point description:

GMTs and 2-sided 95% CIs were calculated by exponentiating the least square (LS) means and the corresponding CIs based on analysis of log-transformed assay results using a linear regression model with baseline assay results (log scale), age and vaccine group as covariates. Assay results below the LLOQ were set to 0.5*LLOQ. GMT is reported in descriptive section and GMR in statistical analysis section. Evaluable immunogenicity population included all eligible assigned participants who received the study intervention to which they were assigned, had at least 1 valid and determinate immunogenicity result from the blood sample collected within 28 to 42 days after the study vaccination, and had no other important protocol deviations as determined by the clinician. Here, Number of Participants Analysed signifies number of participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

At 1 month after vaccination

End point values	SSB: Vaccine-Naïve Substudy B	SSB Control: Vaccine-Experienced Substudy A		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	298	295		
Units: Titer				
geometric mean (confidence interval 95%)	4951.6 (4222.8 to 5806.2)	2566.5 (2186.8 to 3012.1)		

Statistical analyses

Statistical analysis title	Vaccine-Naïve SSB vs Vaccine-Experienced SSA

Statistical analysis description:

GMRs and the corresponding 2-sided 95% CIs were calculated by exponentiating the difference in LS means (Substudy B - Substudy A) and the corresponding CIs based on analysis of log-transformed assay results using a linear regression model with baseline assay results (log scale), age and vaccine group as covariates. Noninferiority of GMR was met if the lower limit of the 95% CI was greater than 0.67.

Comparison groups	SSB: Vaccine-Naïve Substudy B v SSB Control: Vaccine-Experienced Substudy A
Number of subjects included in analysis	593
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Geometric mean ratio
Point estimate	1.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.52
upper limit	2.44

Adverse events information

Timeframe for reporting adverse events:

SSA & SSB: Systematic assessment: Local reactions, systemic events: Day 1 to Day 7 after vaccination (vacc.); Non-systematic assessment: SAEs: Day 1 of vacc. up to 6 months after study vacc. & Non-SAEs: Day 1 of vaccination up to 1 month after study vacc.

Adverse event reporting additional description:

Same event may appear as both AE and SAE but are distinct events. An event may be categorized as serious in 1 participant and non-serious in another, or a participant may have experienced both SAE and non-SAE.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26

Reporting groups

Reporting group title	SSA: Group 1: 12-17 years

Reporting group description:

Participants aged 12 to 17 years who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.

Reporting group title	SSA: Group 2: 18-55 years

Reporting group description:

Participants aged 18 to 55 years who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.

Reporting group title	SSA: Group 3: >55 years

Reporting group description:

Participants aged >55 years who received at least three prior doses of US-authorized mRNA COVID-19 vaccine with the most recent dose being the Omicron BA.4/BA.5 received at least 150 days prior to the study vaccination were included. Participants received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.

Reporting group title	SSB: Group 1: 12-17 years

Reporting group description:

Participants aged 12-17 years who were previously exposed to SARS-CoV-2 and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.

Reporting group title	SSB: Group 2: 18-55 years

Reporting group description:

Participants aged 18-55 years who were previously exposed to SARS-CoV-2 and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this study.

Reporting group title	SSB: Group 3: >55 years

Reporting group description:

Participants aged >55 years who were previously exposed to SARS-CoV-2 and were COVID-19 vaccine–naïve received a single dose of BNT162b2 (Omi XBB.1.5) 30 mcg via IM route on Day 1 of this

Serious adverse events	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 30 (3.33%)	0 / 174 (0.00%)	4 / 208 (1.92%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 30 (0.00%)	0 / 174 (0.00%)	1 / 208 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 30 (0.00%)	0 / 174 (0.00%)	1 / 208 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 30 (0.00%)	0 / 174 (0.00%)	0 / 208 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 30 (0.00%)	0 / 174 (0.00%)	1 / 208 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 30 (0.00%)	0 / 174 (0.00%)	0 / 208 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 174 (0.00%)	1 / 208 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paroxysmal nocturnal			

haemoglobinuria			
subjects affected / exposed	0 / 30 (0.00%)	0 / 174 (0.00%)	1 / 208 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 174 (0.00%)	0 / 208 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 174 (0.00%)	0 / 208 (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
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 174 (0.00%)	1 / 208 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	SSB: Group 1: 12-17 years	SSB: Group 2: 18-55 years	SSB: Group 3: >55 years
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	2 / 253 (0.79%)	1 / 49 (2.04%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Small intestinal obstruction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (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
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 253 (0.40%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (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
Paroxysmal nocturnal haemoglobinuria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (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
Appendicitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 253 (0.40%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (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

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

Non-serious adverse events	SSA: Group 1: 12-17 years	SSA: Group 2: 18-55 years	SSA: Group 3: >55 years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 30 (90.00%)	154 / 174 (88.51%)	134 / 208 (64.42%)
Nervous system disorders			
Restless arm syndrome			
subjects affected / exposed	1 / 30 (3.33%)	0 / 174 (0.00%)	0 / 208 (0.00%)
occurrences (all)	1	0	0
Headache (HEADACHE)			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 30 (36.67%)	76 / 174 (43.68%)	54 / 208 (25.96%)
occurrences (all)	11	76	54
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 30 (0.00%)	2 / 174 (1.15%)	0 / 208 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Fatigue (FATIGUE)			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 30 (56.67%)	99 / 174 (56.90%)	73 / 208 (35.10%)
occurrences (all)	17	99	73
Injection site erythema (REDNESS)			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 30 (10.00%)	7 / 174 (4.02%)	12 / 208 (5.77%)
occurrences (all)	3	7	12
Chills (CHILLS)			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 30 (20.00%)	16 / 174 (9.20%)	19 / 208 (9.13%)
occurrences (all)	6	16	19
Fatigue			

subjects affected / exposed	0 / 30 (0.00%)	2 / 174 (1.15%)	2 / 208 (0.96%)
occurrences (all)	0	2	2
Injection site pruritus			
subjects affected / exposed	1 / 30 (3.33%)	0 / 174 (0.00%)	0 / 208 (0.00%)
occurrences (all)	1	0	0
Injection site swelling (SWELLING)			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 30 (16.67%)	13 / 174 (7.47%)	12 / 208 (5.77%)
occurrences (all)	5	13	12
Injection site pain (PAIN)			
alternative assessment type: Systematic			
subjects affected / exposed	24 / 30 (80.00%)	132 / 174 (75.86%)	107 / 208 (51.44%)
occurrences (all)	24	132	107
Injection site pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 174 (0.00%)	4 / 208 (1.92%)
occurrences (all)	0	0	4
Pyrexia (FEVER)			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 30 (16.67%)	7 / 174 (4.02%)	8 / 208 (3.85%)
occurrences (all)	5	7	8
Non-cardiac chest pain			
subjects affected / exposed	0 / 30 (0.00%)	2 / 174 (1.15%)	1 / 208 (0.48%)
occurrences (all)	0	2	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 30 (0.00%)	3 / 174 (1.72%)	0 / 208 (0.00%)
occurrences (all)	0	3	0
Vomiting (VOMITING)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 30 (0.00%)	4 / 174 (2.30%)	0 / 208 (0.00%)
occurrences (all)	0	4	0
Diarrhoea (DIARRHEA)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 30 (0.00%)	21 / 174 (12.07%)	18 / 208 (8.65%)
occurrences (all)	0	21	18

Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 30 (0.00%)	2 / 174 (1.15%)	0 / 208 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 30 (3.33%)	0 / 174 (0.00%)	0 / 208 (0.00%)
occurrences (all)	1	0	0
Heavy menstrual bleeding			
subjects affected / exposed	1 / 30 (3.33%)	0 / 174 (0.00%)	0 / 208 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 30 (3.33%)	0 / 174 (0.00%)	0 / 208 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Myalgia (MUSCLE PAIN)			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 30 (23.33%)	38 / 174 (21.84%)	25 / 208 (12.02%)
occurrences (all)	7	38	25
Arthralgia (JOINT PAIN)			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 30 (16.67%)	25 / 174 (14.37%)	16 / 208 (7.69%)
occurrences (all)	5	25	16
Pain in extremity			
subjects affected / exposed	0 / 30 (0.00%)	0 / 174 (0.00%)	0 / 208 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Sialoadenitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 174 (0.00%)	0 / 208 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 30 (3.33%)	0 / 174 (0.00%)	0 / 208 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	SSB: Group 1: 12-17 years	SSB: Group 2: 18-55 years	SSB: Group 3: >55 years

Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 9 (44.44%)	167 / 253 (66.01%)	25 / 49 (51.02%)
Nervous system disorders			
Restless arm syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Headache (HEADACHE)			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 9 (11.11%)	76 / 253 (30.04%)	8 / 49 (16.33%)
occurrences (all)	1	76	8
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 9 (0.00%)	1 / 253 (0.40%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue (FATIGUE)			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 9 (11.11%)	87 / 253 (34.39%)	12 / 49 (24.49%)
occurrences (all)	1	87	12
Injection site erythema (REDNESS)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 9 (0.00%)	22 / 253 (8.70%)	1 / 49 (2.04%)
occurrences (all)	0	22	1
Chills (CHILLS)			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 9 (11.11%)	30 / 253 (11.86%)	5 / 49 (10.20%)
occurrences (all)	1	30	5
Fatigue			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Injection site pruritus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Injection site swelling (SWELLING)			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 9 (11.11%)	30 / 253 (11.86%)	5 / 49 (10.20%)
occurrences (all)	1	30	5
Injection site pain (PAIN)			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 9 (44.44%)	142 / 253 (56.13%)	18 / 49 (36.73%)
occurrences (all)	4	142	18
Injection site pain			
subjects affected / exposed	0 / 9 (0.00%)	5 / 253 (1.98%)	0 / 49 (0.00%)
occurrences (all)	0	5	0
Pyrexia (FEVER)			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 9 (11.11%)	6 / 253 (2.37%)	3 / 49 (6.12%)
occurrences (all)	1	6	3
Non-cardiac chest pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Vomiting (VOMITING)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 9 (0.00%)	12 / 253 (4.74%)	1 / 49 (2.04%)
occurrences (all)	0	12	1
Diarrhoea (DIARRHEA)			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 9 (11.11%)	42 / 253 (16.60%)	4 / 49 (8.16%)
occurrences (all)	1	42	4
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0

Heavy menstrual bleeding			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia (MUSCLE PAIN)			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 9 (11.11%)	45 / 253 (17.79%)	9 / 49 (18.37%)
occurrences (all)	1	45	9
Arthralgia (JOINT PAIN)			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 9 (11.11%)	32 / 253 (12.65%)	6 / 49 (12.24%)
occurrences (all)	1	32	6
Pain in extremity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	1
Infections and infestations			
Sialoadenitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 9 (0.00%)	0 / 253 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported