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Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

COMIRNATY

COVID-19 mRNA vaccine

Procedure no: EMEA/H/C/005735/P46/070

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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Status of this report and steps taken for the assessment			
Current step	**Description**	**Planned date**	**Actual Date**
☐	Start of procedure	27 May 2024	27 May 2024
☐	CHMP Rapporteur Assessment Report	01 July 2024	26 June 2024
☐	CHMP members comments	15 July 2024	n/a
☐	Updated CHMP Rapporteur Assessment Report	18 July 2024	18 July 2024
☒	CHMP adoption of conclusions:	25 July 2024	25 July 2024

Table of contents

1. Introduction

On 29 April 2024, the MAH submitted a completed paediatric study for Comirnaty, in accordance with Article 46 of Regulation (EC) No 1901/2006, as amended.

These data are also submitted as part of the post-authorisation measures to assess the safety, tolerability, immunogenicity, and efficacy of the BNT162b2 RNA-based COVID-19 vaccine candidate against COVID-19 in healthy paediatric subjects.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that "Children 6 Months to <16 Years of Age: A Phase 1, Open-Label Dose-Finding Study to Evaluate Safety, Tolerability, and Immunogenicity and Phase 2/3 Placebo-Controlled, Observer-Blinded Safety, Tolerability, and Immunogenicity Study of a SARS-CoV-2 RNA Vaccine Candidate Against COVID-19 in Healthy Children" C4591007 is a stand-alone study.

This report concerns the final clinical study report (CSR) for the phase I/II/III study C4591007, which includes descriptive summary of COVID-19 incidence rate and cases for all study phases, plus data that has not been previously reported in an interim CSR.

2.2. Information on the pharmaceutical formulation used in the study

In the European Union, the Tris/Sucrose vaccine product is supplied as a preservative-free, sterile dispersion of LNPs in aqueous cryoprotectant buffer for intramuscular administration formulated at 0.1 mg/mL RNA in 10 mM Tris buffer, 300 mM sucrose, pH 7.4. The presentations of the vaccine used in this study are:

- 30 µg RNA/dose for individuals ≥12 years of age, not for dilution (0.3 mL administration), EU MA numbers EU/1/20/1528/003 and EU/1/20/1528/002.
- 10 µg RNA/dose for individuals 5 to 11 years of age, requires dilution (0.2 mL administration), EU MA numbers EU/1/20/1528/004 and EU/1/20/1528/005.
- 3 µg RNA/dose of the Tris/Sucrose vaccine product (requires dilution, 0.2 mL administration) for individuals 6 months through 4 years of age, EU MA numbers EU/1/20/1528/010.

2.3. Clinical aspects

2.3.1. Introduction

Study C4591007 is a randomised, placebo-controlled, Phase 1/2/3 paediatric study in healthy children aged 6 months to <12 years of age. For these paediatric groups, the study was designed to evaluate BNT162b2 vaccination in an age-de-escalation Phase 1 dose-finding portion and Phase 2/3 selected-dose portion, in protocol-defined age groups: 5 to <12 years, 2 to <5 years, and 6 months to <2 years of age. Initiation of the study with the oldest paediatric group (5 to <12 years of age) was based on acceptable safety and tolerability demonstrated in adolescents in Study C4591001. The BNT162b2 series was initially planned as a 2-dose series; however, based on emerging clinical and real-world data, the protocol was amended on 04 January 2022 to add a third dose at the selected dose level for each age group.

BNT162b2 10 µg for children aged 5 to 11 years of age was approved in EU on 25 November 2021. Comirnaty 3 µg for children aged 6 months to 4 years was approved in EU on 19 October 2022.

A bivalent (original and Omicron BA.4/BA.5) booster (30 µg) dose was granted EUA in the US for individuals ≥12 years of age on 31 August 2022. An EUA for the bivalent booster (10 µg) in individuals 5 through 11 years of age followed on 12 October 2022. The EUA for the bivalent booster (3 µg) as the third dose in the primary series (3 doses) in children 6 months to <5 years of age was authorised on 08 December 2022. As of 18 April 2023, the US FDA reissued the EUA for the original/Omicron BA.4/BA.5 bivalent mRNA COVID-19 vaccines to be used for all doses administered to individuals 6 months of age and older. In early 2023, the WHO, EMA, and FDA recommended that updated COVID-19 vaccines target the XBB.1.5 Omicron subvariant as a monovalent vaccine.

Previous C4591007 Interim CSRs

Data from Study C4591007 has been previously reported in the following interim CSRs:

Participants 5 to <12 Years of Age

- One-month post–Dose 2 safety, tolerability, immunogenicity, and descriptive efficacy results following administration of a 2-dose primary series of BNT162b2 10 µg in participants 5 to <12 years of age. Safety data were presented for the initial enrollment of 2268 participants (1518 vaccine recipients and 750 placebo recipients) in C4591007 (5 to <12 Years of Age) Interim CSR Version 1.0, dated 30 September 2021.
- Six-month post–Dose 2 safety follow-up data and a formal assessment of per-protocol efficacy for 4647 participants 5 to <12 years of age were previously reported in C4591007 (5 to <12 Years of Age 6-Month Post-Dose 2) Interim CSR Version 1.0, dated 31 October 2022.
- One-month post–Dose 3 (booster) data of BNT162b2 in 401 participants 5 to <12 years of age who received a 2-dose primary series followed by a third (booster) dose of BNT162b2 10 µg were previously submitted in C4591007 (5 to <12 Years of Age Dose 3) Interim CSR Version 2.0, dated 11 May 2022.
- Six-month post–Dose 3 data of BNT162b2 for all participants in the full safety population of participants 5 to <12 years of age who received a 2-dose primary series followed by Dose 3 of BNT162b2 10 µg (2408 participants in the original BNT162b2 group and 955 participants in the original placebo who received BNT162b2 after unblinding) were previously reported in C4591007 (6 Months to <12 Years of Age 6-Month Post-Dose 3) Interim CSR Version 1.0, dated 08 November 2023. (EMEA/H/C/005735/II/0203)

Participants 6 Months to <5 Years of Age

- 1 month after Dose 2 and 1 month after Dose 3 safety, tolerability, immunogenicity, and descriptive efficacy data following the 3-dose primary series of BNT162b2 3 µg for 4526 participants 6 months to <5 years of age
    - 2750 participants 2 to <5 years of age
    - 1776 participants 6 months to <2 years of age
- Data for these participants were previously submitted in C4591007 (6 Months to <5 Years of Age Three-Dose Series) Interim CSR Version 1.0, dated 01 July 2022.

This study was conducted at 111 sites in the US, Spain, Finland, Poland, and Brazil. The data cutoff dates for this interim CSR are 17 June 2022 (efficacy, 6 months to <5 years of age) and 28 February 2023 (6-month post–Dose 3 safety, 6 months to <12 years of age).

- Six-month post–Dose 3 safety data following the 3-dose primary series of BNT162b2 3 µg of BNT162b2 in 5720 participants 6 months to <5 years of age.
    - 3543 participants 2 to <5 years of age
    - 2177 participants 6 months to <2 years of age
- Formal per-protocol assessment of efficacy in 1993 participants 6 months to <5 years of age.

Data for these participants in the full safety population were previously reported in the C4591007 (6 Months to <12 Years of Age Dose 3) Interim CSR Version 1.0, dated 08 November 2023.

The purpose of this report is to describe the results presented in the Study C4591007 Final CSR evaluating Pfizer BioNTech's BNT162b2 in children 6 months to <16 years of age, which includes descriptive summary of COVID-19 incidence rate and cases for all study phases, plus data that have not been previously reported in an interim CSR, as follows:

Phase 1

- Post-Dose 3 safety data (reactogenicity, AE, and SAE) and SAE data from Dose 1 to 6 months after Dose 3 in participants 6 months to <2 years of age, 2 to <5 years of age, and 5 to <12 years of age.
- Description of COVID-19 occurrences, severe COVID-19 occurrences, and multisystem inflammatory syndrome in children (MIS-C) cases (if applicable) in the Dose 1 all-available efficacy population through end of study.

Phase 2/3

- Description of complete safety data for participants in the troponin I testing portion of the study (age groups: 5 to <12 years and 12 to <16 years). This includes description of the reactogenicity and AE data following Doses 1, 2 and 3, frequency of elevated troponin I levels at baseline and after Vaccination 2 and/or 3.
- Description of cell-mediated immune response to the reference strain in a subset of participants 10 to <12 years of age.
- Description of the incidence of confirmed COVID-19 through the entire study follow-up period in participants who received BNT162b2 at initial randomization or subsequently.
- SAE data from Dose 1 to 6 months after Dose 2 in participants 6 months to <2 years of age, 2 to <5 years of age, and 5 to <12 years of age.
- Description of COVID-19 occurrences, severe COVID-19 occurrences, and MIS-C cases (if applicable) in the Dose 1 all-available efficacy population through end of study.

2.3.2. Clinical study

Study C4591007 - Children 6 Months to <16 Years of Age: A Phase 1, Open-Label Dose-Finding Study to Evaluate Safety, Tolerability, and Immunogenicity and Phase 2/3 Placebo-Controlled, Observer-Blinded Safety, Tolerability, and Immunogenicity Study of a SARS-CoV-2 RNA Vaccine Candidate Against COVID-19 in Healthy Children

Study Design

Study C4591007 was a Phase 1/2/3 study in healthy children.

Phase 1 enrolled 16 participants per dose level in each age group (planned); however, an additional 16 participants per dose level (total 32) were enrolled to receive 10 µg in the 2 to <5 years of age group. The doses tested and selected in each age group during Phase 1 were:

- 5 to <12 years of age: dose levels 10, 20, 30 µg – selected dose level 10 µg
- 2 to <5 years of age: dose levels 3, 10 µg – selected dose level 3 µg
- 6 months to <2 years of age: dose level 3 µg – selected dose level 3 µg

Phase 2/3 commenced with the selected vaccine dose level for each age group, with participants randomised 2:1 to receive vaccine or placebo at sites in the US, Finland, Poland, and Spain. Brazil enrolled participants 6 months to <5 years of age randomised 2:1 to receive vaccine or placebo.

Phase 2/3 was planned to evaluate BNT162b2 as a 2-dose series given 21 days apart at the selected dose levels for each age group for safety, tolerability, and immunogenicity, and to include supportive efficacy analyses evaluated within or across age groups in which immunobridging is successful, depending on the accrual of a sufficient number of cases in those age groups.

All Phase 2/3 study participants could be unblinded at the 6-month post–Dose 2 follow-up visit. Participants who originally received placebo for the initial 2 doses were offered the opportunity to receive BNT162b2 (at the age-appropriate dose at the time of vaccination) as part of the study.

For participants 6 months to <5 years of age, the study was unblinded in stages. Unblinding completed once all ongoing participants either had been individually unblinded or had concluded their 6-month post–Dose 2 study visit. Due to several waves of enrollment and stages of unblinding, there were different lengths of follow-up time for participants 6 months to <5 years of age (refer to Section 3.7 and Figure 1 for additional information). The study was unblinded in the following sequence.

The participant:

- became EUA age-eligible at 5 years of age
- enrolled prior to protocol amendment 6 (addition of 3rd dose as primary series for 6m-<5y)
- enrolled after protocol amendment 6

All remaining participants 6 months to <5 years of age were unblinded after the US FDA issued an EUA (17 June 2022) for BNT162b2 3 µg as a 3-dose primary series. Placebo participants were eligible to receive BNT162b2 at the age-appropriate dose level in an open- label manner. As enrolment was ongoing at the time of the EUA, participants may have been unblinded prior to the protocol-specified 6-month post–Dose 2 period. In all case of unblinding, participants who remained in the study were followed in an open-label manner until the end of the study participation.

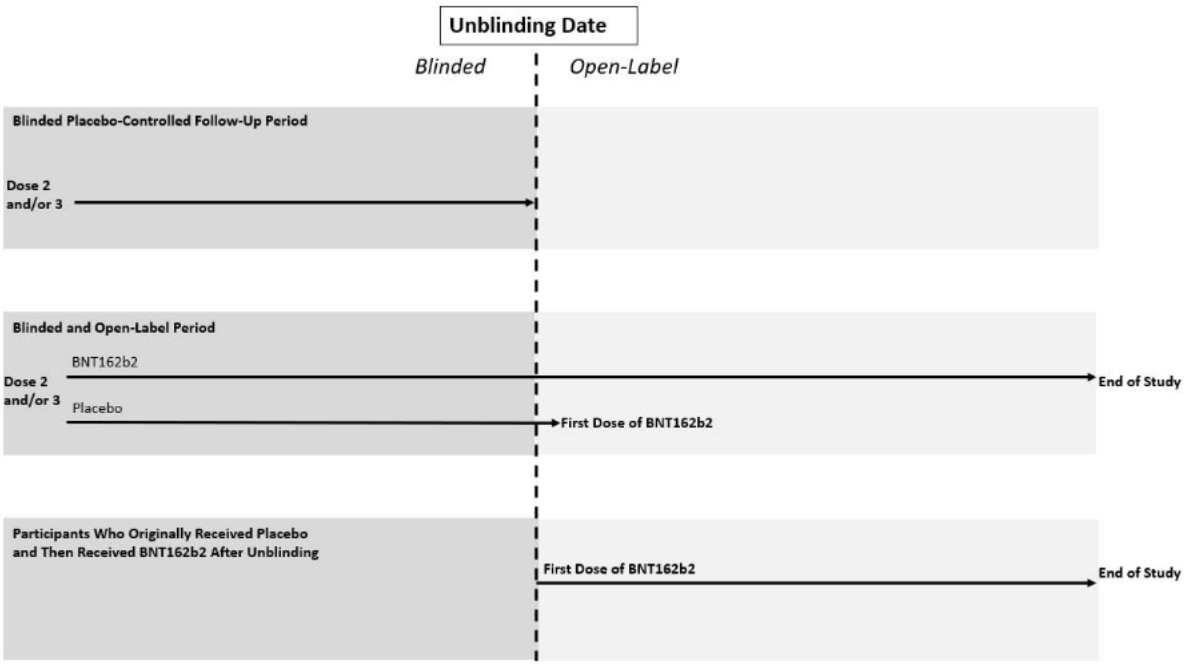

Figure 1 Schematic Diagram of Varied Blinded and open-label follow up time for participants 6 months to <5 years of age after dose 2 and/or dose 3

Troponin group

In the troponin group, troponin I assessment at baseline and after vaccination was performed to evaluate whether elevated troponin I levels, potentially indicative of subclinical myocarditis, occurred following vaccination. Samples were analysed using a High Sensitivity Troponin-I assay. An elevated troponin I result was defined as >35 ng/L in male participants and >17 ng/L in female participants. These values were established as the 99th percentile cut-off in male and female individuals, respectively, in a reference range study conducted by the assay manufacturer.

Troponin I Analyses: At Baseline and After Vaccination in Participants ≥5 to <12 Years of Age and ≥12 to <16 Years of Age (Troponin Group).

Troponin I level in participants ≥5 to <12 years of age and ≥12 to <16 years of age in the participants specifically enrolled for this purpose (troponin group) were drawn at baseline and on Day 4 after Dose 2 of vaccine or placebo (if ≥5 to <12 years). As a result of the 2 dose primary series EUA with BNT162b2 10 µg for individuals ≥5 to <12 years, participants were unblinded prior to the 6 months post-Dose 2 visit in this age group. Participants who received placebo crossed over to the BNT162b2 group and did not have an additional blood draw after Dose 2. With the emergence of Omicron and adult clinical trial data showing an improved Omicron response after Dose 3, a third dose was added for all study participants. Collection of a blood sample for troponin I level analysis was included for the troponin group on Day 4 after Dose 3 for participants ≥5 to <12 years of age who originally received active vaccine and for all participants ≥12 to <16 years of age.

In addition to the scheduled testing of troponin I after Dose 2 and Dose 3 in the troponin group participants, potential symptoms of myocarditis and pericarditis, protocol-specified AESIs in Study C4591007, were monitored in all participants. Per Section 8.14 of the protocol, specified procedures were to be followed for any study participant who reported acute chest pain, shortness of breath, palpitations, or any other symptom(s) that in the medical opinion of the investigator might be indicative of myocarditis or pericarditis within 4 weeks after a study vaccination.

Disposition

This study was conducted at 119 sites in the US, Spain, Finland, Poland, Mexico, and Brazil.

Phase 1

Table 1: Disposition of all assigned participants – Phase 1 – 5 to 12< years of age

	Vaccine Group (as Assigned)			
	BNT162b2 (10 µg) (N^b=16) n^c (%)	BNT162b2 (20 µg) (N^b=17) n^c (%)	BNT162b2 (30[a] µg) (N^b=16) n^c (%)	Total (N^b=49) n^c (%)
Assigned	16 (100.0)	17 (100.0)	16 (100.0)	49 (100.0)
Not vaccinated	0	1 (5.9)	0	1 (2.0)
Vaccinated	16 (100.0)	16 (94.1)	16 (100.0)	48 (98.0)
Dose 1	16 (100.0)	16 (94.1)	16 (100.0)	48 (98.0)
Dose 2	16 (100.0)	16 (94.1)	16 (100.0)	48 (98.0)
Dose 3	16 (100.0)	8 (47.1)	16 (100.0)	40 (81.6)
Completed the study	2 (12.5)	3 (17.6)	3 (18.8)	8 (16.3)
Withdrawn from the study	14 (87.5)	13 (76.5)	13 (81.3)	40 (81.6)
Reason for withdrawal from the study				
Protocol deviation	5 (31.3)	9 (52.9)	7 (43.8)	21 (42.9)
Withdrawal by parent/guardian/participant	1 (6.3)	2 (11.8)	1 (6.3)	4 (8.2)
Other	8 (50.0)	2 (11.8)	5 (31.3)	15 (30.6)

a. Of the 16 participants who received BNT162b2 30 µg at Dose 1, 4 participants received BNT162b2 30 µg at Dose 2 and 12 participants received BNT162b2 10 µg at Dose 2.
b. N = number of assigned participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
c. n = Number of participants with the specified characteristic.
PFIZER CONFIDENTIAL SDTM Creation: 09JAN2024 (03:56) Source Data: adds Table Generation: 23JAN2024 (01:35)
(Database snapshot date : 05JAN2024) Output File: ./nda2_ubped2/C4591007_CSR/adds_s002_disp_p1_12

All participants in the 10 µg and 30-µg groups received Dose 3 of BNT162b2 and 47.1% of participants in the 20-µg group received Dose 3 of BNT162b2. Of the 16 participants assigned to the 30-µg dose level group at Dose 1, the 4 sentinel participants received 30 µg at Dose 2. However, due to increased reactogenicity observed at the 30-µg dose level, the remaining 12 participants received 10 µg at Dose 2 as this dose was selected for Phase 2/3 in this age group. Dose 3 reflects age-appropriate dosing for all Phase 1 participants. The 30-µg dose level was discontinued in the study.

Table 2: Disposition of all assigned participants – Phase 1 – 2 to <5 years of age

	Vaccine Group (as Assigned)		
	BNT162b2 (3 µg) (N^a=16) n^b (%)	BNT162b2 (10 µg) (N^a=33) n^b (%)	Total (N^a=49) n^b (%)
Assigned	16 (100.0)	33 (100.0)	49 (100.0)
Not vaccinated	0	1 (3.0)	1 (2.0)
Vaccinated	16 (100.0)	32 (97.0)	48 (98.0)
Dose 1	16 (100.0)	32 (97.0)	48 (98.0)
Dose 2	16 (100.0)	32 (97.0)	48 (98.0)
Dose 3	13 (81.3)	27 (81.8)	40 (81.6)

Completed the study	7 (43.8)	14 (42.4)	21 (42.9)
Withdrawn from the study	9 (56.3)	18 (54.5)	27 (55.1)
Reason for withdrawal from the study			
Lost to follow-up	1 (6.3)	2 (6.1)	3 (6.1)
Protocol deviation	2 (12.5)	8 (24.2)	10 (20.4)
Withdrawal by parent/guardian/participant	3 (18.8)	4 (12.1)	7 (14.3)
Other	3 (18.8)	4 (12.1)	7 (14.3)

a. N = number of assigned participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic.
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(Database snapshot date : 05JAN2024) Output File: ./nda2_ubped2/C4591007_CSR/adds_s002_disp_p1_5

All participants aged 6 months to <2 years of age received Dose 1 and Dose 2 of BNT162b2 3 µg, and 93.8% received Dose 3. A total of 8 participants (50.0%) completed the study and 8 participants (50.0%) withdrew from the study, with the majority reason due to "other" (37.5%). One participant (6.3%) each withdrew due to protocol deviation and withdrawal by parent/guardian/participant.

Phase 2/3

Table 3: Disposition of all randomized participants – Phase 2/3 – selected dose portion – 5 to<12 years of age

	Vaccine Group (as Randomized)		
	BNT162b2 (10 µg) n[a] (%)	Placebo n[a] (%)	Total n[a] (%)
Randomized[b]	3127 (100.0)	1553 (100.0)	4680 (100.0)
Not vaccinated	19 (0.6)	14 (0.9)	33 (0.7)
Vaccinated	3108 (99.4)	1539 (99.1)	4647 (99.3)
Dose 1	3108 (99.4)	1539 (99.1)	4647 (99.3)
Dose 2	3100 (99.1)	1533 (98.7)	4633 (99.0)
Dose 3	2554 (81.7)	1 (0.1)	2555 (54.6)
Completed the study	1604 (51.3)	636 (41.0)	2240 (47.9)
Withdrawn from study	1504 (48.1)	903 (58.1)	2407 (51.4)
Reason for withdrawal from study			
Lost to follow-up	126 (4.0)	41 (2.6)	167 (3.6)
Protocol deviation	474 (15.2)	272 (17.5)	746 (15.9)
Withdrawal by parent/guardian/participant	816 (26.1)	543 (35.0)	1359 (29.0)
Refused further study procedures	2 (0.1)	0	2 (0.0)
Other	86 (2.8)	47 (3.0)	133 (2.8)

Note: One participant from 5-<12 years of age mis-stratified to 2-<5 age group and randomized to BNT162b2 3 µg is not included in this table.
a. n = Number of participants with the specified characteristic.
b. These values are the denominators for the percentage calculations.
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(Database snapshot date : 05JAN2024) Output File: ./nda2_ubped2/C4591007_CSR/adds_s002_disp_p2_12

Of participants who originally received placebo and then received BNT162b2, the majority (100.0%, 99.4%, and 83.0%) received crossover Dose 1, 2, and 3 of BNT162b2, respectively. Approximately half of the participants (50.4%) who originally received placebo and then received BNT162b2 after unblinding, completed the study after BNT162b2 vaccination. A total of 626 participants (49.6%) who originally received placebo and then received BNT162b2 after unblinding withdrew from the study for non-safety reasons. Most of these withdrawals were due to withdrawal by parent/guardian/participant (26.6%).

Table 4: Disposition of all randomized participants – phase 2/3 – selected dose portion – 2 to <5 years of age

	Vaccine Group (as Randomized)		
	BNT162b2 (3 µg) n[a] (%)	Placebo n[a] (%)	Total n[a] (%)
Randomized[b]	2378 (100.0)	1184 (100.0)	3562 (100.0)
Not vaccinated	13 (0.5)	6 (0.5)	19 (0.5)
Vaccinated	2365 (99.5)	1178 (99.5)	3543 (99.5)
Dose 1	2365 (99.5)	1178 (99.5)	3543 (99.5)
Dose 2	2338 (98.3)	1078 (91.0)	3416 (95.9)
Dose 3	2093 (88.0)	410 (34.6)	2503 (70.3)
Completed the study	1211 (50.9)	411 (34.7)	1622 (45.5)
Withdrawn from study	1154 (48.5)	767 (64.8)	1921 (53.9)
Reason for withdrawal from study			
Adverse event	3 (0.1)	0	3 (0.1)
Lost to follow-up	109 (4.6)	55 (4.6)	164 (4.6)
Physician decision	2 (0.1)	1 (0.1)	3 (0.1)
Protocol deviation	148 (6.2)	82 (6.9)	230 (6.5)
Withdrawal by parent/guardian/participant	428 (18.0)	458 (38.7)	886 (24.9)
Other	464 (19.5)	171 (14.4)	635 (17.8)

a. n = Number of participants with the specified characteristic.
b. These values are the denominators for the percentage calculations.
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(Database snapshot date : 05JAN2024) Output File: ./nda2_ubped2/C4591007_CSR/adds_s002_disp_p2_5

Of participants who originally received placebo and then received BNT162b2, the majority (100%, 98.1%, and 88.2%) received Dose 1, 2, and 3 of BNT162b2, respectively. Approximately half of the participants (48.4%) who originally received placebo and then received BNT162b2 withdrew from the study after BNT162b2 vaccination. Most of the withdrawals were due to other (21.6%) and withdrawal by parent/guardian/participant (17.2%). Most participants who withdrew for "other" reasons, withdrew to be enrolled in Study C4591048.

Table 5: Disposition of all randomized participants – phase 2/3 – selected dose portion – 6 months to <2 years of age

	Vaccine Group (as Randomized)		
	BNT162b2 (3 µg) n[a] (%)	Placebo n[a] (%)	Total n[a] (%)
Randomized[b]	1460 (100.0)	729 (100.0)	2189 (100.0)
Not vaccinated	9 (0.6)	3 (0.4)	12 (0.5)
Vaccinated	1451 (99.4)	726 (99.6)	2177 (99.5)
Dose 1	1451 (99.4)	726 (99.6)	2177 (99.5)
Dose 2	1437 (98.4)	680 (93.3)	2117 (96.7)
Dose 3	1324 (90.7)	245 (33.6)	1569 (71.7)
Completed the study	705 (48.3)	269 (36.9)	974 (44.5)
Withdrawn from study	746 (51.1)	457 (62.7)	1203 (55.0)
Reason for withdrawal from study			
Adverse event	1 (0.1)	0	1 (0.0)
Lost to follow-up	53 (3.6)	23 (3.2)	76 (3.5)
Physician decision	3 (0.2)	1 (0.1)	4 (0.2)
Protocol deviation	25 (1.7)	16 (2.2)	41 (1.9)
Withdrawal by parent/guardian/participant	199 (13.6)	196 (26.9)	395 (18.0)
Other	465 (31.8)	221 (30.3)	686 (31.3)

a. n = Number of participants with the specified characteristic.
b. These values are the denominators for the percentage calculations.
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(Database snapshot date : 05JAN2024) Output File: ./nda2_ubped2/C4591007_CSR/adds_s002_disp_p2_2

Of participants who originally received placebo and then received BNT162b2, the majority (100.0%, 97.8%, and 91.8%) received Dose 1, 2, and 3 of BNT162b2, respectively. A total of 321 participants (55.2%) who originally received placebo and then received BNT162b2 withdrew from the study after BNT162b2 vaccination. Most of the withdrawals were due to other (37.6%). Most participants who withdrew for "other" reasons, withdrew to be enrolled in Study C4591048.

Phase 2/3 Troponin Group

Table 6: Disposition of all randomized participants – phase 2/3 – Troponin Group – 5 to <12 years of age

	Vaccine Group (as Randomized)		
	BNT162b2 (10 µg) n[a] (%)	Placebo n[a] (%)	Total n[a] (%)
Randomized[b]	523 (100.0)	261 (100.0)	784 (100.0)
Not vaccinated	5 (1.0)	1 (0.4)	6 (0.8)
Vaccinated	518 (99.0)	260 (99.6)	778 (99.2)
Dose 1	518 (99.0)	260 (99.6)	778 (99.2)
Dose 2	514 (98.3)	110 (42.1)	624 (79.6)
Dose 3	429 (82.0)	0	429 (54.7)
Completed the study	395 (75.5)	188 (72.0)	583 (74.4)
Withdrawn from study	123 (23.5)	72 (27.6)	195 (24.9)
Reason for withdrawal from study			
Lost to follow-up	14 (2.7)	10 (3.8)	24 (3.1)
Physician decision	1 (0.2)	1 (0.4)	2 (0.3)
Protocol deviation	31 (5.9)	20 (7.7)	51 (6.5)
Withdrawal by parent/guardian/participant	66 (12.6)	37 (14.2)	103 (13.1)
Other	11 (2.1)	4 (1.5)	15 (1.9)

a. n = Number of participants with the specified characteristic.
b. These values are the denominators for the percentage calculations.
PFIZER CONFIDENTIAL SDTM Creation: 09JAN2024 (03:56) Source Data: adds Table Generation: 23JAN2024 (01:37)
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The majority of participants aged 5 to <12 years, who originally received placebo then received BNT162b2 after unblinding received Dose 1 (100.0%), Dose 2 (98.4%) and Dose 3 (86.8%). In participants who originally received placebo and then received BNT162b2 after unblinding, 55 participants (22.6%) withdrew from the study after BNT162b2 vaccination.

The safety population in this age group of the troponin group included a total of 778 (99.2%) of 784 randomised participants. A total of 6 randomised participants (0.8%) did not receive study vaccination and were excluded from the safety population. In the safety population, 518 and 260 participants were in the BNT162b2 group and placebo group, respectively.

Among the participants aged 12 to <16 years, the majority of participants in the BNT162b2 group received Dose 1 (99.8%), Dose 2 (97.8%) and Dose 3 (89.2%). A total of 443 participants (87.4%) in the BNT162b2 group completed the study. Most of the withdrawals in the BNT162b2 group were due to withdrawal by parent/guardian (7.9%). Two participants withdrew from the study due to pregnancy. Both pregnancies had an onset (153 days and 169 days after Dose 2) that was greater than the protocol-specified window of 28 days after vaccination.

The safety population in this age group of the troponin group included 487 (96.1%) of 507 assigned participants. A total of 20 assigned participants (3.9%) were excluded from the safety population, of whom 1 participant (0.2%) did not receive study vaccination and 19 participants' (3.7%) parent/guardian did not provide acceptable dual parental informed consent required per local regulation.

Demographics

Phase 1

In the group 5 to <12 years of age, the majority of participants were White and the median age at vaccination was 6.0 years for participants in the BNT162b2 30/30-µg group and 8.5 years for all other dose level groups.

The overall median follow-up time in this age group from Dose 1, Dose 2, and Dose 3 of BNT162b2 to end of study was 20.2 months, 19.2 months, and 9.3 months, respectively.

In the group 2 to <5 years of age that received BNT162b2 3-µg, there were 9 males (56.3%) and 7 females (43.8%) in the safety population. In the BNT162b2 10-µg group, there were 19 males (59.4%) and 13 females (40.6%) in the safety population. Across both groups, the majority of participants were White. The median age at vaccination was 3.0 years in both groups.

The overall median follow-up time in this age group from Dose 1, Dose 2, and Dose 3 of BNT162b2 to end of study was 23.1 months, 22.3 months, and 12.5 months, respectively.

In the group 6 months to <2 years of age, there were 10 males (62.5%) and 6 females (37.5%) in the safety population and the majority of participants were White. The median age at vaccination was 15.5 months.

The overall median follow-up time in this age group from Dose 1, Dose 2, and Dose 3 of BNT162b2 to end of study was 23.4 months, 22.7 months, and 12.5 months, respectively.

Phase 2/3

In the group 5 to <12 years of age, the percentage of participants who were baseline positive for prior SARS-CoV-2 infection was similar in the BNT162b2 group (9.5%) and placebo group (9.6%). The median age at vaccination was 8.0 years of age for both groups and the majority of participants were White from USA.

The overall median follow-up time in this age group from Dose 1, Dose 2, and Dose 3 of BNT162b2 to end of study was 19.8 months, 19.1 months, and 12.5 months, respectively. The overall median follow-up time from Dose 1 and Dose 2 of placebo to the first dose of open-label BNT162b2 vaccination, withdrawal, or end of study was 3.5 months and 2.8 months, respectively.
In participants who originally received placebo and then received BNT162b2, the overall median follow-up time from Dose 1, Dose 2, and Dose 3 of BNT162b2 to end of study was 18.6 months, 18.1 months, and 11.6 months, respectively.

In the group 2 to <5 years of age, the percentage of participants who were baseline positive for prior SARS-CoV-2 infection was similar in the BNT162b2 group (20.0%) and placebo group (20.1%). The median age at vaccination was 3.0 years for both groups and the majority of participants were White from USA.

In the original blinded placebo-controlled follow-up period in this age group, the overall median follow-up time from Dose 1, Dose 2, and Dose 3 of BNT162b2 to end of study was 16.0 months, 15.3 months, and 12.5 months, respectively. The overall median follow-up time from Dose 1, Dose 2, and Dose 3 of placebo to the first dose of open-label BNT162b2 vaccination, withdrawal, or end of study was 6.8 months, 6.3 months, and 2.8 months, respectively.
As participants in the placebo group crossed over to receive BNT162b2, limited additional follow-up time accrued for these participants, resulting in the lower median time. In participants who originally received placebo and then received BNT162b2 after unblinding, the overall median follow-up time from

Dose 1, Dose 2, and Dose 3 of BNT162b2 to end of study was 13.1 months, 12.3 months, and 10.3 months, respectively.

In the group 6 months to <2 years of age, the percentage of participants who were baseline positive for prior SARS-CoV-2 infection was similar in the BNT162b2 group (13.4%) and placebo group (10.4%). The median age at vaccination was 16.0 months for the BNT162b2 group and 15.0 months for the placebo group and the majority of participants were White from USA.

The overall median follow-up time in this age group from Dose 1, Dose 2, and Dose 3 of BNT162b2 to end of study was 17.5 months, 16.6 months, and 12.5 months, respectively. The overall median follow-up time from Dose 1, Dose 2, and Dose 3 of placebo to the first dose of open-label BNT162b2 vaccination, withdrawal, or end of study was 7.1 months, 6.4 months, and 2.1 months, respectively. As participants in the placebo group crossed over to receive BNT162b2, limited additional follow-up time accrued for these participants, resulting in the lower median time. In participants who originally received placebo and then received BNT162b2, the overall median follow-up time from Dose 1, Dose 2, and Dose 3 of BNT162b2 to end of study was 13.1 months, 12.5 months, and 10.5 months, respectively.

Phase 2/3 Troponin Group

Within the Troponin group aged 5 to <12 years, among the subjects receiving BNT162b2, 51.4% of participants were male and 14.9% of participants had evidence of prior SARS-CoV-2 infection ("baseline positive"). In the placebo group, 53.8% of participants were male and 14.2% of participants were baseline positive. The majority of participants in the BNT162b2 and placebo group were not obese and did not have any comorbidities. All participants were from the US, with 10 to 13.1% of Hispanic/Latino ethnicity). In contrast to participants ≥12 to <16 years of age in the troponin group were prevalent, contributing to the lower percentage of baseline positives compared with that in the ≥12 to <16 years age group.

In the Troponin group aged 12 to <16 years, a total of 55.6% of participants were male. Overall, 88.7% of participants were baseline positive. The majority of participants were from Mexico and of Hispanic/Latino ethnicity. In contrast to participants ≥5 to <12 years of age in the troponin group most participants in this age group were enrolled when Omicron sublineage(s) were prevalent, contributing to the higher percentage of baseline positives compared with that in the ≥5 to <12 years of age group. The majority of participants were not obese and did not have any comorbidities.

Objectives and Endpoints

The objectives and endpoints presented in this report align with protocol amendment 8 (28 April 2023).
The dose-finding/selected-dose age group referred to in the objectives and estimands below included participants 5 to <12 years, 2 to <5 years, and 6 months to <2 years of age. The troponin group referred to in the objectives and estimands below included participants 5 to <12 years (10 µg) and 12 to <16 years of age (30 µg).
Table 1 presents Phase 1 and Table 2 presents Phase 2/3 objectives/estimands/endpoints. Objectives/estimands/endpoints previously reported are shown in gray shading and bold, those reported in this CSR are shown in plain text.

Table 7: Phase 1 objectives, estimands and endpoints

Objectives	Estimands	Endpoints	Reference
Primary:	**Primary:**	**Primary:**	
To describe the safety and tolerability profiles of prophylactic BNT162b2 at each dose level in each age group	In participants receiving at least 1 dose of study intervention, the percentage of participants in each age group reporting: • **Local reactions for up to 7 days following each dose** • **Systemic events for up to 7 days following each dose** • **AEs from Dose 1 to 1 month after Dose 2** • SAEs from Dose 1 to 6 months after Dose 2 • AEs from Dose 3 to 1 month after Dose 3 • SAEs from Dose 3 to 6 months after Dose 3	Participants **≥5 to <12,** and **≥2 to <5 years of age:** • **Local reactions (pain at the injection site, redness, and swelling)** • **Systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain)** • **AEs** • **SAEs** **Participants ≥6 months to <2 years of age:** • **Local reactions (tenderness at the injection site, redness, and swelling)** • **Systemic events (fever, decreased appetite, drowsiness, and irritability)** • **AEs** • **SAEs**	**Data for participants 2 to <5 years and 6 months to <2 years of age were included in the CSR dated 01 July 2022** **Data for participants 5 to <12 years of age were reported in previous CSRs dated 31 October 2022 and 30 September 2021** Post-Dose 3 reactogenicity, AE, and SAE data and SAE from Dose 1 to 6 months after Dose 3 data for participants ≥6 months to <12 years of age are included in this CSR
Secondary:	**Secondary:**	**Secondary:**	
To describe the immune responses elicited by prophylactic BNT162b2 at each dose level in each age group	**In participants complying with the key protocol criteria (evaluable participants) in each age group:** • **GMTs at each time point**	• **SARS-CoV-2 neutralizing titers**	**Data for participants 2 to <5 years and 6 months to <2 years of age groups were reported in a previous CSR dated 01 July 2022** **Data for participants 5 to <12 years of age were reported in a previous CSR dated 30 September 2021**
Exploratory:	**Exploratory:**	**Exploratory:**	
To describe COVID-19 and severe COVID-19 cases with and without serological or virological evidence of past SARS-CoV-2 infection		• Confirmed COVID-19 cases • Confirmed severe COVID-19 cases	Data for participants ≥6 months to <12 years of age are included in this CSR
To describe MIS-C cases with and without evidence of past SARS-CoV-2 infection		• Confirmed cases as per CDC criteria	Data for participants ≥6 months to <12 years of age are included in this CSR

Source: Appendix 16.1.1, Protocol Section 3.1.

Table 8: Phase 2/3 objectives, estimands and endpoints

Objectives	Estimands	Endpoints	Reference
Primary Safety:	**Primary Safety:**	**Primary Safety:**	
To define the safety profile of prophylactic BNT162b2 in all participants (selected-dose, and obtaining-serum-samples-for-potential-troponin I-testing portions of the study) in Phase 2/3 in each age group.	**In participants receiving at least 1 dose of study intervention from each vaccine group, the percentage of participants in each age group reporting:** • **Local reactions for up to 7 days following each dose** • **Systemic events for up to 7 days following each dose** • **AEs from Dose 1 to 1 month after Dose 2** • **SAEs from Dose 1 to 6 months after Dose 2** • **AEs from Dose 3 to 1 month after Dose 3** • **SAEs from Dose 3 to 6 months after Dose 3**	**Participants, ≥12 to <16, ≥5 to <12, and ≥2 to <5 years of age:** • **Local reactions (pain at the injection site, redness, and swelling)** • **Systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain)** • **AEs** • **SAEs** **Participants ≥6 months to <2 years of age:** • **Local reactions (tenderness at the injection site, redness, and swelling)** • **Systemic events (fever, decreased appetite, drowsiness, and irritability)** • **AEs** • **SAEs**	Data for the troponin group are included in this CSR SAE data from Dose 1 to 6 months after Dose 2 or prior to Dose 3 for participants 6 months to <12 years of age in the selected dose portion are included in this CSR **Data for selected-dose participants were reported in previous CSRs listed below:** **Complete 6 Months Post-Dose 3 data for participants 6 months to <12 years of age were reported in a previous CSR dated 08 November 2023** **Complete 6 Months Post-Dose 2 data for participants 5 to <12 years of age were reported in a previous CSR dated 31 October 2022** **Interim data for participants 2 to <5 years and 6 months to <2 years of age were reported in a previous CSR dated 01 July 2022 (3-dose series)** **Interim data for a subset of participants 5 to <12 years of age were reported in previous CSRs dated 30 September 2021 (2-dose series) and 11 May 2022 (3rd dose)**
Objectives	**Estimands**	**Endpoints**	**Reference**
Primary Immunogenicity (Selected-Dose 2-Dose Series):	**Primary Immunogenicity (Selected-Dose 2-Dose Series):**	**Primary Immunogenicity (Selected-Dose 2-Dose Series):**	
To immunobridge the immune response elicited by prophylactic BNT162b2 between Phase 2/3 participants at the dose selected in each age group and participants 16 to 25 years of age from the C4591001 study without serological or virological evidence (up to 1 month after receipt of Dose 2) of past SARS-CoV-2 infection.	**In participants complying with the key protocol criteria (evaluable participants) and no serological or virological evidence (up to 1 month after receipt of Dose 2) of past SARS-CoV-2 infection:**	• **SARS-CoV-2 neutralizing titers**	
• **In participants ≥5 to <12 years of age compared to participants 16 to 25 years of age from Phase 2/3 of the C4591001 study**	• **GMR, estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers in participants ≥5 to <12 years of age to those in participants 16 to 25 years of age 1 month after Dose 2 from Phase 2/3 of the C4591001 study** • **The difference in percentages of participants with seroresponse[a] in participants ≥5 to <12 years of age and participants 16 to 25 years of age from Phase 2/3 of the C4591001 study**		**Data for participants 5 to <12 years of age were reported in a previous CSR dated 30 September 2021**
• **In participants 2 to <5 years of age compared to participants 16 to 25 years of age from Phase 2/3 of the C4591001 study**	• **GMR, estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers in participants ≥2 to <5 years of age to those in participants 16 to 25 years of age 1 month after Dose 2**		**Data for participants 2 to <5 years of age were reported in a previous CSR dated 01 July 2022**

Exploratory:	**Exploratory:**	**Exploratory:**	
To describe COVID-19 and severe COVID-19 cases with and without serological or virological evidence of past SARS-CoV-2 infection		• Confirmed COVID-19 cases • Confirmed severe COVID-19 cases	Data for participants ≥6 months to <12 years of age are included in this CSR
To describe MIS-C cases with and without evidence of past SARS-CoV-2 infection		• Confirmed cases as per CDC criteria	Data for participants ≥6 months to <12 years of age are included in this CSR

Source: Appendix 16.1.1, Protocol Section 3.1.

Results

Efficacy results

Phase 1 – Confirmed COVID-19 Occurrences

Participants 5 to <12 Years of Age

In the Dose 1 all-available efficacy population, 17 participants reported at least 1 occurrence of COVID-19. Of these 17 participants, 5 participants were assigned to BNT162b2 10 µg, 7 participants were assigned to BNT162b2 20 µg, and 5 participants were assigned to BNT162b2 30 µg. One participant assigned to BNT162b2 20 µg reported multiple COVID-19 occurrences, with the first occurrence after Dose 2 and the second occurrence after Dose 3.

Participants 2 to <5 Years of Age

In the Dose 1 all-available efficacy population, 8 participants reported at least 1 occurrence of COVID-19. Of these 8 participants, 2 participants were assigned to BNT162b2 3 µg, 4 participants were assigned to BNT162b2 10 µg, and 2 participants were assigned to BNT162b2 30 µg. No participants reported multiple occurrences of COVID-19.

Participants 6 Months to <2 Years of Age

In the Dose 1 all-available efficacy population, 4 participants assigned to BNT162b2 3 µg reported at least 1 occurrence of COVID-19. No participants reported multiple occurrences of COVID-19.

Phase 1 – Severe COVID-19 Illness and MIS-C

There were no participants in any age group that met 1 or more severe COVID-19 illness criteria. No cases of MIS-C were reported.

Phase 2/3 – Selected Dose Portion – COVID-19 Incidence

This section presents results of analyses for participants 5 to <12 years of age, 2 to <5 years of age, and 6 months to <2 years of age, for the following protocol exploratory objective

- COVID-19 incidence per 1000 person-years of follow-up through the entire study follow- up period in participants who received BNT162b2 at initial randomization or subsequently

5 Years to <12 Years of Age

In the Dose 1 all-available efficacy population, the IR of first COVID-19 occurrence after vaccination from 07 June 2021 to 30 September 2021, when Delta variant was the predominant strain, was 11.691 and 88.804 per 1000 person-years of follow up in the original BNT162b2 10-µg group and original placebo prior to crossover group, respectively. The substantially lower IR in the BNT162b2 group comparing to the placebo group was consistent with the high VE in the blinded placebo-controlled period reported previously.

During the transition of the Delta variant to Omicron variant in late 2021 to early 2022, a large increase in IR was observed for all groups. To note, with EUA issued on 29 October 2021 for this age group, study participants were offered to be unblinded and placebo participants started to receive BNT162b2. The majority of placebo participants completed the switch to BNT162b2 by 01 January 2022, with very limited placebo-controlled surveillance afterwards.

Table 9: Incidence rates of first COVID-19 occurrence after vaccination, by calendar period – phase 2/3 – selected dose portion – 5 to <12 years of age – dose 1 all-available efficacy population

	Vaccine Group								
	Original BNT162b2 (10 µg)			Original Placebo Prior to Crossover			Placebo Crossover to BNT162b2 (10 µg)		
Efficacy Endpoint	n1[a]	Surveillance Time[b] (n2[c])	IR (/1000 PY)[d]	n1[a]	Surveillance Time[b] (n2[c])	IR (/1000 PY)[d]	n1[a]	Surveillance Time[b] (n2[c])	IR (/1000 PY)[d]
First COVID-19 occurrence from 07JUN2021[e] to 30SEP2021	6	0.513 (2654)	11.691	25	0.282 (1493)	88.804	0	0.000 (0)	NE
First COVID-19 occurrence from 01OCT2021 to 31DEC2021	91	0.659 (2642)	138.098	29	0.183 (1453)	158.529	25	0.132 (1058)	189.870
First COVID-19 occurrence from 01JAN2022 to 31MAR2022	379	0.535 (2514)	707.758	0	0.002 (43)	0.000	125	0.237 (1062)	527.141
First COVID-19 occurrence from 01APR2022 to 30JUN2022	142	0.459 (1971)	309.093	0	0.000 (1)	0.000	101	0.211 (921)	477.587
First COVID-19 occurrence from 01JUL2022 to 30SEP2022	171	0.392 (1690)	436.279	0	0.000 (1)	0.000	52	0.178 (759)	291.957
First COVID-19 occurrence from 01OCT2022 to 31DEC2022	44	0.296 (1409)	148.811	0	0.000 (0)	NE	24	0.137 (659)	174.824
First COVID-19 occurrence from 01JAN2023 to 31MAR2023	26	0.183 (970)	141.900	0	0.000 (0)	NE	10	0.098 (430)	101.894
First COVID-19 occurrence from 01APR2023 to 30JUN2023	3	0.051 (345)	59.345	0	0.000 (0)	NE	4	0.068 (378)	59.116
First COVID-19 occurrence from 01JUL2023 to 30SEP2023	0	0.010 (102)	0.000	0	0.000 (0)	NE	1	0.010 (90)	98.690
First COVID-19 occurrence from 01OCT2023 to 16OCT2023[f]	0	0.000 (1)	0.000	0	0.000 (0)	NE	0	0.000 (5)	0.000
First COVID-19 occurrence after vaccination	862	3.099 (2654)	278.165	54	0.467 (1493)	115.624	342	1.072 (1093)	319.092

Abbreviation: NE = not estimable.

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years (PY) for the given endpoint across all participants within each group at risk for the endpoint. For the original BNT162b2 and original placebo prior to crossover group, time period for COVID-19 case accrual is from latest of Dose 1 vaccination date or the start date of each calendar time period to the earliest of confirmed case, death, withdrawn from the study, study completion date, their first dose of BNT162b2 vaccination date (original placebo group only), or the end date of each calendar time period. For the placebo crossover to BNT162b2 (10 µg) group, the time period is from latest of first dose of BNT162b2 vaccination date or the start date of each calendar time period to the earliest of confirmed case, death, withdrawn from the study, study completion date, or the end date of each calendar time period.

c. n2 = Number of participants at risk for the endpoint.

d. Incidence rate (IR) is calculated as number of participants meeting the endpoint definition/total surveillance time across all participants at risk for the endpoint within the specific group.

e. Date of the first participant receiving vaccination.

f. Date of last visit for the last participant.

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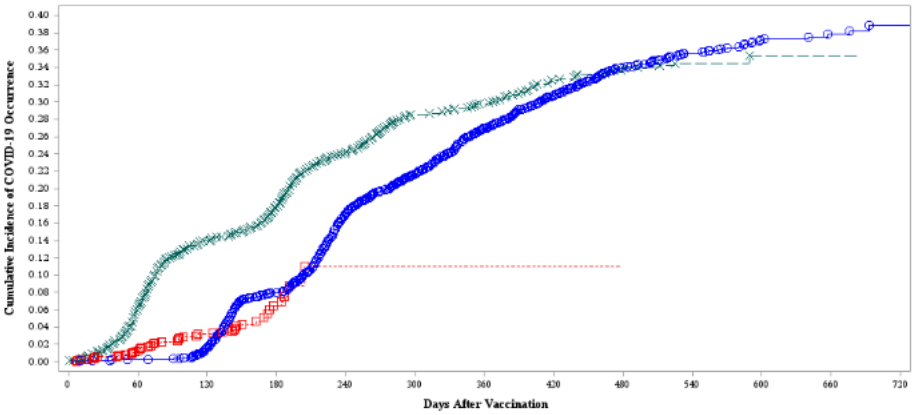
Table 10: Cumulative incidence curves for the first COVID-19 occurrence after vaccination – Phase 2/3 – selected dose portion –5 to <12 years of age – dose 1 all available efficacy population



Participants at Risk

A:	2654	2641	2594	2392	2025	1829	1646	1439	1182	976	480	215	145
B:	1493	1407	697	204	3	1	1	0	0	0	0	0	0
C:	1093	1023	925	865	768	673	571	416	382	359	42	0	0

Cumulative Number of Events

A:	0	6	42	210	488	545	668	750	813	840	856	859	862
B:	0	19	36	49	54	54	54	54	54	54	54	54	54
C:	0	69	151	193	259	300	311	330	337	341	342	342	342

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2 to <5 Years of Age

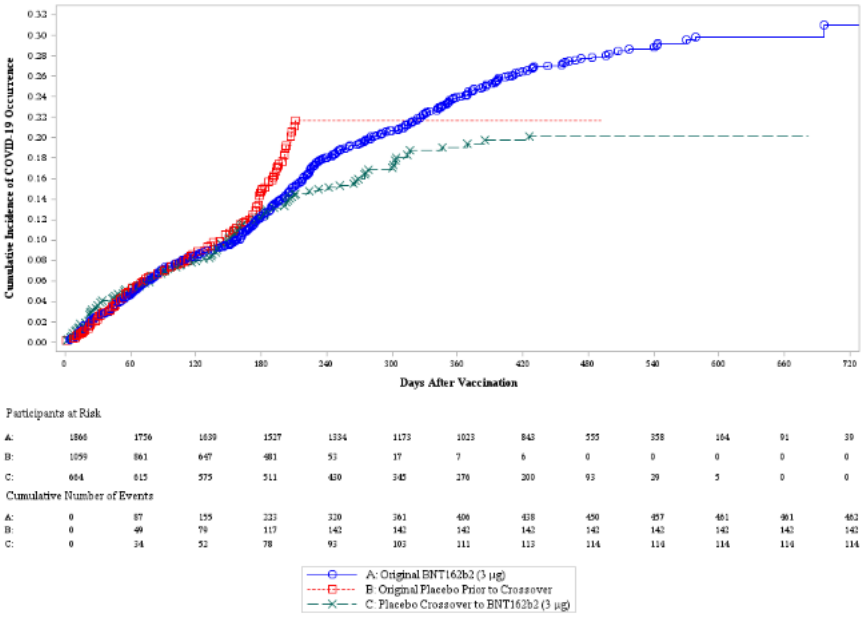
In the Dose 1 all-available efficacy population, the IR of first COVID-19 occurrence after vaccination from 21 June 2021 to 30 September 2021 after vaccination, when Delta variant was the predominant strain, was 38.084 and 41.155, per 1000 person-years of follow up in the original BNT162b2 3-µg group and original placebo prior to crossover group, respectively. During the transition of the Delta variant to Omicron variant in late 2021 to early 2022, large increase in IR was observed for all groups.

Table 11: Incidence rates of first COVID-19 occurrence after vaccination, by calendar period – Phase 2/3 – selected dose portion – 2 to <5 years of age – dose 1 all available efficacy population

	Vaccine Group								
	Original BNT162b2 (3 µg)			Original Placebo Prior to Crossover			Placebo Crossover to BNT162b2 (3 µg)		
Efficacy Endpoint	n1[a]	Surveillance Time[b] (n2[c])	IR (/1000 PY)[d]	n1[a]	Surveillance Time[b] (n2[c])	IR (/1000 PY)[d]	n1[a]	Surveillance Time[b] (n2[c])	IR (/1000 PY)[d]
First COVID-19 occurrence from 21JUN2021[e] to 30SEP2021	5	0.131 (652)	38.084	3	0.073 (367)	41.155	0	0.000 (0)	NE
First COVID-19 occurrence from 01OCT2021 to 31DEC2021	20	0.213 (1125)	94.083	18	0.113 (615)	159.424	1	0.004 (32)	274.418
First COVID-19 occurrence from 01JAN2022 to 31MAR2022	138	0.279 (1417)	494.433	66	0.107 (740)	617.846	17	0.042 (289)	400.881
First COVID-19 occurrence from 01APR2022 to 30JUN2022	106	0.342 (1621)	310.012	51	0.109 (648)	466.908	24	0.077 (503)	311.481
First COVID-19 occurrence from 01JUL2022 to 30SEP2022	125	0.332 (1446)	376.004	3	0.015 (195)	196.125	43	0.134 (602)	321.694
First COVID-19 occurrence from 01OCT2022 to 31DEC2022	46	0.275 (1223)	167.182	1	0.002 (14)	488.302	13	0.121 (529)	107.814
First COVID-19 occurrence from 01JAN2023 to 31MAR2023	15	0.174 (952)	86.446	0	0.001 (5)	0.000	12	0.091 (430)	132.457
First COVID-19 occurrence from 01APR2023 to 30JUN2023	5	0.088 (458)	57.060	0	0.001 (4)	0.000	4	0.062 (305)	65.026
First COVID-19 occurrence from 01JUL2023 to 30SEP2023	1	0.034 (213)	29.580	0	0.001 (3)	0.000	0	0.026 (164)	0.000
First COVID-19 occurrence from 01OCT2023 to 08DEC2023[f]	1	0.007 (71)	137.519	0	0.000 (3)	0.000	0	0.004 (47)	0.000
First COVID-19 occurrence after vaccination	462	1.875 (1866)	246.438	142	0.422 (1059)	336.232	114	0.560 (664)	203.630

Abbreviation: NE = not estimable.
a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years (PY) for the given endpoint across all participants within each group at risk for the endpoint. For the original BNT162b2 and original placebo prior to crossover group, time period for COVID-19 case accrual is from latest of Dose 1 vaccination date or the start date of each calendar time period to the earliest of confirmed case, death, withdrawn from the study, study completion date, their first dose of BNT162b2 vaccination date (original placebo group only), or the end date of each calendar time period. For the placebo crossover to BNT162b2 (3 µg) group, the time period is from latest of first dose of BNT162b2 vaccination date or the start date of each calendar time period to the earliest of confirmed case, death, withdrawn from the study, study completion date, or the end date of each calendar time period.
c. n2 = Number of participants at risk for the endpoint.
d. Incidence rate (IR) is calculated as number of participants meeting the endpoint definition/total surveillance time across all participants at risk for the endpoint within the specific group.
e. Date of the first participant receiving vaccination.
f. Date of last visit for the last participant.
PFIZER CONFIDENTIAL SDTM Creation: 12JAN2024 (08:40) Source Data: adc19eu Table Generation: 02FEB2024 (19:05)
(Database snapshot date : 05JAN2024) Output File: ./nda2_ubped2/C4591007_CSR/adc19ef_pd1_d1aa_5

Table 12: Cumulative incidence curves for the first COVID-19 occurrence after vaccination – phase 2/3 – selected dose portion – 2 to <5 years of age – dose 1 all available efficacy population



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6 Months to <2 Years of Age

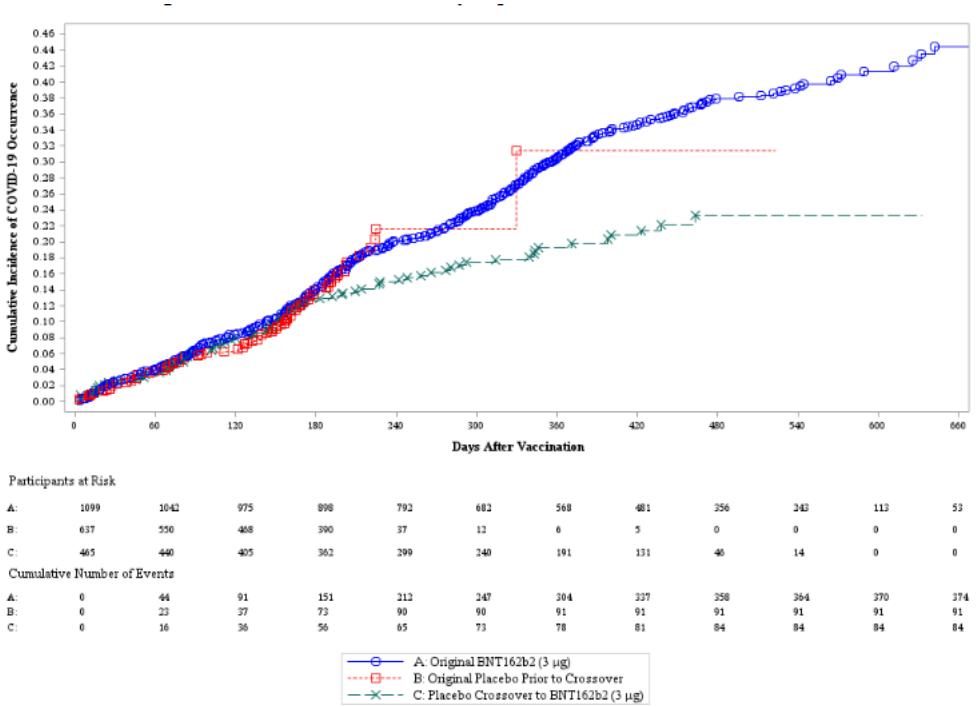
In the Dose 1 all-available efficacy population, the IR of first COVID-19 occurrence after vaccination from 21 June 2021 to 30 September 2021, when Delta variant was the predominant strain, was 0 and 55.937 per 1000 person-years of follow up in the original BNT162b2 3-µg group and original placebo prior to crossover group, respectively. During the transition of the Delta variant to Omicron variant in late 2021 to early 2022, large increase in IR was observed for all groups.

Table 13: Incidence rates of first COVID-19 occurrence after vaccination, by calendar period – Phase 2/3 – selected dose portion – 6 months to <2 years of age – dose 1 all available efficacy population

	Vaccine Group								
	Original BNT162b2 (3 µg)			Original Placebo Prior to Crossover			Placebo Crossover to BNT162b2 (3 µg)		
Efficacy Endpoint	n1[a]	Surveillance Time[b] (n2[c])	IR (/1000 PY)[d]	n1[a]	Surveillance Time[b] (n2[c])	IR (/1000 PY)[d]	n1[a]	Surveillance Time[b] (n2[c])	IR (/1000 PY)[d]
First COVID-19 occurrence from 21JUN2021[e] to 30SEP2021	0	0.093 (544)	0.000	3	0.054 (325)	55.937	0	0.000 (0)	NE
First COVID-19 occurrence from 01OCT2021 to 31DEC2021	15	0.154 (711)	97.504	9	0.090 (421)	99.892	0	0.000 (0)	NE
First COVID-19 occurrence from 01JAN2022 to 31MAR2022	107	0.174 (864)	615.364	47	0.076 (502)	619.358	8	0.028 (226)	283.002
First COVID-19 occurrence from 01APR2022 to 30JUN2022	77	0.204 (952)	377.928	22	0.054 (356)	409.327	23	0.067 (367)	343.941
First COVID-19 occurrence from 01JUL2022 to 30SEP2022	100	0.189 (834)	529.432	8	0.010 (108)	791.441	28	0.091 (419)	306.739
First COVID-19 occurrence from 01OCT2022 to 31DEC2022	44	0.147 (685)	298.479	1	0.002 (9)	550.075	13	0.083 (378)	155.910
First COVID-19 occurrence from 01JAN2023 to 31MAR2023	23	0.087 (500)	263.528	1	0.001 (5)	901.852	7	0.058 (290)	120.955
First COVID-19 occurrence from 01APR2023 to 30JUN2023	6	0.042 (224)	142.324	0	0.001 (4)	0.000	3	0.039 (187)	77.504
First COVID-19 occurrence from 01JUL2023 to 30SEP2023	2	0.016 (112)	126.625	0	0.001 (4)	0.000	2	0.019 (106)	107.490
First COVID-19 occurrence from 01OCT2023 to 08DEC2023[f]	0	0.003 (31)	0.000	0	0.000 (4)	0.000	0	0.003 (39)	0.000
First COVID-19 occurrence after vaccination	374	1.109 (1099)	337.288	91	0.289 (637)	315.047	84	0.388 (465)	216.750

Abbreviation: NE = not estimable.
a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years (PY) for the given endpoint across all participants within each group at risk for the endpoint. For the original BNT162b2 and original placebo prior to crossover group, time period for COVID-19 case accrual is from latest of Dose 1 vaccination date or the start date of each calendar time period to the earliest of confirmed case, death, withdrawn from the study, study completion date, their first dose of BNT162b2 vaccination date (original placebo group only), or the end date of each calendar time period. For the placebo crossover to BNT162b2 (3 µg) group, the time period is from latest of first dose of BNT162b2 vaccination date or the start date of each calendar time period to the earliest of confirmed case, death, withdrawn from the study, study completion date, or the end date of each calendar time period.
c. n2 = Number of participants at risk for the endpoint.
d. Incidence rate (IR) is calculated as number of participants meeting the endpoint definition/total surveillance time across all participants at risk for the endpoint within the specific group.
e. Date of the first participant receiving vaccination.
f. Date of last visit for the last participant.
PFIZER CONFIDENTIAL SDTM Creation: 12JAN2024 (08:40) Source Data: adc19eu Table Generation: 02FEB2024 (19:01) (Database snapshot date : 05JAN2024) Output File: ./nda2_ubped2/C4591007_CSR/adc19ef_pd1_d1aa_2

Table 14: Cumulative incidence curves for the first COVID-19 occurrence after vaccination – phase 2/3 – selected dose portion – 6 months to <2 years of age – dose 1 all available efficacy population



PFIZER CONFIDENTIAL SDTM Creation: 08JAN2024 (02:13) Source Data: adc19eu Table Generation: 31JAN2024 (00:45)(Database snapshot date : 05JAN2024) Output File: /nda2_ubped2/C4591007_CSR/adc19ef_f001_aa2_p2

Phase 2/3 – Selected Dose Portion –Severe COVID-19 Illness and MIS-C

This section presents Phase 2/3 severe COVID-19 occurrences and MIS-C from Dose 1 through end of the study. No cases of MIS-C were reported in Phase 2/3.

5 Years to <12 Years of Age

Fifteen participants had COVID-19 that met 1 or more severe illness criteria. Criteria for severe illness were fulfilled for 13 cases in the BNT162b2 group and 2 occurrences in the placebo group (noting 2:1 randomization and significantly shortened surveillance period for placebo group due to unblinding and crossover). All occurrences in the placebo group met protocol-defined severe illness criteria. In the BNT162b2 group, 10 occurrences met protocol-defined severe illness criteria, 1 case met CDC-defined severe illness criteria, and 2 cases met both severe illness criteria.

2 to <5 Years of Age

Thirteen participants had COVID-19 that met 1 or more severe illness criteria. Criteria for severe illness were fulfilled for 9 occurrences in the BNT162b2 group and 4 occurrences in the placebo group (noting 2:1 randomization and significantly shortened surveillance period for placebo group due to unblinding and crossover). One occurrence in the BNT162b2 group met both severe illness criteria. All other occurrences across BNT162b2 and placebo groups met a single protocol-defined criterion for severe illness.

6 Months to <2 Years of Age

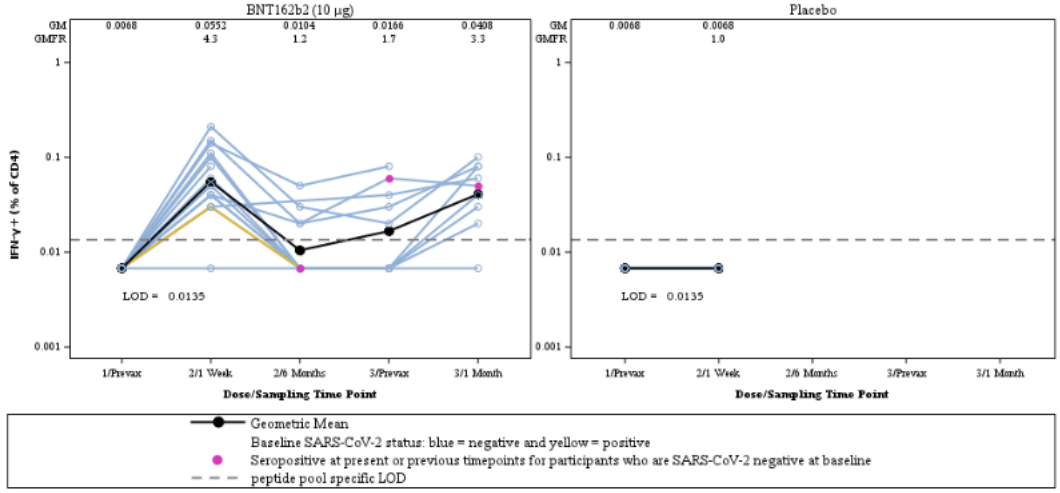
Seven participants had COVID-19 that met 1 or more severe illness criteria. Criteria for severe illness were fulfilled for 6 occurrences in the BNT162b2 group and 1 occurrence in the placebo group (noting 2:1 randomization and significantly shortened surveillance period for placebo group due to unblinding and crossover). No participants with occurrences meeting severe criteria had evidence of prior infection with SARS-CoV-2. Two occurrences in the BNT162b2 group met both criteria for severe illness, and all other occurrences met a single protocol-defined criterion for severe illness.

Phase 2/3 – Peripheral Blood Mononuclear Cell Analysis (PBMC) Subset – 10 to <12 Years of Age

Blood samples were obtained prior to Dose 1, at 7 days and 6 months after Dose 2, and prior to and 1 month after Dose 3 from 55 participants ≥10 to <12 years of age for isolation of peripheral blood mononuclear cell (PBMCs). The analysis included the frequency of T-cell specific responses to epitopes (amino acid 1-643) in the spike protein S1 subunit of the wild-type virus.

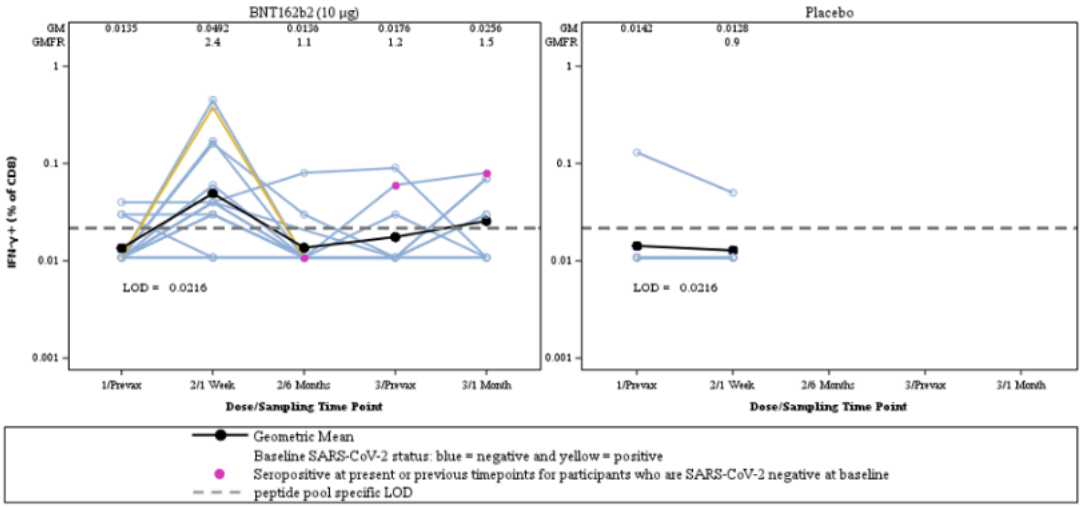
Frequencies of CD4+ T cells secreting interferon gamma in response to S1 peptide stimulation increased 7 days after Dose 1 and 1 month after Dose 2 for some participants.

Frequencies of CD8+ T cells secreting interferon gamma in response to S1 stimulation increased 7 days after Dose 1. The geometric mean interferon gamma responses in CD8. T cells remained relatively unchanged for the rest of the sampling period.



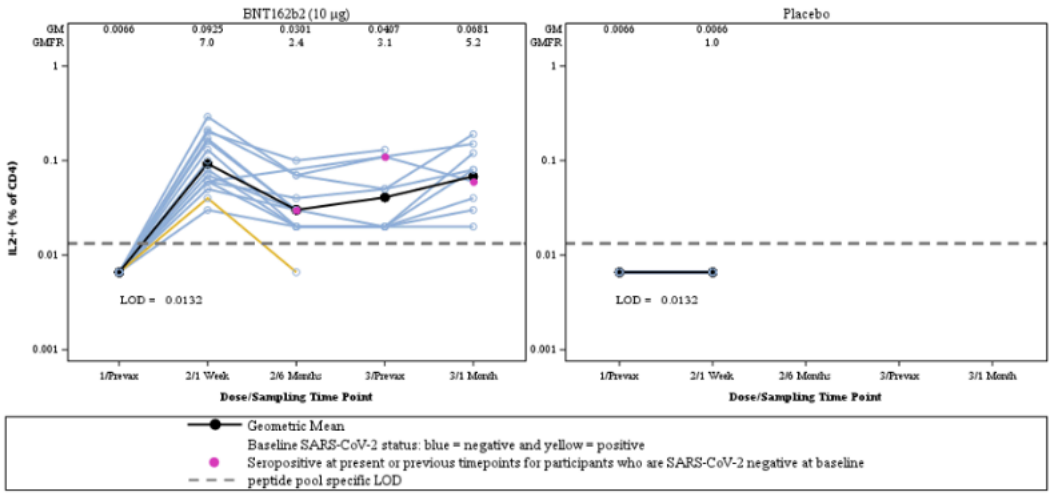
Abbreviations: GM = geometric mean; GMFR = geometric mean fold rise; IFN-γ = interferon gamma; LOD = limit of detection; NAAT = nucleic acid amplification test; PBMC = peripheral blood mononuclear cell; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Seronegative or seropositive is determined per timepoint by N-binding result (potentially available NAAT results not considered).
Note: SARS-CoV-2 positive at baseline: Positive N-binding antibody result at Dose 1, positive NAAT result at Dose 1, or medical history of COVID-19.
Note: SARS-CoV-2 negative at baseline: Negative N-binding antibody result at Dose 1, negative NAAT result at Dose 1, and no medical history of COVID-19.
Note: Spike pool 1 refers to a pool of 158 overlapping peptides representing amino acids 1-643 of the spike protein sequence as encoded by the virus.
Note: Assay results below the LOD were set to LOD when calculating GMFRs and set to 0.5 × LOD in other analyses.
Note: Geometric means were calculated by exponentiating the mean logarithm of the percentages.
Note: GMFRs were calculated by exponentiating the mean logarithm of fold rises.
PFIZER CONFIDENTIAL SDTM Creation: 17JAN2024 (06:13) Source Data: adva Table Generation: 05FEB2024 (21:53)
Output File: /nda2_ubped2/C4591007_PBMC/adva_f006_wtsp1_r1_aai

Figure 2: Plot of CD4 T cell responses to wild type spike pool 1 of PBMCs – Response IFN γ+(% of CD4) – Phase 2/3 PBMC subset – 10 to <12 years of age – all available immunogenicity population



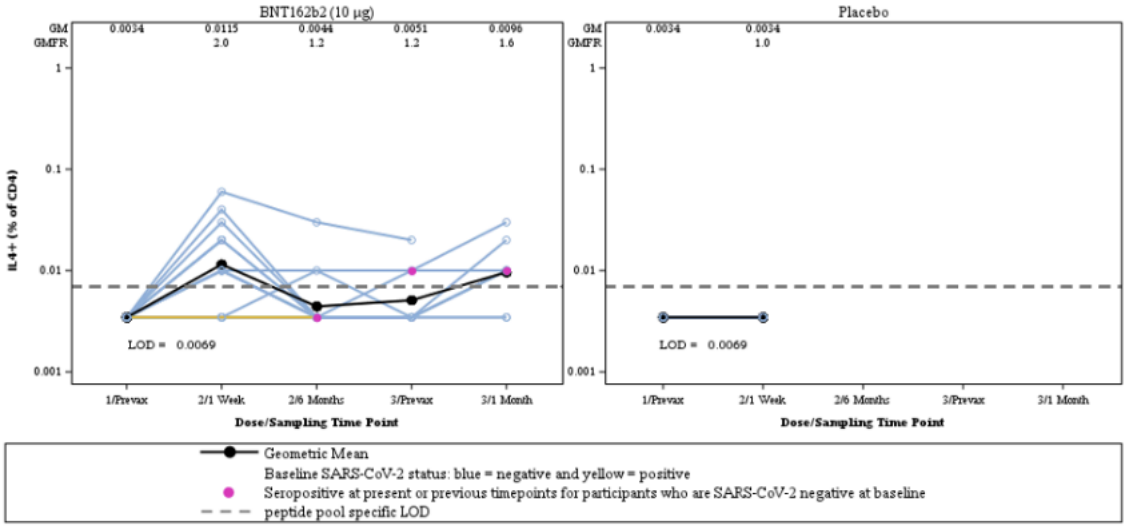
Abbreviations: GM = geometric mean; GMFR = geometric mean fold rise; IFN-γ = interferon gamma; LOD = limit of detection; NAAT = nucleic acid amplification test; PBMC = peripheral blood mononuclear cell; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Seronegative or seropositive is determined per timepoint by N-binding result (potentially available NAAT results not considered).
Note: SARS-CoV-2 positive at baseline: Positive N-binding antibody result at Dose 1, positive NAAT result at Dose 1, or medical history of COVID-19.
Note: SARS-CoV-2 negative at baseline: Negative N-binding antibody result at Dose 1, negative NAAT result at Dose 1, and no medical history of COVID-19.
Note: Spike pool 1 refers to a pool of 158 overlapping peptides representing amino acids 1-643 of the spike protein sequence as encoded by the virus.
Note: Assay results below the LOD were set to LOD when calculating GMFRs and set to 0.5 × LOD in other analyses.
Note: Geometric means were calculated by exponentiating the mean logarithm of the percentages.
Note: GMFRs were calculated by exponentiating the mean logarithm of fold rises.
PFIZER CONFIDENTIAL SDTM Creation: 17JAN2024 (06:13) Source Data: adva Table Generation: 05FEB2024 (21:53)
Output File: /nda2_ubped2/C4591007_PBMC/adva_f006_wtsp1_r2_aai

Figure 3: Plot of CD8 T cell responses to wild type spike pool 1 of PBMCs – Response IFN γ+(% of CD8) – Phase 2/3 PBMC subset – 10 to <12 years of age – all available immunogenicity population



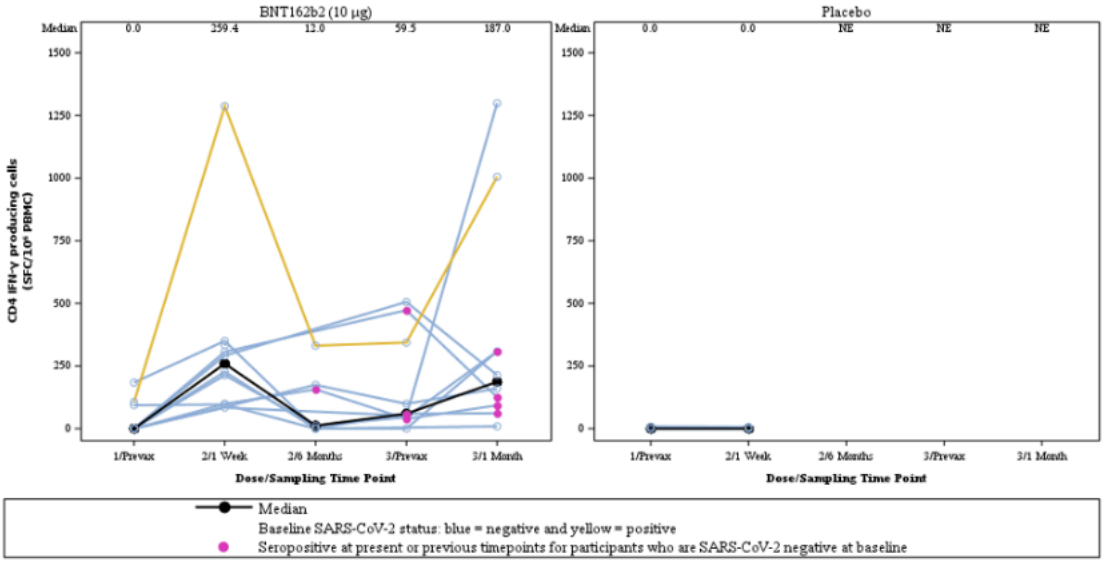
Abbreviations: GM = geometric mean; GMFR = geometric mean fold rise; IL = interleukin; LOD = limit of detection; NAAT = nucleic acid amplification test; PBMC = peripheral blood mononuclear cell; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Seronegative or seropositive is determined per timepoint by N-binding result (potentially available NAAT results not considered).
Note: SARS-CoV-2 positive at baseline: Positive N-binding antibody result at Dose 1, positive NAAT result at Dose 1, or medical history of COVID-19.
Note: SARS-CoV-2 negative at baseline: Negative N-binding antibody result at Dose 1, negative NAAT result at Dose 1, and no medical history of COVID-19.
Note: Spike pool 1 refers to a pool of 158 overlapping peptides representing amino acids 1-643 of the spike protein sequence as encoded by the virus.
Note: Assay results below the LOD were set to LOD when calculating GMFRs and set to 0.5 × LOD in other analyses.
Note: Geometric means were calculated by exponentiating the mean logarithm of the percentages.
Note: GMFRs were calculated by exponentiating the mean logarithm of fold rises.
PFIZER CONFIDENTIAL SDTM Creation: 17JAN2024 (06:13) Source Data: adva Table Generation: 05FEB2024 (21:53)
Output File: /nda2_ubped2/C4591007_PBMC/adva_f006_wtsp1_r3_aai

Figure 4: Plot of CD4 T cell responses to wild type spike pool 1 of PBMCs – Response IL2+ (% of CD4) – Phase 2/3 PBMC subset – 10 to <12 years of age – all available immunogenicity population



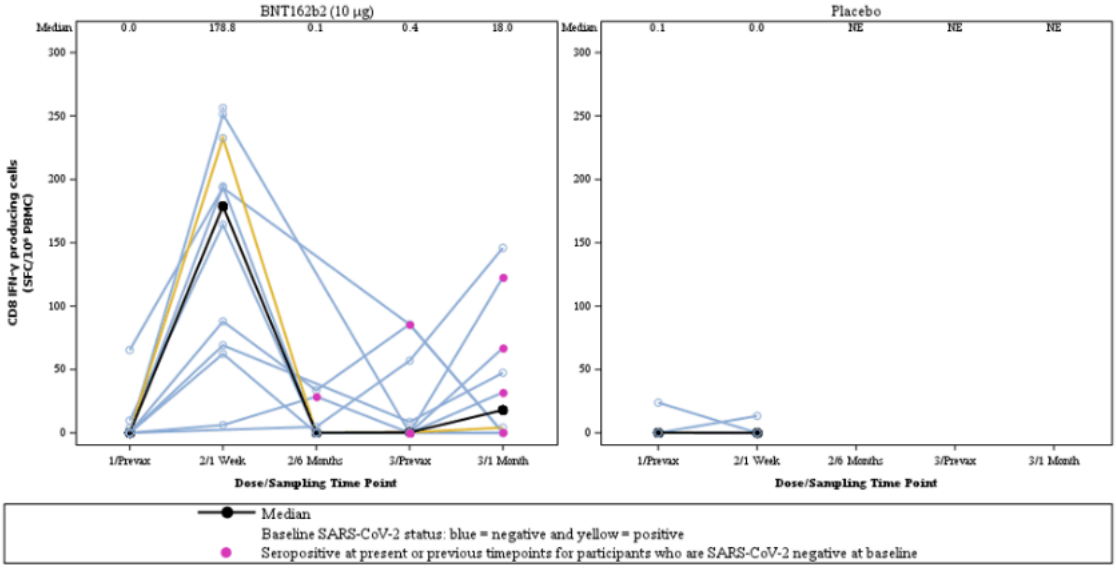
Abbreviations: GM = geometric mean; GMFR = geometric mean fold rise; IL = interleukin; LOD = limit of detection; NAAT = nucleic acid amplification test; PBMC = peripheral blood mononuclear cell; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Seronegative or seropositive is determined per timepoint by N-binding result (potentially available NAAT results not considered).
Note: SARS-CoV-2 positive at baseline: Positive N-binding antibody result at Dose 1, positive NAAT result at Dose 1, or medical history of COVID-19.
Note: SARS-CoV-2 negative at baseline: Negative N-binding antibody result at Dose 1, negative NAAT result at Dose 1, and no medical history of COVID-19.
Note: Spike pool 1 refers to a pool of 158 overlapping peptides representing amino acids 1-643 of the spike protein sequence as encoded by the virus.
Note: Assay results below the LOD were set to LOD when calculating GMFRs and set to 0.5 × LOD in other analyses.
Note: Geometric means were calculated by exponentiating the mean logarithm of the percentages.
Note: GMFRs were calculated by exponentiating the mean logarithm of fold rises.
PFIZER CONFIDENTIAL SDTM Creation: 17JAN2024 (06:13) Source Data: adva Table Generation: 05FEB2024 (21:53)
Output File: /nda2_ubped2/C4591007_PBMC/adva_f006_wtsp1_r4_aai

Figure 5: Plot of CD4 T cell responses to wild type spike pool 1 of PBMCs – Response IL4+ (% of CD4) – Phase 2/3 PBMC subset – 10 to <12 years of age – all available immunogenicity population



Abbreviations: NAAT = nucleic acid amplification test; PBMC = peripheral blood mononuclear cell; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SFC= spot-forming cell.
Note: Seronegative or seropositive is determined per timepoint by N-binding result (potentially available NAAT results not considered).
Note: SARS-CoV-2 positive at baseline: Positive N-binding antibody result at Dose 1, positive NAAT result at Dose 1, or medical history of COVID-19.
Note: SARS-CoV-2 negative at baseline: Negative N-binding antibody result at Dose 1, negative NAAT result at Dose 1, and no medical history of COVID-19.
Note: Spike pool 1 refers to a pool of 158 overlapping peptides representing amino acids 1-643 of the spike protein sequence as encoded by the virus.
PFIZER CONFIDENTIAL SDTM Creation: 17JAN2024 (06:13) Source Data: adva Table Generation: 05FEB2024 (21:53)
Output File: /nda2_ubped2/C4591007_PBMC/adva_f006_wtsp1_r5_aai

Figure 6: Plot of CD4 T cell responses to wild type spike pool 1 of PBMCs – Response CD4 IFN-γ producing cells (SFC/10^6 PBMC) – Phase 2/3 PBMC subset – 10 to <12 years of age – all available immunogenicity population



Abbreviations: NAAT = nucleic acid amplification test; PBMC = peripheral blood mononuclear cell; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SFC= spot-forming cell.
Note: Seronegative or seropositive is determined per timepoint by N-binding result (potentially available NAAT results not considered).
Note: SARS-CoV-2 positive at baseline: Positive N-binding antibody result at Dose 1, positive NAAT result at Dose 1, or medical history of COVID-19.
Note: SARS-CoV-2 negative at baseline: Negative N-binding antibody result at Dose 1, negative NAAT result at Dose 1, and no medical history of COVID-19.
Note: Spike pool 1 refers to a pool of 158 overlapping peptides representing amino acids 1-643 of the spike protein sequence as encoded by the virus.
PFIZER CONFIDENTIAL SDTM Creation: 17JAN2024 (06:13) Source Data: adva Table Generation: 05FEB2024 (21:53)
Output File: /nda2_ubped2/C4591007_PBMC/adva_f006_wtsp1_r6_aai

Figure 7: Plot of CD8 T cell responses to wild type spike pool 1 of PBMCs – Response CD8 IFN-γ producing cells (SFC/10^6 PBMC) – Phase 2/3 PBMC subset – 10 to <12 years of age – all available immunogenicity population

Safety results

The local and systemic reactions as well as AEs and SAEs for the phase I/II/III have already been presented in previous reports (EMEA/H/C/005735/X/0138, EMEA/H/C/005735/II/0160 and EMEA/H/C/005735/II/0203) and therefore not included here. The main safety focus in this report includes safety data for the Troponin group. Furthermore, MIS-C cases are also a target for this report.

Participants 6 Months to <2 Years of Age

During the blinded placebo-controlled follow-up period from Dose 1 to 6 months after Dose 2 or prior to Dose 3, 24 participants (1.7%) in the BNT162b2 3-µg group and 17 participants (2.4%) in the placebo group reported at least 1 SAE.
During the blinded placebo-controlled follow-up period from Dose 3 to 6 months after Dose 3, 1 participant (0.1%) in the BNT162b2 3-µg group reported an SAE of respiratory syncytial virus bronchiolitis.

Table 15: Number (%) of participants reporting at least 1 serious adverse event from dose 1 to 6 months after dose 2 or prior to dose 3, by system organ class and preferred term – blinded placebo-controlled follow up period – phase 2/3 – 6 months to <2 years of age – safety population

	Vaccine Group (as Administered)			
	BNT162b2 (3 µg) (N[a]=1447)		Placebo (N[a]=718)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any adverse event	24 (1.7)	(1.1, 2.5)	17 (2.4)	(1.4, 3.8)
Gastrointestinal disorders	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Vomiting	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Immune system disorders	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.8)
Anaphylactic reaction	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.8)
Infections and infestations	20 (1.4)	(0.8, 2.1)	8 (1.1)	(0.5, 2.2)
Bronchiolitis	3 (0.2)	(0.0, 0.6)	3 (0.4)	(0.1, 1.2)
Respiratory syncytial virus bronchiolitis	5 (0.3)	(0.1, 0.8)	1 (0.1)	(0.0, 0.8)
Gastroenteritis	3 (0.2)	(0.0, 0.6)	0	(0.0, 0.5)
Gastroenteritis rotavirus	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.8)
Gastroenteritis viral	2 (0.1)	(0.0, 0.5)	0	(0.0, 0.5)
Pneumonia	2 (0.1)	(0.0, 0.5)	0	(0.0, 0.5)
Anal abscess	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Enterovirus infection	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Exanthema subitum	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Gastroenteritis norovirus	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
HCoV-NL63 infection	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Large intestine infection	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Lower respiratory tract infection	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Lower respiratory tract infection viral	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Metapneumovirus infection	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Otitis media acute	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Parainfluenzae virus infection	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Respiratory syncytial virus infection	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Rhinovirus infection	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Tonsillitis	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Viral infection	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Injury, poisoning and procedural complications	1 (0.1)	(0.0, 0.4)	4 (0.6)	(0.2, 1.4)
Accidental overdose	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Burns second degree	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Concussion	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Fall	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Head injury	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Thermal burn	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Metabolism and nutrition disorders	0	(0.0, 0.3)	2 (0.3)	(0.0, 1.0)
Feeding intolerance	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Hypoglycaemia	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Nervous system disorders	2 (0.1)	(0.0, 0.5)	0	(0.0, 0.5)
Febrile convulsion	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Seizure	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Respiratory, thoracic and mediastinal disorders	0	(0.0, 0.3)	2 (0.3)	(0.0, 1.0)
Acute respiratory failure	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Pneumomediastinum	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Respiratory distress	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.8)
Vascular disorders	0	(0.0, 0.3)	2 (0.3)	(0.0, 1.0)
Cyanosis	0	(0.0, 0.3)	2 (0.3)	(0.0, 1.0)

Note: MedDRA (v25.1) coding dictionary applied.
a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants reporting at least 1 occurrence of the specified event. For "any adverse event," n = number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided CI, based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 03AUG2023 (14:20) Source Data: adaexa Table Generation: 24JAN2024 (18:23)
(Cutoff Date: 28FEB2023, Snapshot Date: 29MAR2023) Output File: ./nda2_ubped2/C4591007_6MPD3_sBLA_UPDATE/adae_s151_d1pd3_soc_bp_p2_2

Phase 2/3 – Troponin Group – 5 to <12 Years of Age

Reactogenicity AE and SAE data, including troponin I analyses, are summarized for 778 participants 5 to <12 years of age in the troponin group safety population (518 participants in the BNT162b2 group and 260 participants in the placebo group) are presented below.

Reactogenicity

Local reactions

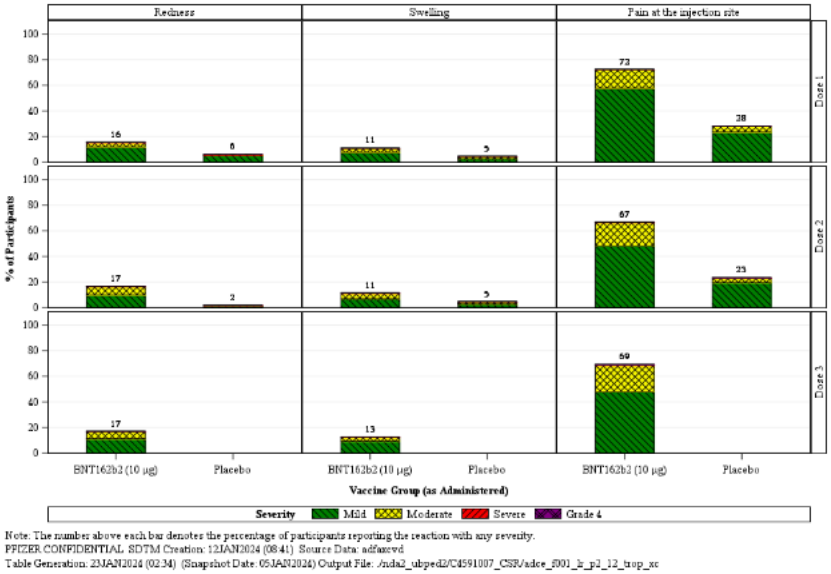


Figure 8: Local reactions, by maximum severity, within 7 days after each dose (E-diary only) – phase 2/3 – Troponin group – 5 to <12 years of age – safety population

In the BNT162b2 group, most local reactions were mild or moderate. Two participants (0.5%) reported severe local reactions of pain at the injection site after Dose 3. In the placebo group, 1 participant (0.4%) reported a severe local reaction of redness after Dose 1. No Grade 4 local reactions were reported after any dose in either group.
Median time to onset for any local reaction after receiving any dose of BNT162b2 occurred on Day 1.0 and also occurred on Day 1.0 after receiving Doses 1 and 2 of placebo. All local reactions resolved with a median duration of 1.0 to 2.0 days after any dose of BNT162b2 10 µg and with a median duration of 1.0 day after Dose 1 and 1.0 to 1.5 days after Dose 2 of placebo.

Systemic events

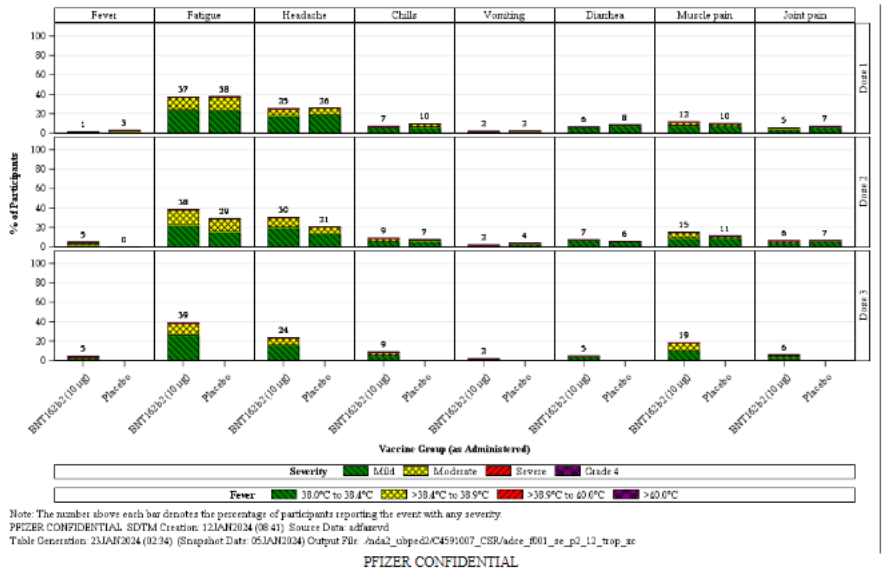


Figure 9: Systematic events, by maximum severity, within 7 days after each dose (E-diary only) – phase 2/3 – Troponin group – 5 to <12 years of age – safety population

In both groups, the majority of systemic events were mild or moderate. After any dose in the BNT162b2 10-µg group, severe cases of headache (0.8%), fatigue (0.6%), chills (0.4%), and diarrhea (0.2%) were reported infrequently. After any dose in the placebo group, 2 participants (0.8%) reported severe cases of fatigue. No Grade 4 systemic events were reported after any dose.
After any dose, 43 participants (8.3%) in the BNT162b2 10-µg group and 8 participants (3.1%) in the placebo group reported fever ≥38.0°C. Of the 43 participants in the BNT162b2 group, 20 participants (3.9%) reported fevers ≥38.0°C to 38.4°C, 14 participants (2.7%) reported fevers >38.4°C to 38.9°C, and 9 participants (1.7%) reported fevers >38.9°C to 40.0°C. No participants reported fever >40°C.
Antipyretic or pain medication use after any dose was reported by 199 participants (38.5%) and 31 participants (11.9%) in the BNT162b2 10-µg group and placebo group, respectively.
Median time to onset for any systemic event after Dose 1 of BNT162b2 10 µg occurred on Day 1.0, while median time to onset for any systemic event after Dose 2 and Dose 3 occurred on Day 2.0. Median time to onset for any systemic event after Dose 1 of placebo occurred on Day 2.0 and on Day 1.0 for Dose 2. All events resolved with a median duration of 1.0 day after any dose of BNT162b2. All events resolved with a median duration of 1.0 day after Dose 1 or Dose 2 of placebo, except for fever, which resolved with a median duration of 2.0 days after Dose 1.

Adverse Events

<u>AEs from dose 1 to 1 month after dose 2</u>

Table 16: Number (%) of participants reporting at least 1 adverse event from dose 1 to 1 month after dose 2 – phase 2/3 – blinded placebo-controlled follow up period – Troponin group – 5 to <12 years of age – safety population

	Vaccine Group (as Administered)	
Adverse Event	BNT162b2 (10 µg) (N[a]=518) n[b] (%)	Placebo (N[a]=260) n[b] (%)
Any adverse event	37 (7.1)	21 (8.1)
Related[c]	12 (2.3)	4 (1.5)
Severe	1 (0.2)	0
Life-threatening	0	0
Any serious adverse event	1 (0.2)	0
Related[c]	0	0
Severe	1 (0.2)	0
Life-threatening	0	0
Any nonserious adverse event	37 (7.1)	21 (8.1)
Related[c]	12 (2.3)	4 (1.5)
Severe	0	0
Life-threatening	0	0
Any adverse event leading to withdrawal	0	0
Related[c]	0	0
Serious	0	0
Severe	0	0
Life-threatening	0	0
Death	0	0

a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants reporting at least 1 occurrence of the specified event category. For "any adverse event," n = number of participants reporting at least 1 occurrence of any adverse event.
c. Assessed by the investigator as related to the study intervention.
PFIZER CONFIDENTIAL SDTM Creation: 12JAN2024 (08:40) Source Data: adaexa Table Generation: 23JAN2024 (02:11)
(Database snapshot date : 05JAN2024) Output File: ./nda2_ubped2/C4591007_CSR/adae_s130_d1md2_p2_trop_12

Note that participants who originally received placebo and then received BNT162b2 after unblinding did not complete a reactogenicity e-diary after BNT162b2 vaccination as, per protocol, local reactions and systemic events were reported as AEs.

The SOC containing the most frequently reported AEs in both the BNT162b2 group and placebo group was infections and infestations (2.5% and 2.7%, respectively), respiratory, thoracic and mediastinal disorders (1.4% and 2.3%, respectively), general disorders and administration site conditions (1.9% and 0.8%, respectively), and gastrointestinal disorders (1.0% and 1.2%, respectively). One participant (0.2%) in the BNT162b2 group reported noncardiac chest pain.
From Dose 1 to 1 month after Dose 2, 61 participants (25.1%) who originally received placebo and then received BNT162b2 after unblinding reported any AE. The SOC containing the most frequently reported AEs was general disorders and administration site conditions (19.3%), infections and infestations (3.7%), nervous system disorders (3.3%), respiratory, thoracic and mediastinal disorders (2.5%), and musculoskeletal and connective tissue disorders (1.6%). One participant (0.4%) each reported chest pain and noncardiac chest pain. Many of the AEs were reflective of reactogenicity events that were reported as AEs (eg, injection site pain, fatigue, headache).

Table 17: Number (%) of participants reporting at least 1 adverse event from dose 1 to 1 month after dose 2 –, by system organ class and preferred term - phase 2/3 – blinded placebo-controlled follow up period – Troponin group – 5 to <12 years of age – safety population

	Vaccine Group (as Administered)			
	BNT162b2 (10 µg) (N[a]=518)		Placebo (N[a]=260)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any adverse event	37 (7.1)	(5.1, 9.7)	21 (8.1)	(5.1, 12.1)
Eye disorders	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Lacrimation increased	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Gastrointestinal disorders	5 (1.0)	(0.3, 2.2)	3 (1.2)	(0.2, 3.3)
Vomiting	3 (0.6)	(0.1, 1.7)	2 (0.8)	(0.1, 2.8)
Diarrhoea	2 (0.4)	(0.0, 1.4)	0	(0.0, 1.4)
Gingival bleeding	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Nausea	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)
General disorders and administration site conditions	10 (1.9)	(0.9, 3.5)	2 (0.8)	(0.1, 2.8)
Injection site pain	5 (1.0)	(0.3, 2.2)	0	(0.0, 1.4)
Pyrexia	3 (0.6)	(0.1, 1.7)	1 (0.4)	(0.0, 2.1)
Injection site erythema	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Injection site swelling	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Non-cardiac chest pain	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Injection site rash	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)
Infections and infestations	13 (2.5)	(1.3, 4.3)	7 (2.7)	(1.1, 5.5)
Upper respiratory tract infection	4 (0.8)	(0.2, 2.0)	3 (1.2)	(0.2, 3.3)
Staphylococcal infection	3 (0.6)	(0.1, 1.7)	1 (0.4)	(0.0, 2.1)
Pharyngitis streptococcal	2 (0.4)	(0.0, 1.4)	0	(0.0, 1.4)
COVID-19	1 (0.2)	(0.0, 1.1)	1 (0.4)	(0.0, 2.1)
Cellulitis	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Eczema herpeticum	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Nasopharyngitis	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Otitis media	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Vulvovaginitis	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Molluscum contagiosum	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)
Sinusitis	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)
Viral upper respiratory tract infection	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)
Injury, poisoning and procedural complications	3 (0.6)	(0.1, 1.7)	1 (0.4)	(0.0, 2.1)
Ankle fracture	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Contusion	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Fall	1 (0.2)	(0.0, 1.1)	1 (0.4)	(0.0, 2.1)
Limb injury	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Lip injury	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)
Investigations	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)
SARS-CoV-2 test positive	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)
Metabolism and nutrition disorders	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Decreased appetite	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Musculoskeletal and connective tissue disorders	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Pain in extremity	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Nervous system disorders	2 (0.4)	(0.0, 1.4)	1 (0.4)	(0.0, 2.1)
Headache	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Paraesthesia	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Syncope	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)
Psychiatric disorders	1 (0.2)	(0.0, 1.1)	1 (0.4)	(0.0, 2.1)
Anxiety	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Insomnia	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)
Respiratory, thoracic and mediastinal disorders	7 (1.4)	(0.5, 2.8)	6 (2.3)	(0.9, 5.0)
Rhinorrhoea	3 (0.6)	(0.1, 1.7)	1 (0.4)	(0.0, 2.1)
Asthma	1 (0.2)	(0.0, 1.1)	1 (0.4)	(0.0, 2.1)
Cough	1 (0.2)	(0.0, 1.1)	2 (0.8)	(0.1, 2.8)
Oropharyngeal pain	1 (0.2)	(0.0, 1.1)	2 (0.8)	(0.1, 2.8)
Respiratory disorder	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Wheezing	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Haemoptysis	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)
Skin and subcutaneous tissue disorders	3 (0.6)	(0.1, 1.7)	2 (0.8)	(0.1, 2.8)
Night sweats	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Petechiae	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Urticaria	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Rash	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)
Rash pruritic	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)

Note: MedDRA (v26.1) coding dictionary applied.
a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants reporting at least 1 occurrence of the specified event. For "any adverse event," n = number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided CI, based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 12JAN2024 (08:40) Source Data: adaexa Table Generation: 23JAN2024 (02:12)
(Database snapshot date : 05JAN2024) Output File: ./nda2_ubped2/C4591007_CSR/adae_s150_d1md2_soc_p2_trop_12

From Dose 3 to 1 month after Dose 3, the percentage of participants reporting any AE was 11.5% in the original BNT162b2 group and 15.3% in the original placebo/BNT162b2 group. The higher percentage of any AE reported in the original placebo/BNT162b2 group is due to these participants having their reactogenicity events reported as AEs. The percentage of participants reporting any AEs assessed as related to study intervention by the investigator was 4.5% in the original BNT162b2 group and 10.4% in the original placebo/BNT162b2 group. All related AEs were nonserious. One participant

(0.2%) in the original BNT162b2 group and 1 participant (0.5%) in the original placebo/BNT162b2 group reported a nonserious, severe AE. No SAEs, AEs leading to withdrawal, life-threatening AEs, or deaths were reported in either the original BNT162b2 group or the original placebo/BNT162b2 group during this time period.

The SOCs containing the most frequently reported AEs in the original BNT162b2 and original placebo/BNT162b2 group were general disorders and administration site conditions (4.1% and 9.9%, respectively), infections and infestations (3.8% and 3.5%, respectively), respiratory, thoracic and mediastinal disorders (1.9% and 2.0%, respectively), and gastrointestinal disorders (1.7% and 1.0%, respectively).
Many of the AEs were reflective of reactogenicity events that were reported as AEs (eg, injection site pain, fatigue, headache

Table 18: Number (%) of participants reporting at least 1 adverse event from dose 3 to 1 month after dose 3, by system organ class and preferred term – phase 2/3 – Troponin group – 5 to <12 years of age – safety population

	Vaccine Group (as Administered at Dose 3)			
	Original BNT162b2 (10 µg) (N[a]=418)		Original Placebo/ BNT162b2 (10 µg) (N[a]=202)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any adverse event	48 (11.5)	(8.6, 14.9)	31 (15.3)	(10.7, 21.1)
Blood and lymphatic system disorders	4 (1.0)	(0.3, 2.4)	1 (0.5)	(0.0, 2.7)
Lymphadenopathy	2 (0.5)	(0.1, 1.7)	1 (0.5)	(0.0, 2.7)
Lymph node pain	2 (0.5)	(0.1, 1.7)	0	(0.0, 1.8)
Ear and labyrinth disorders	0	(0.0, 0.9)	1 (0.5)	(0.0, 2.7)
Ear pain	0	(0.0, 0.9)	1 (0.5)	(0.0, 2.7)
Gastrointestinal disorders	7 (1.7)	(0.7, 3.4)	2 (1.0)	(0.1, 3.5)
Vomiting	3 (0.7)	(0.1, 2.1)	1 (0.5)	(0.0, 2.7)
Abdominal pain upper	2 (0.5)	(0.1, 1.7)	0	(0.0, 1.8)
Diarrhoea	2 (0.5)	(0.1, 1.7)	0	(0.0, 1.8)
Gastritis	1 (0.2)	(0.0, 1.3)	0	(0.0, 1.8)
Nausea	0	(0.0, 0.9)	1 (0.5)	(0.0, 2.7)
General disorders and administration site conditions	17 (4.1)	(2.4, 6.4)	20 (9.9)	(6.2, 14.9)
Injection site pain	7 (1.7)	(0.7, 3.4)	17 (8.4)	(5.0, 13.1)
Pyrexia	2 (0.5)	(0.1, 1.7)	4 (2.0)	(0.5, 5.0)
Axillary pain	5 (1.2)	(0.4, 2.8)	0	(0.0, 1.8)
Chills	1 (0.2)	(0.0, 1.3)	2 (1.0)	(0.1, 3.5)
Fatigue	0	(0.0, 0.9)	3 (1.5)	(0.3, 4.3)
Injection site swelling	0	(0.0, 0.9)	2 (1.0)	(0.1, 3.5)
Vessel puncture site bruise	2 (0.5)	(0.1, 1.7)	0	(0.0, 1.8)
Vessel puncture site pain	2 (0.5)	(0.1, 1.7)	0	(0.0, 1.8)
Injection site erythema	0	(0.0, 0.9)	1 (0.5)	(0.0, 2.7)
Pain	0	(0.0, 0.9)	1 (0.5)	(0.0, 2.7)
Swelling	1 (0.2)	(0.0, 1.3)	0	(0.0, 1.8)
Infections and infestations	16 (3.8)	(2.2, 6.1)	7 (3.5)	(1.4, 7.0)
COVID-19	8 (1.9)	(0.8, 3.7)	2 (1.0)	(0.1, 3.5)
Nasopharyngitis	1 (0.2)	(0.0, 1.3)	2 (1.0)	(0.1, 3.5)
Viral infection	2 (0.5)	(0.1, 1.7)	0	(0.0, 1.8)
Viral upper respiratory tract infection	1 (0.2)	(0.0, 1.3)	1 (0.5)	(0.0, 2.7)
Ear infection	1 (0.2)	(0.0, 1.3)	0	(0.0, 1.8)
External ear cellulitis	1 (0.2)	(0.0, 1.3)	0	(0.0, 1.8)
Gastroenteritis viral	1 (0.2)	(0.0, 1.3)	0	(0.0, 1.8)

Influenza	0	(0.0, 0.9)	1 (0.5)	(0.0, 2.7)
Pharyngitis streptococcal	1 (0.2)	(0.0, 1.3)	0	(0.0, 1.8)
Upper respiratory tract infection	1 (0.2)	(0.0, 1.3)	0	(0.0, 1.8)
Viral rhinitis	0	(0.0, 0.9)	1 (0.5)	(0.0, 2.7)
Injury, poisoning and procedural complications	1 (0.2)	(0.0, 1.3)	0	(0.0, 1.8)
Upper limb fracture	1 (0.2)	(0.0, 1.3)	0	(0.0, 1.8)
Musculoskeletal and connective tissue disorders	1 (0.2)	(0.0, 1.3)	1 (0.5)	(0.0, 2.7)
Arthralgia	1 (0.2)	(0.0, 1.3)	1 (0.5)	(0.0, 2.7)
Myalgia	0	(0.0, 0.9)	1 (0.5)	(0.0, 2.7)
Nervous system disorders	1 (0.2)	(0.0, 1.3)	1 (0.5)	(0.0, 2.7)
Headache	1 (0.2)	(0.0, 1.3)	1 (0.5)	(0.0, 2.7)
Psychiatric disorders	1 (0.2)	(0.0, 1.3)	0	(0.0, 1.8)
Anxiety	1 (0.2)	(0.0, 1.3)	0	(0.0, 1.8)
Respiratory, thoracic and mediastinal disorders	8 (1.9)	(0.8, 3.7)	4 (2.0)	(0.5, 5.0)
Oropharyngeal pain	4 (1.0)	(0.3, 2.4)	2 (1.0)	(0.1, 3.5)
Cough	3 (0.7)	(0.1, 2.1)	1 (0.5)	(0.0, 2.7)
Rhinorrhoea	2 (0.5)	(0.1, 1.7)	0	(0.0, 1.8)
Nasal congestion	0	(0.0, 0.9)	1 (0.5)	(0.0, 2.7)
Skin and subcutaneous tissue disorders	1 (0.2)	(0.0, 1.3)	0	(0.0, 1.8)
Rash	1 (0.2)	(0.0, 1.3)	0	(0.0, 1.8)

Note: MedDRA (v26.1) coding dictionary applied.
a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants reporting at least 1 occurrence of the specified event. For "any adverse event," n = number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided CI, based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 12JAN2024 (08:40) Source Data: adaexa Table Generation: 01FEB2024 (04:53)
(Database snapshot date : 05JAN2024) Output File: ./nda2_ubped2/C4591007_CSR/adae_s150_d3md3_soc_p2_trop_12

Related AEs

During the blinded placebo-controlled follow-up period, from Dose 1 to 1 month after Dose 2, AEs assessed as related to study intervention by the investigator were reported by 12 participants (2.3%) and 4 participants (1.5%) in the BNT162b2 and placebo groups, respectively. These AEs were all nonserious.
Most related AEs reported by participants in the BNT162b2 group were reactogenicity events in the general disorders and administration site conditions SOC (1.5%) and the most commonly reported PT in this SOC was injection site pain (1.0%). One participant (0.2%) reported noncardiac chest pain. Related AEs (injection site rash, vomiting, syncope, insomnia, and oropharyngeal pain) in the placebo group were reported by 1 participant (0.4%) each.

From Dose 3 to 1 month after Dose 3, AEs assessed as related to study intervention by the investigator were reported by 19 participants (4.5%) and 21 participants (10.4%) in the original BNT162b2 group and original placebo/BNT162b2 group, respectively. These AEs were all nonserious. Most related AEs reported by participants in the original BNT162b2 group and in the original placebo/BNT162b2 group were reactogenicity events in the general disorders and administration site conditions SOC (3.1% and 9.9%, respectively). The most commonly reported PT in this SOC in the original BNT162b2 group and original placebo/BNT162b2 group was injection site pain (1.7% and 8.4%, respectively).

Immediate AEs

Five participants (1.0%) in the BNT162b2 group and 1 participant (0.4%) in the placebo group reported any immediate adverse events (Table 14.100).

Table 19: Number (%) of participants reporting at least 1 immediate adverse event, by system organ class and preferred term – phase 2/3 – Troponin group – 5 to <12 years of age – safety population

	Vaccine Group (as Administered)			
	BNT162b2 (10 µg) (N[a]=518)		Placebo (N[a]=260)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any adverse event	5 (1.0)	(0.3, 2.2)	1 (0.4)	(0.0, 2.1)
Gastrointestinal disorders	1 (0.2)	(0.0, 1.1)	1 (0.4)	(0.0, 2.1)
Vomiting	1 (0.2)	(0.0, 1.1)	1 (0.4)	(0.0, 2.1)
General disorders and administration site conditions	2 (0.4)	(0.0, 1.4)	0	(0.0, 1.4)
Injection site erythema	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Injection site pain	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Musculoskeletal and connective tissue disorders	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Pain in extremity	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Nervous system disorders	1 (0.2)	(0.0, 1.1)	1 (0.4)	(0.0, 2.1)
Paraesthesia	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Syncope	0	(0.0, 0.7)	1 (0.4)	(0.0, 2.1)
Psychiatric disorders	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)
Anxiety	1 (0.2)	(0.0, 1.1)	0	(0.0, 1.4)

Note: MedDRA (v26.1) coding dictionary applied.
a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants reporting at least 1 occurrence of the specified event. For "any adverse event," n = number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided CI, based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 12JAN2024 (08:40) Source Data: adaexa Table Generation: 02FEB2024 (18:55)
(Database snapshot date : 05JAN2024) Output File: ./nda2_ubped2/C4591007_CSR/adae_s150_imm_p2_tp_12

Deaths

No deaths were reported in participants 12 to <16 years of age in the troponin group during the study.

Serious Adverse Events

Serious Adverse Events from Dose 1 to 6 Months After Dose 2 (Prior to Dose 3)

From Dose 1 to 6 months after Dose 2 (prior to Dose 3), 1 participant (0.2%) each reported an SAE of abortion spontaneous and ovarian cyst. The spontaneous abortion occurred in a participant who developed worsening abdominal pain and underwent an abdominal ultrasound 187 days after vaccination, which confirmed pregnancy at approximately 8 weeks' gestation. On postvaccination Day 193, the participant experienced vaginal hemorrhage, vomiting, and diarrhea for which the participant was evaluated in the emergency department. The participant was diagnosed with 'latent abortion' and received treatment with progesterone. The following day, a repeat ultrasound was performed which demonstrated absence of product in the uterus and uterine aspiration was performed. The participant recovered the same day. This spontaneous abortion was assessed as not related to study intervention.

Serious Adverse Events from Dose 3 to 6 Months After Dose 3

From Dose 3 to 6 months after Dose 3, no participants reported an SAE.

Elevated Troponin I Level At Baseline and After Vaccination – Troponin Group – 12 to <16 Years of Age

At baseline, a total of 2 male participants (0.4%) (95% CI: 0.0, 1.5) had an abnormal troponin I value range of >50 to 100 ng/mL (Table 50), with no further abnormal troponin I levels.
At Day 4 after Dose 2, a total of 2 participants (0.4%) (95% CI: 0.1, 1.5) had an abnormal troponin I result: one male participant with a troponin value range of >35 to 50 ng/mL, and 1 female participant (0.5%) (95% CI: 0.0, 2.6) with a troponin value range of >17 to 35 ng/mL (Table 50). Neither participant had abnormal troponin I levels at baseline or at the after Dose 3 visit.

At Day 4 after Dose 3, a total of 3 participants (0.7%) (95% CI: 0.1, 2.1) had an abnormal troponin I result: two male participants and 1 female participant (Table 50). One male participant had a troponin value range of >35 to 50 ng/mL, and the other male participant had a troponin value range of >50 to 100 ng/mL. The female participant had a troponin value range of >35 to 50 ng/mL. None of these participants had abnormal troponin I levels at baseline or at the after Dose 2 visit. No participant in the troponin group with elevated troponin I levels at baseline or after study vaccination reported symptoms of potential myocarditis/pericarditis.

Table 20: Number (%) of participants with elevated Troponin I results at each time point, by sex and Troponin value range – phase 2/3 – Troponin group – 12 to <16 years of age – safety population

		Vaccine Group (as Administered)					
		BNT162b2 (30 µg)					
		Male		Female		Total	
Dose No. /Sampling Time Point	Troponin Value Range (ng/L)	N[a]	n[b] (%) (95% CI[c])	N[a]	n[b] (%) (95% CI[c])	N[a]	n[b] (%) (95% CI[c])
1/Prevax	Any abnormality	270	2 (0.7) (0.1, 2.7)	216	0 (0.0, 1.7)	486	2 (0.4) (0.0, 1.5)
	>17 to 35[d]		NA		0 (0.0, 1.7)		0 (0.0, 0.8)
	>35 to 50		0 (0.0, 1.4)		0 (0.0, 1.7)		0 (0.0, 0.8)
	>50 to 100		2 (0.7) (0.1, 2.7)		0 (0.0, 1.7)		2 (0.4) (0.0, 1.5)
	>100 to 200		0 (0.0, 1.4)		0 (0.0, 1.7)		0 (0.0, 0.8)
	>200		0 (0.0, 1.4)		0 (0.0, 1.7)		0 (0.0, 0.8)
2/Day 4	Any abnormality	256	1 (0.4) (0.0, 2.2)	209	1 (0.5) (0.0, 2.6)	465	2 (0.4) (0.1, 1.5)
	>17 to 35[d]		NA		1 (0.5) (0.0, 2.6)		1 (0.2) (0.0, 1.2)
	>35 to 50		1 (0.4) (0.0, 2.2)		0 (0.0, 1.7)		1 (0.2) (0.0, 1.2)
	>50 to 100		0 (0.0, 1.4)		0 (0.0, 1.7)		0 (0.0, 0.8)
	>100 to 200		0 (0.0, 1.4)		0 (0.0, 1.7)		0 (0.0, 0.8)
	>200		0 (0.0, 1.4)		0 (0.0, 1.7)		0 (0.0, 0.8)
3/Day 4	Any abnormality	235	2 (0.9) (0.1, 3.0)	188	1 (0.5) (0.0, 2.9)	423	3 (0.7) (0.1, 2.1)
	>17 to 35[d]		NA		0 (0.0, 1.9)		0 (0.0, 0.9)
	>35 to 50		1 (0.4) (0.0, 2.3)		1 (0.5) (0.0, 2.9)		2 (0.5) (0.1, 1.7)
	>50 to 100		1 (0.4) (0.0, 2.3)		0 (0.0, 1.9)		1 (0.2) (0.0, 1.3)
	>100 to 200		0 (0.0, 1.6)		0 (0.0, 1.9)		0 (0.0, 0.9)
	>200		0 (0.0, 1.6)		0 (0.0, 1.9)		0 (0.0, 0.9)

Abbreviation: NA = not applicable.
Note: One participant who received BNT162b2 10 µg at Dose 1 and 30 µg at Dose 2 and Dose 3 is also included in the analysis.
a. N = number of participants with troponin I test result in the specified sex and age group. These values are the denominators for the percentage calculations.
b. n = Number of participants with an elevated troponin I result.
c. Exact 2-sided CI, based on the Clopper and Pearson method.
d. An elevated troponin I result is defined as >35 ng/L in males or >17 ng/L in females.
PFIZER CONFIDENTIAL SDTM Creation: 11MAY2023 (15:34) Source Data: adlb Table Generation: 05JUN2023 (15:40)
(Cutoff Date: 13MAR2023, Snapshot Date: 08MAY2023) Output File: ./nda2_ubped2/C4591007_5LT12_Troponin/adlb_s201_trop_sex_tvr_vs_16

Multisystem Inflammatory Syndrome in Children

No cases of MIS-C were reported in any of the Phase I/II/III study.

2.3.3. Discussion on clinical aspects

This is the final report for the Phase 1/2/3 study C4591007, which is a randomised, placebo-controlled, study in healthy children aged 6 months to <12 years of age. For these paediatric groups, the study was designed to evaluate BNT162b2 vaccination in an age-de-escalation Phase 1 dose-finding portion and Phase 2/3 selected-dose portion, in protocol-defined age groups: 5 to <12 years, 2 to <5 years, and 6 months to <2 years of age. Initiation of the study with the oldest paediatric group (5 to <12 years of age) was based on acceptable safety and tolerability demonstrated in adolescents in Study C4591001. The BNT162b2 series was initially planned as a 2-dose series; however, based on emerging clinical and real-world data, the protocol was amended on 04 January 2022 to add a third dose at the selected dose level for each age group.

BNT162b2 were administered at the following dose levels: 5 to <12 years of age (10 µg), 2 to <5 years of age (3 µg) and 6 months to <2 years of age (3 µg).

Interim data from this study has previously been presented and assessed in EMEA/H/C/005735/X/0138, EMEA/H/C/005735/II/0160 and EMEA/H/C/005735/II/0203.

Efficacy

The incidence rate of COVID-19 was monitored for approximately one year post dose 3. During this period, the epidemiological situation of COVID-19 strains changed drastically. Breakthrough cases started to appear during the Delta strain wave. The high vaccine efficacy, which was recorded earlier, (7 days to 2 months post last dose) in placebo-controlled settings, vanished later on, when Omicron strains became prevalent. The incidence rate (IR) increase was observed in all study arms in all studied age groups. Also, severe cases appeared in all study arms, but no MIS-C case was reported. Interestingly, among children below 5 years, who received 3 doses of 3 µg Original Comirnaty, the IR was lower in the cross-over arm than in original active arm, showing, that recent vaccination protected better than vaccination with the same vaccine longer time ago. This observation shows the importance of the level of circulating antibodies, which is constantly decreasing with time since vaccination.

Exploratory PBMC analysis revealed that CD4+ and CD8+ T cells stimulated with S1 peptide responded with interferon gamma, IL2 and IL4 secretion in some vaccinated subjects, whereas such secretion was not observed in placebo recipients. This data supports the mechanism of action for Comirnaty as some T cell mediated immunity is also recorded besides of the B cell and neutralising antibody mediated immunity.

The data provided do not raise new concerns and are in agreement with other data.

Safety

The local and systemic reactions as well as adverse events (AEs) and serious adverse events (SAEs) for the phase I/II/III have already been presented in previous reports (EMEA/H/C/005735/X/0138, EMEA/H/C/005735/II/0160 and EMEA/H/C/005735/II/0203) and therefore not included here.

Among the participants aged 6 months to <2 years of age, any AEs were reported at a frequency of 1.7% in the vaccine group and by 2.4% in the placebo group.

The main safety focus in this report includes safety data for the Troponin group. Among the 778 participants aged 5 to <12 years of age (518 participants in the BNT162b2 group and 260 participants in the placebo group) pain at injection site was the most commonly reported local reaction at all three doses of vaccine (67-73%). The most reported systemic events for all three doses of vaccine were fatigue (37-39%) followed by headache (24-30%) and muscle pain (12-19%). Fever was reported

among 1-3% of the subjects in the vaccine group. Most of the local and systemic events were mild to moderate at intensity and resolved within 1-2 days.

Up to one month after dose 2, any AEs were reported in 7,1% of the subjects in the vaccine group and in 8,1% of the subjects in the placebo group. The system organ class (SOC) containing the most frequently reported AEs in both the vaccine group and placebo group was infections and infestations (2.5% and 2.7%, respectively). Most related AEs reported in the vaccine group were reactogenicity events in the general disorders and administration site conditions SOC (1.5%) and the most commonly reported PT in this SOC was injection site pain (1.0%). One participant (0.2%) reported noncardiac chest pain.

From dose 3 to 1 month after dose 3, the percentage of participants reporting any AE was 11.5% in the original vaccine group and 15.3% in the original placebo and then switched to the vaccine group. The higher percentage of any AE reported in the original the last group is explained by these participants having their reactogenicity events reported as AEs. The AEs considered related to vaccination were reported by 19 participants (4.5%) and 21 participants (10.4%) in the original vaccine group and original placebo/vaccine group, respectively. These AEs were all nonserious. The most commonly reported preferred term (PT) in this SOC in the original vaccine group and original placebo/vaccine group was injection site pain (1.7% and 8.4%, respectively).

Two male participants had abnormal troponin I values at baseline (>50-100 ng/L), at day 4 after dose 2 one male reported >35-50 ng/L and one female>17-34 ng/L. At day 4 after dose 3 one male and one female reported >35-50 ng/L, and one male reported a troponin I level of >35-50 ng/L. No participants reported levels >100 or >200 ng/L. No participant in the troponin group with elevated troponin I levels at baseline or after study vaccination reported symptoms of potential myocarditis/pericarditis.

MIS-C cases are also a target for this report; however, no such cases were reported in this study.

The presented safety data are in line with previous reported results. No new safety concern was identified in this report.

3. CHMP overall conclusion and recommendation

The efficacy data provided are in agreement with other available data. among children below 5 years, who received 3 doses of 3 µg Original Comirnaty, the IR was lower in the cross-over arm than in original active arm, showing, that recent vaccination protected better than vaccination with the same vaccine longer time ago. This observation shows the importance of the level of circulating antibodies, which is constantly decreasing with time since vaccination.

The presented safety data are in line with previous reported results. No new safety concern was identified.

☒ Fulfilled:

No regulatory action required.