For each dose, the number and percentage of participants reporting at least one local reaction or systemic reaction (i.e., solicited data collected using participant diaries) were summarized for predefined reaction types.

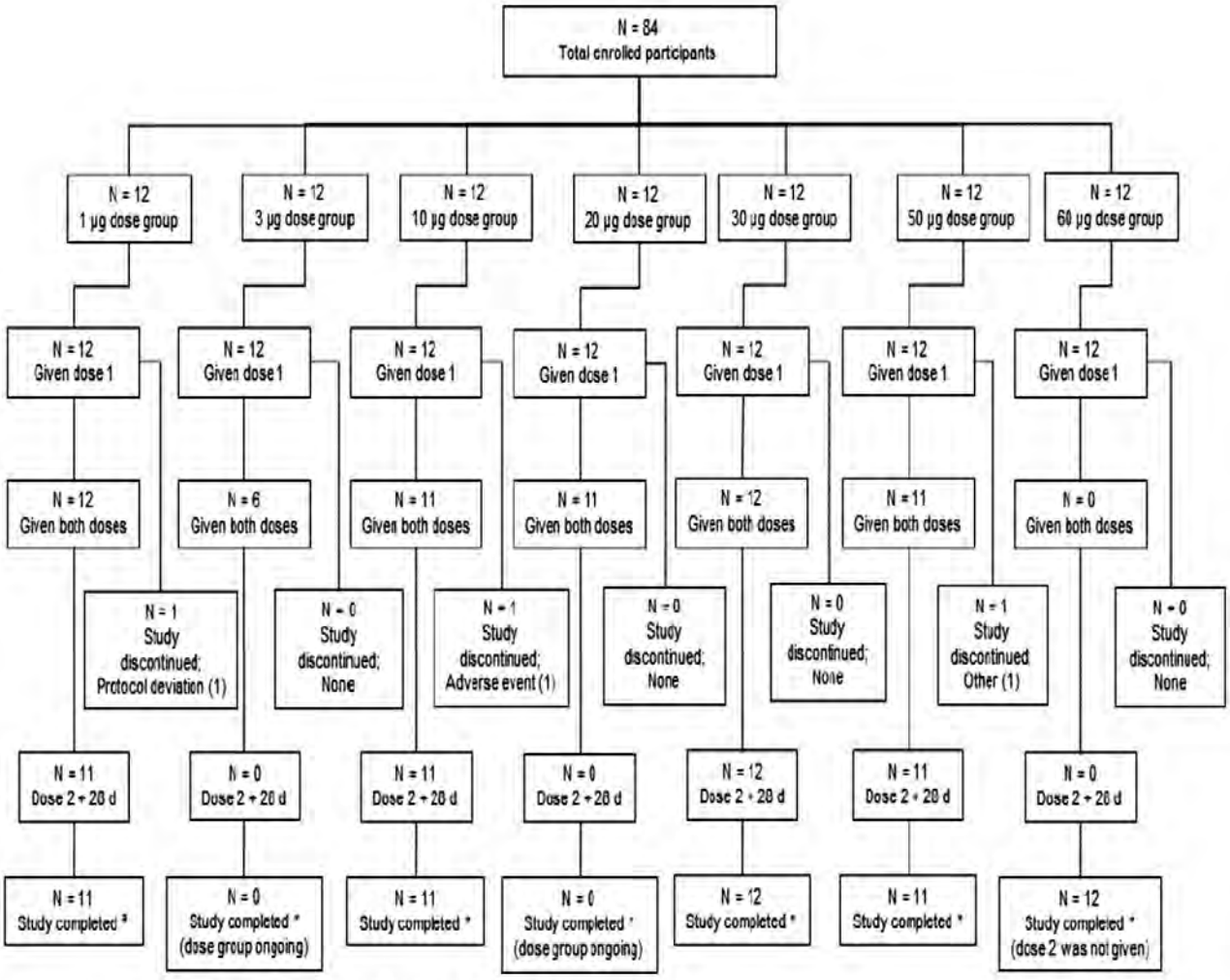
8.2.1.6. Baseline data

All participants met the inclusion criteria for age, weight, and body mass index (BMI).

In total 84 participants were treated with BNT162b1 and included in the Safety Set. Of these participants, 44 were male and 40 were female. Eighty-one were White, two were Asian, and one was Black. Two participants were of Hispanic or Latino origin. Across the dose groups, the mean age ranged from 19.9 yrs to 55.8 yrs, the mean weight ranged from 50.1 kg to 110.2 kg, and the mean BMI ranged from 19.6 kg/m2 to 29.9 kg/m2.

In total 60 participants were treated with BNT162b2 and included in the Safety Set. Of these participants, 26 were male and 34 were female. All participants were White and no participants were of Hispanic or Latino origin. Across the dose groups, the mean age ranged from 19.0 yrs to 55.8 yrs, mean weight ranged from 55.7 kg to 99.1 kg, and mean BMI ranged from 19.5 kg/m2 to 29.8 kg/m2

Figure 20: **Disposition of participants – BNT162b1**

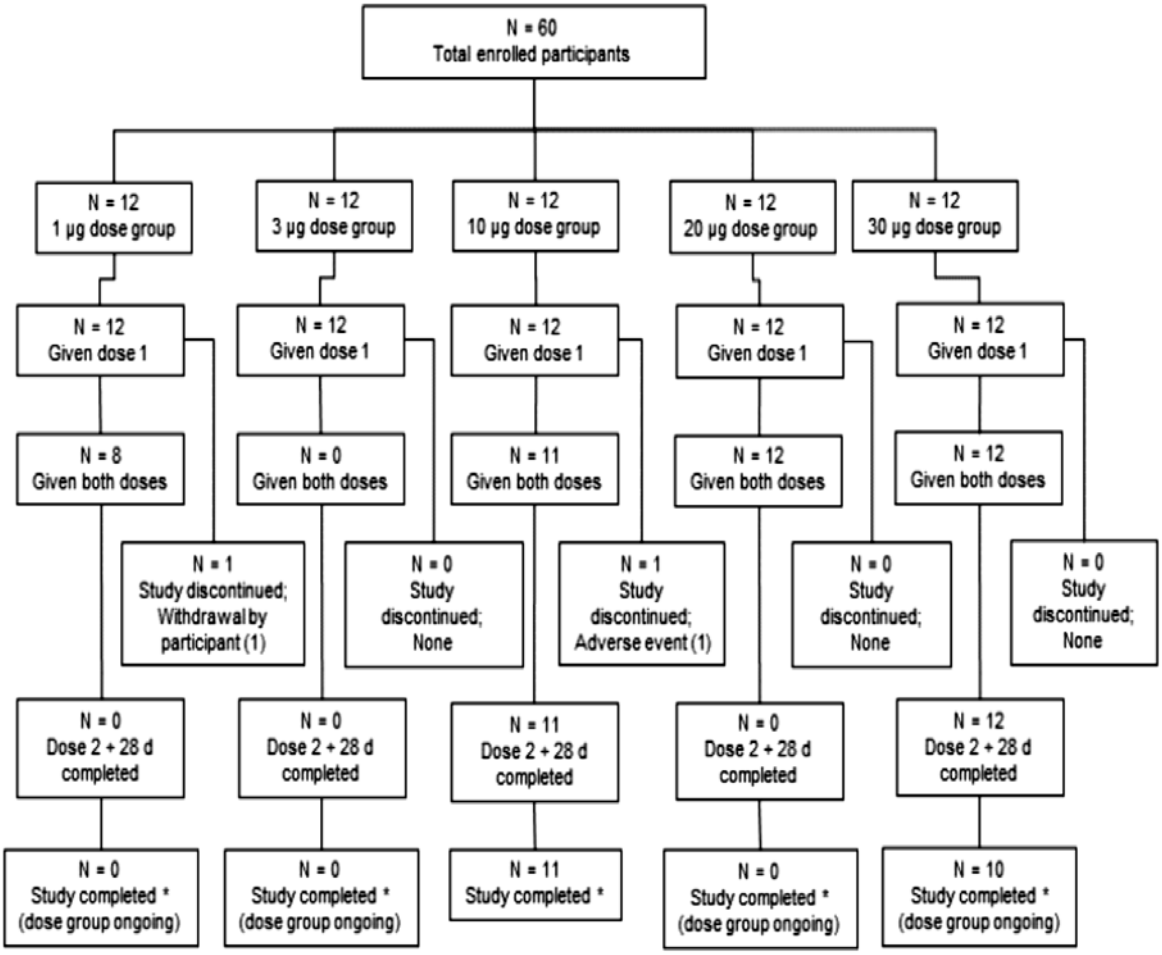


)isposition of participants – BNT162b1

I = number of participants; * Study completed denotes that participants completed Visit 7 (the end of study visit).

)ource: Based on data from Table 14.1-2-1 and Table 14.1-3.1-1, and Listing 16.2.1-1-1

Figure 21: Disposition of participants – BNT162b2



8.2.1.7. Results for the primary safety outcome

The provided data for BNT162b1 and BNT162b2 was collected up until Visit 7 (the EoS visit at ~28 d after the dose 2, i.e., Day 50) in Part A of this study.

Table 15: Summary of solicited local reactions – BNT162b1 (SAF)

Time interval		1 µg (N=12)	3 µg (N=12)	10 µg (N=12)	20 µg (N=12)	30 µg (N=12)	50 µg (N=12)	60 µg (N=12)	Total (N=84)
Dose 1 up to Day 7 after dose 1	nn	12	12	12	12	12	12	12	84
	Any local reaction n (%)	6 (50)	5 (42)	10 (83)	12 (100)	11 (92)	12 (100)	12 (100)	68 (81)
	Any grade >= 3 local reaction n (%)	0 (0)	0 (0)	1 (8)	2 (17)	4 (33)	2 (17)	1 (8)	10 (12)
Dose 2 up to Day 7 after dose 2	nn	12	6	11	10	12	11	N/A	62
	Any local reaction n (%)	7 (58)	3 (50)	10 (91)	10 (100)	11 (92)	11 (100)	N/A	52 (84)
	Any grade >= 3 local reaction n (%)	2 (17)	0 (0)	0 (0)	0 (0)	2 (17)	3 (27)	N/A	7 (11)
Combined interval	nn	12	12	12	12	12	12	12	84
	Any local reaction n (%)	7 (58)	6 (50)	11 (92)	12 (100)	12 (100)	12 (100)	12 (100)	72 (86)
	Any grade >= 3 local reaction n (%)	2 (17)	0 (0)	1 (8)	2 (17)	5 (42)	4 (33)	1 (8)	15 (18)

The combined interval is the union of the intervals 'Dose 1 up to Day 7 after dose 1' and 'Dose 2 up to Day 7 after dose 2'. The denominator for the percentage calculation is nn.

N = number of participants in the analysis set; n = number of participants with the respective local reactions; nn = number of participants with any information on local reactions available; N/A = not available, SAF = Safety Set.

Source: Table 14.3.1-1.1-1.

Table 16: Frequency of participants with solicited local reactions by grade - BNT162b1 (SAF)

Time interval			1 µg (N=12)	3 µg (N=12)	10 µg (N=12)	20 µg (N=12)	30 µg (N=12)	50 µg (N=12)	60 µg (N=12)	Total (N=84)
Combined interval		nn	12	12	12	12	12	12	12	84
	Any	Any n (%)	7 (58)	6 (50)	11 (92)	12 (100)	12 (100)	12 (100)	12 (100)	72 (86)
		Mild n (%)	7 (58)	6 (50)	11 (92)	12 (100)	12 (100)	12 (100)	12 (100)	72 (86)
		Moderate n (%)	5 (42)	1 (8)	5 (42)	6 (50)	11 (92)	10 (83)	7 (58)	45 (54)
		Severe n (%)	2 (17)	0 (0)	1 (8)	2 (17)	5 (42)	4 (33)	1 (8)	15 (18)
	Pain	Any n (%)	6 (50)	4 (33)	9 (75)	12 (100)	12 (100)	12 (100)	12 (100)	67 (80)
		Mild n (%)	5 (42)	4 (33)	9 (75)	12 (100)	12 (100)	11 (92)	12 (100)	65 (77)
		Moderate n (%)	3 (25)	1 (8)	2 (17)	5 (42)	9 (75)	8 (67)	2 (17)	30 (36)
		Severe n (%)	1 (8)	0 (0)	1 (8)	2 (17)	4 (33)	3 (25)	1 (8)	12 (14)
	Tenderness	Any n (%)	7 (58)	6 (50)	11 (92)	12 (100)	11 (92)	12 (100)	11 (92)	70 (83)
		Mild n (%)	6 (50)	6 (50)	10 (83)	12 (100)	10 (83)	12 (100)	11 (92)	67 (80)
		Moderate n (%)	5 (42)	1 (8)	5 (42)	6 (50)	11 (92)	10 (83)	7 (58)	45 (54)
		Severe n (%)	2 (17)	0 (0)	1 (8)	1 (8)	4 (33)	3 (25)	0 (0)	11 (13)
	Erythema / Redness	Any n (%)	0 (0)	0 (0)	0 (0)	1 (8)	3 (25)	3 (25)	0 (0)	7 (8)
		Mild n (%)	0 (0)	0 (0)	0 (0)	1 (8)	3 (25)	3 (25)	0 (0)	7 (8)
		Moderate n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (25)	0 (0)	3 (4)
		Severe n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Induration / Swelling	Any n (%)	2 (17)	0 (0)	1 (8)	2 (17)	2 (17)	4 (33)	1 (8)	12 (14)
		Mild n (%)	0 (0)	0 (0)	1 (8)	2 (17)	2 (17)	3 (25)	1 (8)	9 (11)
		Moderate n (%)	2 (17)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	1 (8)	4 (5)
		Severe n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

The combined interval is the union of the intervals 'Dose 1 up to Day 7 after dose 1' and 'Dose 2 up to Day 7 after dose 2'. The denominator for the percentage calculation is nn.

N = number of participants in the analysis set; n = number of participants with the respective local reaction; nn = number of participants with any information on local reactions available; SAF = Safety Set.

Source: modified from Table 14.3.1-1.3-1.

Table 17 : Summary of solicited local reactions – BNT162b2 (SAF)

Summary of solicited local reactions – BNT162b2 (SAF)

Time interval		1 µg (N=12)	3 µg (N=12)	10 µg (N=12)	20 µg (N=12)	30 µg (N=12)	Total (N=60)
Dose 1 up to Day 7 after dose 1	nn	12	12	12	12	12	60
	Any local reaction n (%)	6 (50)	9 (75)	12 (100)	12 (100)	10 (83)	49 (82)
	Any grade >= 3 local reaction n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Dose 2 up to Day 7 after dose 2	nn	8	0	11	12	12	43
	Any local reaction n (%)	4 (50)	- (-)	10 (91)	10 (83)	11 (92)	35 (81)
	Any grade >= 3 local reaction n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Combined interval	nn	12	12	12	12	12	60
	Any local reaction n (%)	7 (58)	9 (75)	12 (100)	12 (100)	11 (92)	51 (85)
	Any grade >= 3 local reaction n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

The combined interval is the union of the intervals 'Dose 1up to Day 7 after dose 1' and 'Dose 2 up to Day 7 after dose 2'. The denominator for the percentage calculation is nn.

N = number of participants in the analysis set; n = number of participants with the respective local reactions; nn = number of participants with any information on local reactions available; - = not estimable; SAF = Safety Set.

Source: Table 14.3.1-1.1-3.

Table 18 : Frequency of participants with solicited local reactions by grade for – BNT162b2 (SAF)

Time interval			1 µg (N=12)	3 µg (N=12)	10 µg (N=12)	20 µg (N=12)	30 µg (N=12)	Total (N=60)
		nn	12	12	12	12	12	60
Combined interval	Any	Any n (%)	7 (58)	9 (75)	12 (100)	12 (100)	11 (92)	51 (85)
		Mild n (%)	7 (58)	8 (67)	12 (100)	12 (100)	11 (92)	50 (83)
		Moderate n (%)	2 (17)	2 (17)	7 (58)	7 (58)	3 (25)	21 (35)
		Severe n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Pain	Any n (%)	5 (42)	5 (42)	12 (100)	12 (100)	10 (83)	44 (73)
		Mild n (%)	5 (42)	5 (42)	12 (100)	12 (100)	10 (83)	44 (73)
		Moderate n (%)	0 (0)	0 (0)	1 (8)	4 (33)	1 (8)	6 (10)
		Severe n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Tenderness	Any n (%)	5 (42)	9 (75)	12 (100)	10 (83)	11 (92)	47 (78)
		Mild n (%)	5 (42)	8 (67)	9 (75)	10 (83)	11 (92)	43 (72)
		Moderate n (%)	2 (17)	2 (17)	7 (58)	6 (50)	3 (25)	20 (33)
		Severe n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Erythema/ Redness	Any n (%)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	1 (2)
		Mild n (%)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	1 (2)
		Moderate n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
		Severe n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Induration/ Swelling	Any n (%)	0 (0)	0 (0)	1 (8)	0 (0)	3 (25)	4 (7)
		Mild n (%)	0 (0)	0 (0)	1 (8)	0 (0)	3 (25)	4 (7)
		Moderate n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
		Severe n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

The combined interval is the union of the intervals 'dose 1 up to Day 7 after dose 1' and 'Dose 2 up to Day 7 after dose 2'. The denominator for the percentage calculation is nn.

s47 [redacted]

Table 20: Summary of solicited systemic reactions – BNT162b2 (SAF)

Time interval		1 µg (N=12)	3 µg (N=12)	10 µg (N=12)	20 µg (N=12)	30 µg (N=12)	Total (N=60)
Dose 1 up to Day 7 after dose 1	nn	12	12	12	12	12	60
	Any systemic reaction n (%)	9 (75)	9 (75)	12 (100)	9 (75)	9 (75)	48 (80)
	Any grade >= 3 systemic reaction n (%)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	1 (2)
Dose 2 up to Day 7 after dose 2	nn	8	0	11	12	12	43
	Any systemic reaction n (%)	4 (50)	- (-)	7 (64)	10 (83)	10 (83)	31 (72)
	Any grade >= 3 systemic reaction n (%)	0 (0)	- (-)	1 (9)	1 (8)	3 (25)	5 (12)
Combined interval	nn	12	12	12	12	12	60
	Any systemic reaction n (%)	9 (75)	9 (75)	12 (100)	11 (92)	12 (100)	53 (88)
	Any grade >= 3 systemic reaction n (%)	0 (0)	0 (0)	1 (8)	2 (17)	3 (25)	6 (10)

The combined interval is the union of the intervals 'Dose 1 up to Day 7 after dose 1' and 'Dose 2 up to Day 7 after dose 2'. The denominator for the percentage calculation is nn.

N = number of participants in the analysis set; n = number of participants with the respective systemic reactions; nn = number of participants with any information on systemic reactions available; - = not estimable; SAF = Safety Set.

s47

s47

Primary endpoints - Unsolicited TEAEs after BNT162b2 dosing

Table 23: Summary of TEAEs without AEs based on solicited reporting via diaries – BNT162b2 (SAF)

Time interval		1 µg (N=12) n (%) E	3 µg (N=12) n (%) E	10 µg (N=12) n (%) E	20 µg (N=12) n (%) E	30 µg (N=12) n (%) E	Total (N=60) n (%) E
Dose 1 up to dose 2 or Day 28 after dose 1 (whatever comes first)	Any TEAE	1 (8) 2	5 (42) 6	5 (42) 7	1 (8) 1	4 (33) 5	16 (27) 21
	Related TEAE	0 (0) 0	2 (17) 2	0 (0) 0	0 (0) 0	0 (0) 0	2 (3) 2
	Grade >=3 TEAE	0 (0) 0	0 (0) 0	1 (8) 1	0 (0) 0	0 (0) 0	1 (2) 1
	Related grade >=3 TEAE	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0
	Any TESAE	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0
	Related TESAE	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0
Dose 1 up to Day 28 after dose 2 or after dose 1 (if no dose 2)	Any TEAE	3 (25) 4	5 (42) 6	7 (58) 11	2 (17) 3	5 (42) 8	22 (37) 32
	Related TEAE	0 (0) 0	2 (17) 2	1 (8) 1	1 (8) 2	1 (8) 3	5 (8) 8
	Grade >=3 TEAE	0 (0) 0	0 (0) 0	1 (8) 1	0 (0) 0	0 (0) 0	1 (2) 1
	Related grade >=3 TEAE	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0
	Any TESAE	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0
	Related TESAE	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0
Dose 2 up to Day 28 after dose 2	Any TEAE	2 (17) 2	0 (0) 0	4 (33) 4	1 (8) 2	1 (8) 3	8 (13) 11
	Related TEAE	0 (0) 0	0 (0) 0	1 (8) 1	1 (8) 2	1 (8) 3	3 (5) 6
	Grade >=3 TEAE	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0
	Related grade >=3 TEAE	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0
	Any TESAE	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0
	Related TESAE	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0	0 (0) 0

The denominator for the percentage calculation is N.

AE = adverse event; E = number of events; N = number of participants in the analysis set; n = number of participants with the specified characteristic; TEAE = treatment-emergent adverse event; TESAE = treatment-emergent serious adverse event; SAF = Safety Set.

Source: modified from Table 14.3.1-3.1.3-3.

8.2.1.8. Evaluator's Overall Safety Comments

The frequency of local and systemic reactogenicity was noted to be lower for BNT162b2 as compared to BNT162b1 across all dose levels.

In the BNT162b2, a total of 51 participants (85%) reported solicited local reactions and 53 participants (88%) reported solicited systemic reactions. Total 6 participants (10%) reported grade ≥3 solicited systemic reactions. One subject (10 µg group) discontinued due to an AE (mild external ear Inflammation) and no serious adverse events were reported. Most of the reported solicited systemic events in the 10-µg and 30-µg groups were due to reactogenicity, with a onset within the first 24 h of immunization. Injection site reactions within 7 days of the prime or boost doses mainly involved pain and tenderness. In the 7 days following either Dose 1 or 2 of BNT162b2, pain and tenderness at the injection site was the most frequent solicited local reaction (73% and 78% respectively).

Reactogenicity was dose-dependent and noted to be more pronounced after the dose 2. The associated symptomatology, such as fever, chills, headache, muscle pain, joint pain, injection site pain, and tenderness, was mostly mild or moderate, with occasional severe (grade 3) manifestations. Because of the reactogenicity reported after the 50-µg boost dose, participants who had received an initial 60-µg dose did not receive a boost injection.

No relevant change in routine clinical laboratory values occurred after Investigational medicinal product (IMP) dosing. However, there were few transient increases in CRP and temporary reduction of blood lymphocyte counts observed in a dose-dependent manner.

The frequency of local and systemic reactogenicity was generally lower for BNT162b2 compared to BNT162b1. BNT162b2 generally had a milder and therefore more favourable reactogenicity profile than BNT162b1 across dose levels. Due to this favourable safety profile, BNT162b2 was chosen for Phase 2/3 of clinical trials.

8.2.1.9. Evaluator safety conclusion

Overall both candidates showed good tolerability. Majority of the AEs were mild and related to the reactogenicity. The AEs were mostly dose dependent. No relevant change in routine clinical laboratory values occurred after any of the two candidates dosing.

Candidate BNT162b2 showed better safety profile and hence was chosen for phase 2/3 of the clinical trials.

8.2.2. Study C4591001

8.2.2.1. Study overview

Study C4591001 is an ongoing , multicentre , Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals.

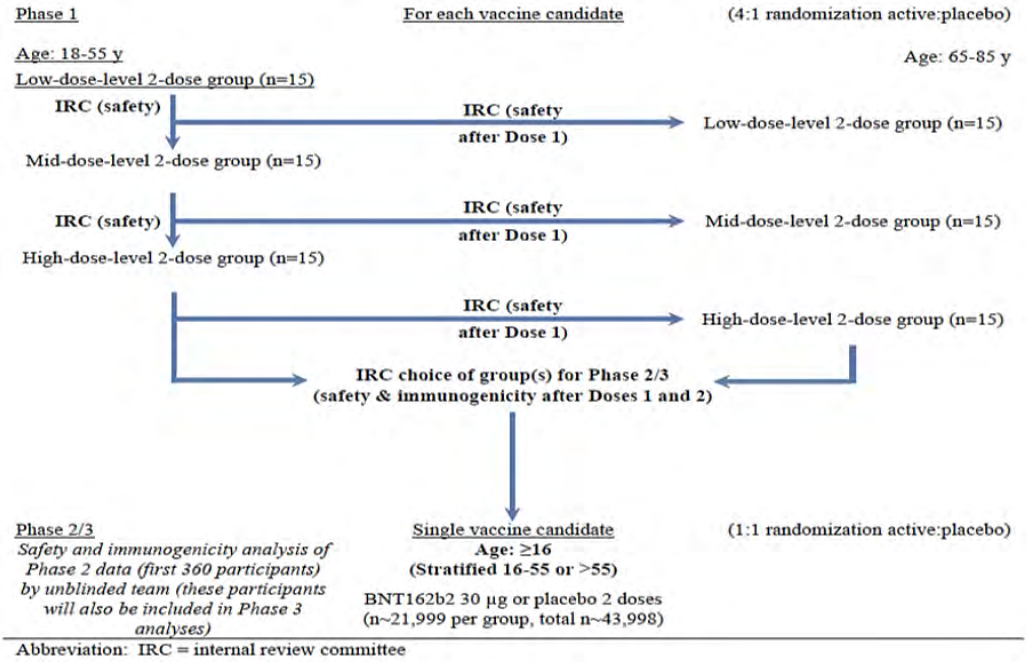
This study is discussed in detail under the efficacy section. Here only Phase 1 of the study is being discussed.

This study commenced on 29th April 2020 at 4 study centres in the United States.

The study consists of 2 parts: Phase 1 to identify preferred vaccine candidate(s) and dose level(s); and Phase 2/3 as an expanded cohort and efficacy part. These parts, and the progression between them, are detailed in following **Figure 16**.

Study included healthy(or pre-existing stable disease) male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive (Phase 1), or ≥16 years (Phase 2/3), at randomization.

Figure 16 : Study Schema



Abbreviation: IRC = internal review committee

8.2.2.2. Objectives (Safety)

Primary objective of this study was to describe the safety and tolerability profiles of prophylactic BNT162 vaccines in healthy adults after 1 or 2 doses. Following are estimands and the safety endpoints.

Table 24: Phase 1 Objectives, Estimands, and Endpoints

Objectives	Estimands	Endpoints
Primary:	**Primary:**	**Primary:**
To describe the safety and tolerability profiles of prophylactic BNT162 vaccines in healthy adults after 1 or 2 doses	In participants receiving at least 1 dose of study intervention, the percentage of participants reporting: • Local reactions for up to 7 days following each dose • Systemic events for up to 7 days following each dose • Adverse events (AEs) from Dose 1 to 1 month after the last dose • SAEs from Dose 1 to 6 months after the last dose In addition, the percentage of participants with: • Abnormal hematology and chemistry laboratory values 1 and 7 days after Dose 1; and 7 days after Dose 2 • Grading shifts in hematology and chemistry laboratory assessments between baseline and 1 and 7 days after Dose 1; and before Dose 2 and 7 days after Dose 2	• 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 Hematology and chemistry laboratory parameters

8.2.2.3. Medicine (Investigational Product)

- BNT162b1 (10 µg,20 µg, 30 µg, and100 µg) and BNT162b2 (10 µg, 20 µg, and 30 µg)
- Placebo - Normal saline (0.9% sodium chloride solution for injection)

8.2.2.4. Safety Evaluations

The primary end points in phase 1 of this trial were , solicited local reactions (i.e., specific local reactions as prompted by and recorded in an electronic diary), systemic events, and use of antipyretic or pain medication within 7 days after the receipt of vaccine or placebo, as prompted by and recorded in an electronic diary.

Unsolicited adverse events and serious adverse events (i.e., those reported by the participants, without electronic- diary prompts) were assessed from the receipt of the first dose through 1 month and 6 months, respectively, after the receipt of the second dose.

Clinical laboratory abnormalities were assessed 1 day and 7 days after the receipt of vaccine or placebo; and grading shifts in laboratory assessments between baseline and 1 day and 7 days after the first dose and between 2 days and 7 days after the second dose.

Protocol-specified safety stopping rules were in effect for all the participants in the phase 1 portion of the trial. An internal review committee and an external data and safety monitoring committee reviewed all safety data.

8.2.2.5. Statistical Methods:

The primary safety objective was evaluated by descriptive summary statistics for local reactions, systemic events, AEs/SAEs, and abnormal hematology and chemistry laboratory parameters, for each vaccine group. Descriptive summary statistics included counts and percentages of participants with the indicated endpoint and the associated 2-sided Clopper-Pearson 95% CIs.

8.2.2.6. Safety Results:

Subject Disposition and Demography

Overall, most participants were white in the younger age group (39 [86.7%]), and all participants were white in the older age group (45 [100%]). Median age was 37.0 years in the younger age group and 68.0 years in the older age group. There was a higher representation of females in both the younger (26 [57.8%]) and older (28 [62.2%]) age groups.

Local reactions

Local reactions in both age groups(16-55yrs and 55yrs or above) included pain at the injection site (58.3% to 100.0%), redness (0% to 16.7%), and swelling (0% to 25.0%) were reported for BNT162b1 recipients.For BNT162b2 recipients, pain at the injection site (33.3% to 91.7%), redness (0% to 8.3%), and swelling (0% to 16.7%) were reported. In general, frequencies of local reactions were observed to be higher with increased dose level and in the BNT162b1 group.

The frequency of local reactions was lower in the older age group compared to the younger age group.

Systemic AEs

Overall, frequencies of systemic events were observed to be higher in the BNT162b1 group and with increased dose level. As expected, the frequency of systemic events was lower in the older age group compared to the younger age group.

Common systemic events in both age groups after Dose 1 or Dose 2 included fatigue (16.7% to 83.3%), headache (25.0% to 100%), chills (8.3% to 66.7%), fever (0% to 75.0%), and muscle pain (8.3% to 75.0%) for BNT162b1 recipients(up to 30 μg). BNT162b2 recipients (up to 30 μg) developed fatigue (8.3% to 75.0%), headache (0% to 66.7%), chills (0% to 58.3%), fever (0% to 16.7%), and muscle pain (0% to 58.3%).

There were no SAEs, deaths, or discontinuations due to AEs.

Laboratory Evaluations

A transient decreases in the lymphocyte count across all age groups was noted 1-3 days after Dose 1, which increased in frequency with increasing dose. It was were mostly Grade 1-2, generally normalized at the next laboratory assessment 6-8 days after Dose 1 and did not occur after Dose 2.

8.2.2.7. Evaluator's overall safety Comment:

In this Phase 1 study, BNT162b2 at 30 µg demonstrated a satisfactory reactogenicity profile, including the older adults.

The most common AEs overall by SOC and PT across dose levels in the younger group were general disorders and administration site conditions, which included injection site pain and injection site erythema. The most common AEs overall by SOC and PT across dose levels in the older group were nervous system disorders, which included sciatica and radiculopathy. No AEs were reported for >1 participant in either age group for BNT162b2 or placebo recipients.

In the younger group, general disorders and administration site conditions was the most commonly reported SOC for related AEs, which included injection site pain and injection site erythema. In the older group, only 1 participant in the 20 µg dose group reported a related AE of nausea.

A transient, reversible decrease in lymphocytes of Grade 1 -2 across all age groups was noted 1-3 days after Dose 1, which increased in frequency with increasing dose.

Additional follow-up from 1 months to 4 months after Dose 2 to the data cutoff date (14 November 2020) included 1 severe SAE (neuritis) reported by 1 participant in the younger BNT162b2 30 µg group. The investigator considered there was a reasonable possibility that the event of neuritis, was related to clinical trial procedure (blood draw) but unrelated to vaccination. The AE profile for remaining non-serious events was unchanged. No additional participants had related AEs.

8.3. Pivotal and/or main efficacy studies (Safety Analysis)

8.3.1. Study C4591001

In this section, safety data from Phase 2/3 of Study C4591001 is discussed. Subjects from phase 2 in study BNT162-01a are included in this safety dataset.

Primary Safety Objectives and Endpoints for Study:

Objectives[a]	Estimands	Endpoints
	Primary Safety	
To define the safety profile of prophylactic BNT162b2 in the first 360 participants randomized (Phase 2)	In participants receiving at least 1 dose of study intervention, the percentage of participants 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 7 days after the second dose • SAEs from Dose 1 to 7 days after the second dose	• 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
To define the safety profile of prophylactic BNT162b2 in all participants randomized in Phase 2/3	In participants receiving at least 1 dose of study intervention, the percentage of participants 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 the second dose • SAEs from Dose 1 to 6 months after the second dose	• AEs • SAEs • In a subset of at least 6000 participants: ○ 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)
To define the safety profile of prophylactic BNT162b2 in participants 12 to 15 years of age in Phase 3	In participants receiving at least 1 dose of study intervention, the percentage of participants 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 the second dose • SAEs from Dose 1 to 6 months after the second dose	• 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

8.3.1.1. Overview of Adverse Events

An adverse event (AE) was defined as any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. As expected, adverse events were reported in higher proportion among the vaccine recipients as compared with placebo recipients. This difference was mainly driven by the reactogenicity (solicited adverse events) reported in the 7 days following vaccination and unsolicited adverse events corresponding to reactogenicity symptoms among participants not in the reactogenicity subset. Severe AEs, SAEs, and AEs leading to withdrawal were few and reported by ≤1.2%, ≤0.5%, and ≤0.2%, respectively, in both groups. Discontinuations due to related AEs were reported in 14 participants in the BNT162b2 group and 7 participants in the placebo group.

There were 6 participants, all in Phase 2/3, who died through the data cutoff date of 14 November 2020 **(Table 25).** This included 2 participants in the BNT162b2 group and 4 participants in the placebo group. Three Phase 3 subjects died, 1 in the BNT162b2 group and 2 in the placebo group. The subject in the BNT162b2 group, who died 3 days after dose 1, experienced an SAE of arteriosclerosis, which was assessed by the investigator as not related to study intervention.

Proportions of participants with serious adverse events, deaths, and withdrawals due to adverse events were balanced between the age, sex, race/ethnicity, or baseline SARS-CoV-2 status subgroups.

Table 25. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to Data Cutoff Date (14NOV2020) – Phase 2/3 (All Subjects) – Safety Population

	Vaccine Group (as Administered)	
Adverse Event	BNT162b2 (30 µg) (N[a]=21621) n[b] (%)	Placebo (N[a]=21631) n[b] (%)
Any event	5770 (26.7)	2638 (12.2)
Related[c]	4484 (20.7)	1095 (5.1)
Severe	240 (1.1)	139 (0.6)
Life-threatening	21 (0.1)	24 (0.1)
Any serious adverse event	126 (0.6)	111 (0.5)
Related[c]	4 (0.0)	0
Severe	71 (0.3)	68 (0.3)
Life-threatening	21 (0.1)	23 (0.1)
Any adverse event leading to withdrawal	37 (0.2)	30 (0.1)
Related[c]	16 (0.1)	9 (0.0)
Severe	13 (0.1)	9 (0.0)
Life-threatening	3 (0.0)	6 (0.0)
Death	2 (0.0)	4 (0.0)

Note: Data for subjects randomized on or after 10OCT2020 are included to comprehensively show all data reported but are subject to change with additional follow-up.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event", n = the number of subjects reporting at least 1 occurrence of any event.
c. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adae Table Generation: 17NOV2020 (16:29)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File:
./nda2 unblinded/C4591001 IA P3 2MPD2/adae s091 all p23 saf

Table 26. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – ~38000 Subjects for Phase 2/3 Analysis – Safety Population

	Vaccine Group (as Administered)	
Adverse Event	BNT162b2 (30 µg) (N[a]=18801) n[b] (%)	Placebo (N[a]=18785) n[b] (%)
Any event	5071 (27.0)	2356 (12.5)
Related[c]	3915 (20.8)	953 (5.1)
Severe	220 (1.2)	109 (0.6)
Life-threatening	18 (0.1)	20 (0.1)
Any serious adverse event	103 (0.5)	81 (0.4)
Related[c]	3 (0.0)	0
Severe	57 (0.3)	48 (0.3)
Life-threatening	18 (0.1)	19 (0.1)
Any adverse event leading to withdrawal	34 (0.2)	25 (0.1)
Related[c]	14 (0.1)	7 (0.0)
Severe	13 (0.1)	7 (0.0)
Life-threatening	2 (0.0)	4 (0.0)
Death	1 (0.0)	2 (0.0)

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event", n = the number of subjects reporting at least 1 occurrence of any event.
c. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adae Table Generation: 17NOV2020 (16:21)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File:
./nda2_unblinded/C4591001_IA_P3_2MPD2/adae_s091_all_pd2_p3_saf

Table 27. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to Data Cutoff Date (14NOV2020) – Subjects With 2 Months Follow-Up Time After Dose 2 for Phase 2/3 Analysis – Safety Population

	Vaccine Group (as Administered)		
Adverse Event	BNT162b2 (30 µg) (N[a]=9531) n[b] (%)	Placebo (N[a]=9536) n[b] (%)	Total (N[a]=19067) n[b] (%)
Any event	2044 (21.4)	1197 (12.6)	3241 (17.0)
Related[c]	1297 (13.6)	343 (3.6)	1640 (8.6)
Severe	105 (1.1)	69 (0.7)	174 (0.9)
Life-threatening	10 (0.1)	11 (0.1)	21 (0.1)
Any serious adverse event	57 (0.6)	53 (0.6)	110 (0.6)
Related[c]	2 (0.0)	0	2 (0.0)
Severe	32 (0.3)	33 (0.3)	65 (0.3)
Life-threatening	10 (0.1)	11 (0.1)	21 (0.1)
Any adverse event leading to withdrawal	1 (0.0)	0	1 (0.0)
Related[c]	0	0	0
Severe	0	0	0
Life-threatening	1 (0.0)	0	1 (0.0)
Death	1 (0.0)	0	1 (0.0)

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event", n = the number of subjects reporting at least 1 occurrence of any event.
c. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adae Table Generation: 17NOV2020 (16:28)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File:
./nda2_unblinded/C4591001_IA_P3_2MPD2/adae_s091_all_2mpd2_p23_saf

8.3.1.2. Solicited Local Reactions

Subgroup analyses by age

For each age group in the reactogenicity subset (younger: 16 to 55 years, older: >55 years) and overall (18 years and older), the median onset of local reactions in the vaccine group was day 1

(day of vaccination) to 2 days after either dose and lasted a median duration between 1 and 2 days.

For both age groups, injection site pain was the most frequent solicited local adverse reaction. After dose 2, the younger age group reported any pain more frequently than the older age group (77.8% vs 66.1%) and pain characterized as moderate (27.1% vs. 18.0%). The frequency was similar after Dose 1 compared with Dose 2 of BNT162b2 in the younger age group (83.1% vs 77.8%) and in the older group (71.1% vs 66.1%). Injection site redness and swelling after each dose were generally similar for both age groups.

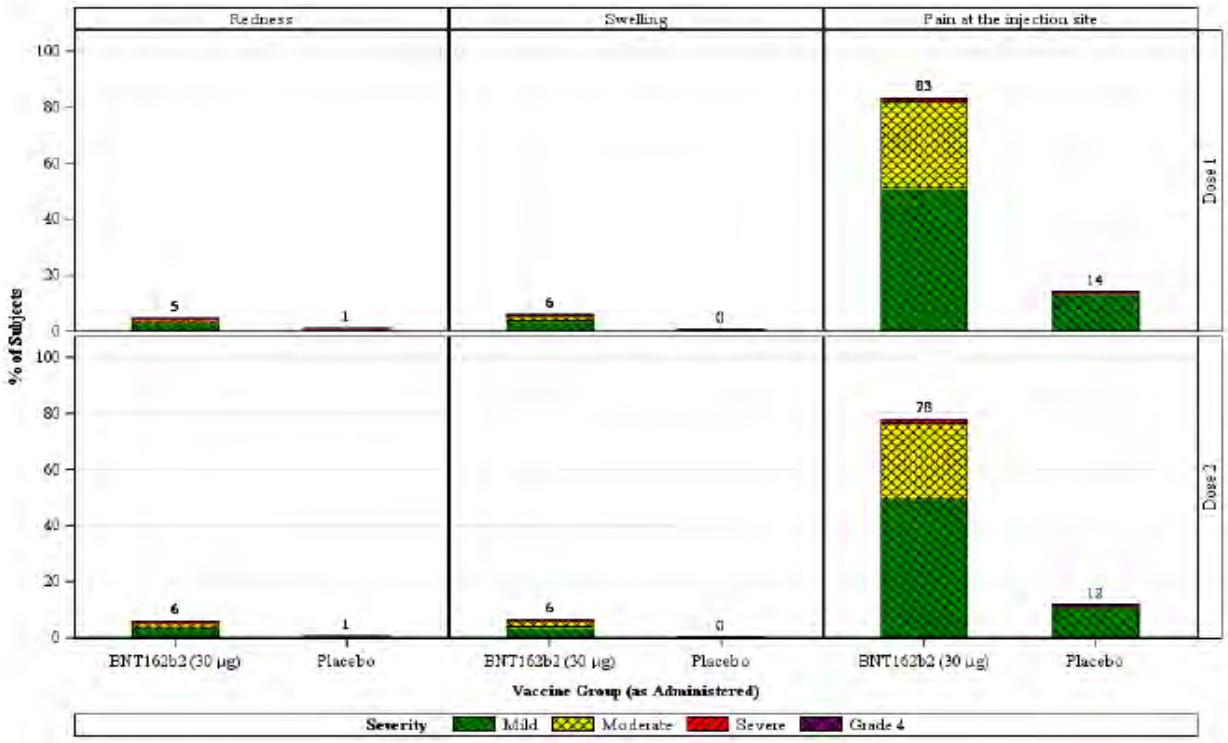
Table 28: Frequency of Solicited Local Reactions Within 7 Days After Each Vaccination, Reactogenicity Subset of the Phase 2/3 Safety Population*, 16 to 55 Years of Age

Table 15. Frequency of Solicited Local Reactions Within 7 Days After Each Vaccination, Reactogenicity Subset of the Phase 2/3 Safety Population*, 18 to 55 Years of Age

Local Reaction	BNT162b2 Dose 1 N=2238 n (%)	Placebo Dose 1 N=2248 n (%)	BNT162b2 Dose 2 N=2045 n (%)	Placebo Dose 2 N=2053 n (%)
Pain[a]				
Any	1904 (83.1)	322 (14.0)	1632 (77.8)	245 (11.7)
Mild	1170 (51.1)	308 (13.4)	1039 (49.5)	225 (10.7)
Moderate	710 (31.0)	12 (0.5)	568 (27.1)	20 (1.0)
Severe	24 (1.0)	2 (0.1)	25 (1.2)	0 (0.0)
Redness[b]				
Any	104 (4.5)	26 (1.1)	123 (5.9)	14 (0.7)
Mild	70 (3.1)	16 (0.7)	73 (3.5)	8 (0.4)
Moderate	28 (1.2)	6 (0.3)	40 (1.9)	6 (0.3)
Severe	6 (0.3)	4 (0.2)	10 (0.5)	0 (0.0)
Swelling[b]				
Any	132 (5.8)	11 (0.5)	132 (6.3)	5 (0.2)
Mild	88 (3.8)	3 (0.1)	80 (3.8)	3 (0.1)
Moderate	39 (1.7)	5 (0.2)	45 (2.1)	2 (0.1)
Severe	5 (0.2)	3 (0.1)	7 (0.3)	0 (0.0)

Source: adapted from EUA 27034, amendment 3, Table 17.
n = number of participants with the specified reaction.
N = number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
[a] Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity.
[b] Mild: 2.0 to ≤5.0 cm; moderate: 5.0 to ≤10.0 cm; severe: >10.0 cm.
* Participants in the reactogenicity subset of the safety population ≥16 years of age enrolled by October 9, 2020 and received at least 1 dose of vaccine or placebo.
Data analysis cutoff date: November 14, 2020.

Figure 17. Participants Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose, by Age Group – Reactogenicity Subset for Phase 2/3 Analysis – Safety Population Age Group: 16-55 Years



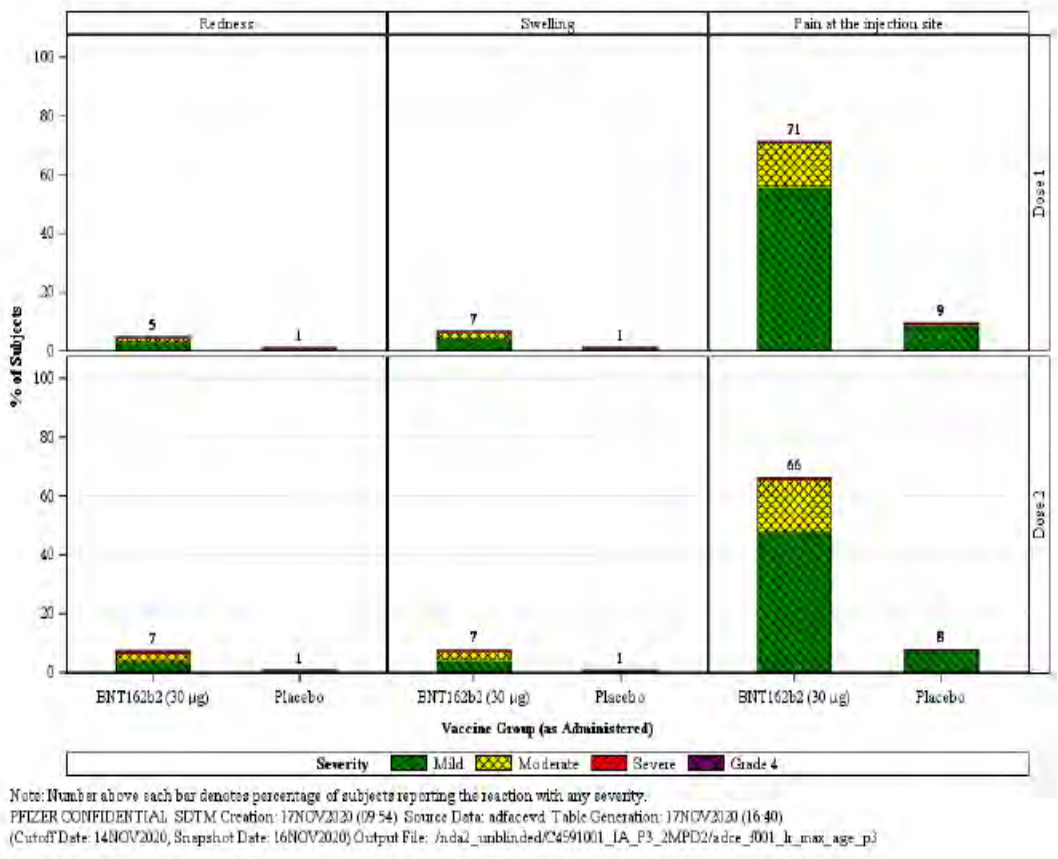
Note: Number above each bar denotes percentage of subjects reporting the reaction with any severity.
PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:54) Source Data: adfacevd Table Generation: 17NOV2020 (16:40)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: /nda2_unblinded/C4591001_IA_P3_2MPD2/adce_f001_lt_max_age_p3

Table 29. Frequency of Solicited Local Reactions Within 7 Days After Each Vaccination, Reactogenicity Subset of the Phase 2/3 Safety Population*, >55 Years of Age and Older

Local Reaction	BNT162b2 Dose 1 N=1802 n (%)	Placebo Dose 1 N=1792 n (%)	BNT162b2 Dose 2 N=1660 n (%)	Placebo Dose 2 N=1646 n (%)
Pain[a]				
Any	1282 (71.1)	166 (9.3)	1098 (66.1)	127 (7.7)
Mild	1008 (55.9)	160 (8.9)	792 (47.7)	125 (7.6)
Moderate	270 (15.0)	6 (0.3)	298 (18.0)	2 (0.1)
Severe	4 (0.2)	0 (0.0)	8 (0.5)	0 (0.0)
Redness[b]				
Any	85 (4.7)	19 (1.1)	120 (7.2)	12 (0.7)
Mild	55 (3.1)	12 (0.7)	59 (3.6)	8 (0.5)
Moderate	27 (1.5)	5 (0.3)	53 (3.2)	3 (0.2)
Severe	3 (0.2)	2 (0.1)	8 (0.5)	1 (0.1)
Swelling[b]				
Any	118 (6.5)	21 (1.2)	124 (7.5)	11 (0.7)
Mild	71 (3.9)	10 (0.6)	68 (4.1)	5 (0.3)
Moderate	45 (2.5)	11 (0.6)	53 (3.2)	5 (0.3)
Severe	2 (0.1)	0 (0.0)	3 (0.2)	1 (0.1)

Source: EUA 27036, amendment 3, Table 21.
n = number of participants with the specified reaction.
N = number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
[a] Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity.
[b] Mild: 2.0 to ≤5.0 cm; moderate: 5.0 to ≤10.0 cm; severe: >10.0 cm.
* Participants in the reactogenicity subset of the safety population ≥16 years of age enrolled by October 9, 2020 and received at least 1 dose of vaccine or placebo.
Data analysis cutoff date: November 14, 2020.

Figure 18. Participants Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose, by Age Group – Reactogenicity Subset for Phase 2/3 Analysis – Safety Population Age Group: >55 Years



Note: Number above each bar denotes percentage of subjects reporting the reaction with any severity.
PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:54) Source Data: adfacevd Table Generation: 17NOV2020 (16:40)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: /ada2_unblinded/C4591001_IA_P3_2MPD2/adce_f001_lr_max_age_p3

8.3.1.3. Solicited Systemic AEs

Subgroup analyses by age

Systemic events were generally increased in frequency and severity in the younger group **(Figure 19)** compared with the older group **(Figure20),** with frequencies and severity increasing with number of doses (Dose 1 vs Dose 2), except for vomiting and diarrhoea, which was generally similar regardless of dose.

For both age groups, fatigue, headache and new/worsened muscle pain were most common.

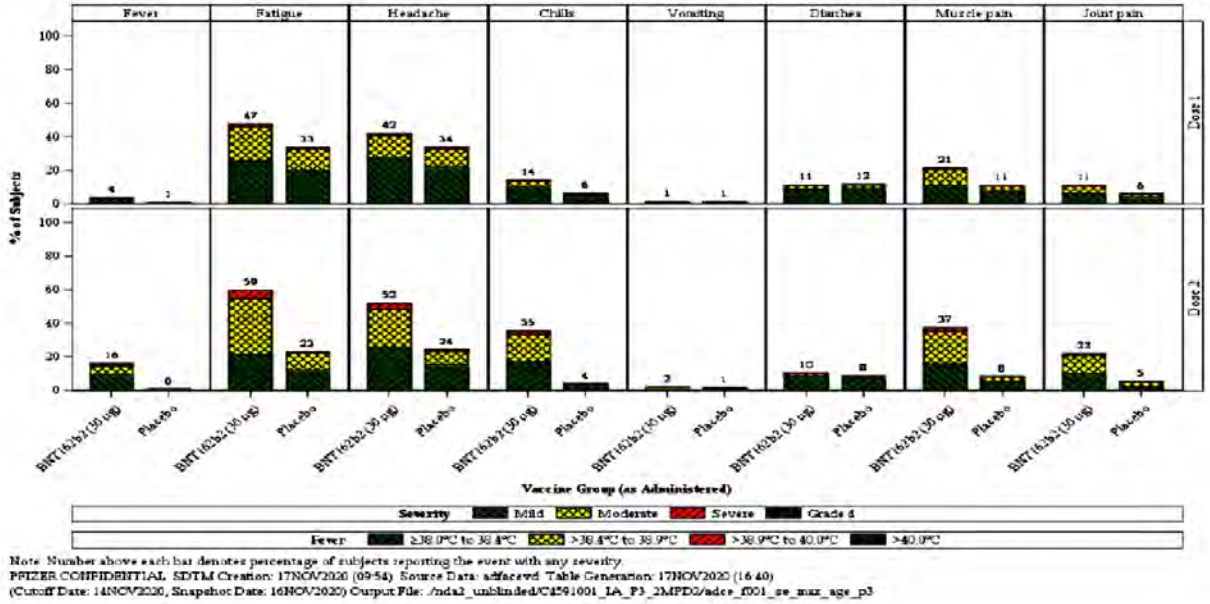
For each age group in the reactogenicity subset (younger: 18 to 55 years, older: >55 years) and overall (18 years and older), the median onset of systemic AEs in the vaccine group in general was day 2 to day 3 after either dose and lasted a median duration of 1 day.

Table 29. Frequency of Solicited Systemic Adverse Events Within 7 Days After Each Vaccination- Reactogenicity Subset of the Phase 2/3 Safety Population*, 18 to 55 Years of Age

Adverse Event	BNT162b2 Dose 1 N=2238 n (%)	Placebo Dose 1 N=2248 n (%)	BNT162b2 Dose 2 N=2045 n (%)	Placebo Dose 2 N=2053 n (%)
Fever				
≥38.0°C	85 (3.7)	20 (0.9)	331 (15.8)	10 (0.5)
>38.0°C to 38.4°C	64 (2.8)	10 (0.4)	194 (9.2)	5 (0.2)
>38.4°C to 38.9°C	15 (0.7)	5 (0.2)	110 (5.2)	3 (0.1)
>38.9°C to 40.0°C	6 (0.3)	3 (0.1)	26 (1.2)	2 (0.1)
>40.0°C	0 (0.0)	2 (0.1)	1 (0.0)	0 (0.0)
Fatigue[a]				
Any	1085 (47.4)	767 (33.4)	1247 (59.4)	479 (22.8)
Mild	597 (26.1)	46 (20.3)	442 (21.1)	248 (11.8)
Moderate	455 (19.9)	289 (12.6)	708 (33.7)	217 (10.3)
Severe	33 (1.4)	11 (0.5)	97 (4.6)	14 (0.7)
Headache[a]				
Any	959 (41.9)	775 (33.7)	1085 (51.7)	506 (24.1)
Mild	628 (27.4)	505 (22.0)	538 (25.6)	321 (15.3)
Moderate	308 (13.4)	251 (10.9)	480 (22.9)	170 (8.1)
Severe	23 (1.0)	19 (0.8)	67 (3.2)	15 (0.7)
Chills[a]				
Any	321 (14.0)	146 (6.4)	737 (35.1)	79 (3.8)
Mild	230 (10.0)	111 (4.8)	359 (17.1)	65 (3.1)
Moderate	82 (3.6)	33 (1.4)	333 (15.9)	14 (0.7)
Severe	9 (0.4)	2 (0.1)	45 (2.1)	0 (0.0)
Vomiting[b]				
Any	28 (1.2)	28 (1.2)	40 (1.9)	25 (1.2)
Mild	24 (1.0)	22 (1.0)	28 (1.3)	16 (0.8)
Moderate	4 (0.2)	5 (0.2)	8 (0.4)	9 (0.4)
Severe	0 (0.0)	1 (0.0)	4 (0.2)	0 (0.0)
Diarrhea[c]				
Any	255 (11.1)	270 (11.7)	219 (10.4)	177 (8.4)
Mild	206 (9.0)	217 (9.4)	179 (8.5)	144 (6.8)
Moderate	46 (2.0)	52 (2.3)	36 (1.7)	32 (1.5)
Severe	3 (0.1)	1 (0.0)	4 (0.2)	1 (0.0)
New or worsened muscle pain[a]				
Any	487 (21.3)	249 (10.8)	783 (37.3)	173 (8.2)
Mild	256 (11.2)	175 (7.6)	326 (15.5)	111 (5.3)
Moderate	218 (9.5)	72 (3.1)	410 (19.5)	59 (2.8)
Severe	13 (0.6)	2 (0.1)	47 (2.2)	3 (0.1)
New or worsened joint pain[a]				
Any	251 (11.0)	138 (6.0)	459 (21.9)	109 (5.2)
Mild	147 (6.4)	95 (4.1)	205 (9.8)	54 (2.6)
Moderate	99 (4.3)	43 (1.9)	234 (11.2)	51 (2.4)
Severe	5 (0.2)	0 (0.0)	20 (1.0)	4 (0.2)
Use of antipyretic or pain medication	638 (27.8)	332 (14.4)	945 (45.0)	266 (12.6)

Source: adapted from EUA 27036, amendment 3, Table 19.
n = number of participants with the specified reaction.
N = number of participants in the reactogenicity subset reporting at least 1 yes or no response for the specified reaction after the specified dose.
[a] Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity.
[b] Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration.
[c] Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours.
* Participants in the reactogenicity subset of the safety population ≥16 years of age enrolled by October 9, 2020 and received at least 1 dose of vaccine or placebo.
Data analysis cutoff date: November 14, 2020.

Figure 19: Participants Reporting Systemic Events, by Maximum Severity, Within 7 Days After Each Dose, by Age Group – Reactogenicity Subset for Phase 2/3 Analysis – Age Group: 16-55 Years – Safety Population



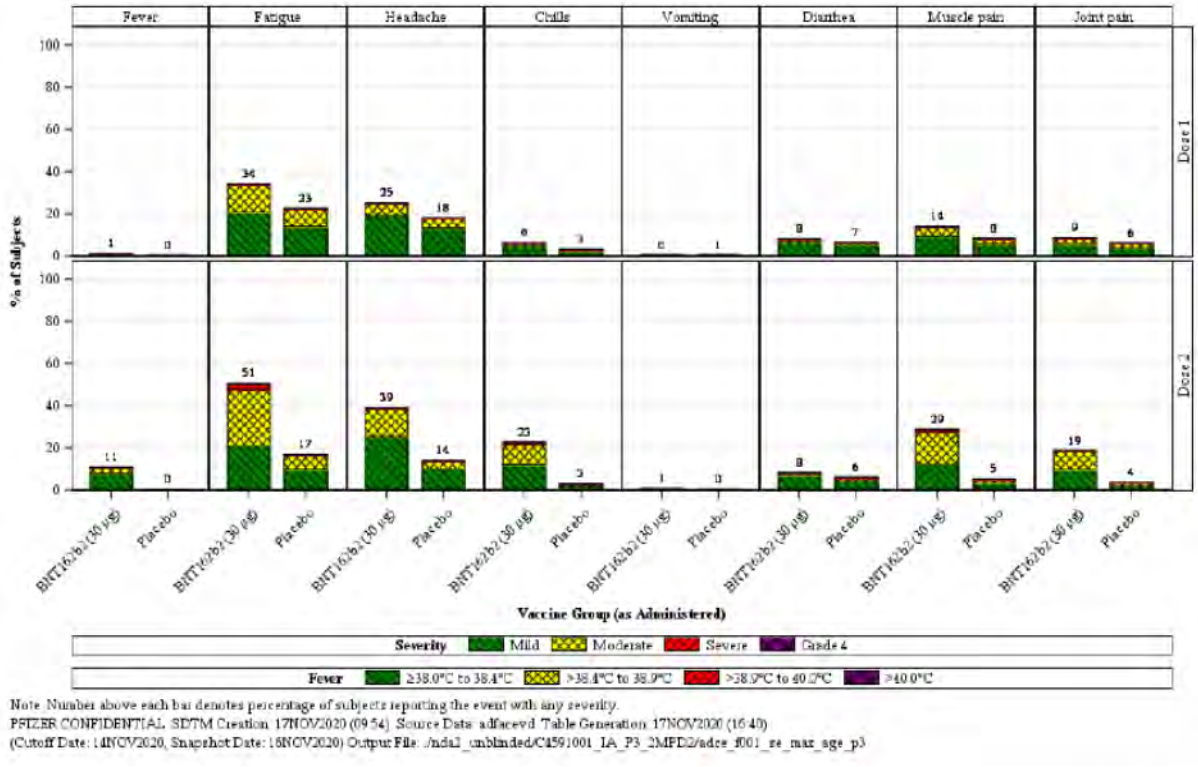
Note: Number above each bar denotes percentage of subjects reporting the event with any severity.
PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:54) Source Data: adfaceve Table Generation: 17NOV2020 (16:40)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: /nda2_unblinded/C4591001_1A_P3_2MPD2/adce_f001_se_max_age_p3

Table 30. Frequency of Solicited Systemic Adverse Events Within 7 Days After Each Vaccination- Reactogenicity Subset of the Phase 2/3 Safety Population*, >55 Years of Age and Older

Adverse Event	BNT162b2 Dose 1 N=1802 n (%)	Placebo Dose 1 N=1792 n (%)	BNT162b2 Dose 2 N=1660 n (%)	Placebo Dose 2 N=1646 n (%)
Fever				
≥38.0°C	26 (1.4)	7 (0.4)	181 (10.9)	4 (0.2)
>38.0°C to 38.4°C	23 (1.3)	2 (0.1)	131 (7.9)	2 (0.1)
>38.4°C to 38.9°C	1 (0.1)	3 (0.2)	45 (2.7)	1 (0.1)
>38.9°C to 40.0°C	1 (0.1)	2 (0.1)	5 (0.3)	1 (0.1)
>40.0°C	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue[a]				
Any	615 (34.1)	405 (22.6)	839 (50.5)	277 (16.8)
Mild	373 (20.7)	252 (14.1)	351 (21.1)	161 (9.8)
Moderate	240 (13.3)	150 (8.4)	442 (26.6)	114 (6.9)
Severe	2 (0.1)	3 (0.2)	46 (2.8)	2 (0.1)
Headache[a]				
Any	454 (25.2)	325 (18.1)	647 (39.0)	229 (13.9)
Mild	348 (19.3)	242 (13.5)	422 (25.4)	165 (10.0)
Moderate	104 (5.8)	80 (4.5)	216 (13.0)	60 (3.6)
Severe	2 (0.1)	3 (0.2)	9 (0.5)	4 (0.2)
Chills[a]				
Any	113 (6.3)	57 (3.2)	377 (22.7)	46 (2.8)
Mild	87 (4.8)	40 (2.2)	199 (12.0)	35 (2.1)
Moderate	26 (1.4)	16 (0.9)	161 (9.7)	11 (0.7)
Severe	0 (0.0)	1 (0.1)	17 (1.0)	0 (0.0)
Vomiting[b]				
Any	9 (0.5)	9 (0.5)	11 (0.7)	5 (0.3)
Mild	8 (0.4)	9 (0.5)	9 (0.5)	5 (0.3)
Moderate	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
Diarrhea[c]				
Any	147 (8.2)	118 (6.6)	137 (8.3)	99 (6.0)
Mild	118 (6.5)	100 (5.6)	114 (6.9)	73 (4.4)
Moderate	26 (1.4)	17 (0.9)	21 (1.3)	22 (1.3)
Severe	3 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[a]				
Any	251 (13.9)	149 (8.3)	477 (28.7)	87 (5.3)
Mild	168 (9.3)	100 (5.6)	202 (12.2)	57 (3.5)
Moderate	82 (4.6)	46 (2.6)	259 (15.6)	29 (1.8)
Severe	1 (0.1)	3 (0.2)	16 (1.0)	1 (0.1)
New or worsened joint pain[a]				
Any	155 (8.6)	109 (6.1)	313 (18.9)	61 (3.7)
Mild	101 (5.6)	68 (3.8)	161 (9.7)	35 (2.1)
Moderate	52 (2.9)	40 (2.2)	145 (8.7)	25 (1.5)
Severe	2 (0.1)	1 (0.1)	7 (0.4)	1 (0.1)
Use of antipyretic or pain medication	358 (19.9)	213 (11.9)	625 (37.7)	161 (9.8)

Source: EUA 27036, amendment 3, Table 23.
n = number of participants with the specified reaction.
N = number of participants in the reactogenicity subset reporting at least 1 yes or no response for the specified reaction after the specified dose.
[a] Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity.
[b] Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration.
[c] Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours.
* Participants in the reactogenicity subset of the safety population ≥16 years of age enrolled by October 9, 2020 and received at least 1 dose of vaccine or placebo.
Data analysis cutoff date: November 14, 2020.

Figure 20: Participants Reporting Systemic Events, by Maximum Severity, Within 7 Days After Each Dose, by Age Group – Reactogenicity Subset for Phase 2/3 Analysis – Age Group: >55 Years – Safety Population



Note: Number above each bar denotes percentage of subjects reporting the event with any severity.
PFIZER CONFIDENTIAL. SDTM Creation: 17NOV2020 (09:54). Source Data: adfacevd. Table Generation: 17NOV2020 (16:40)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./ndal_unblinded/C4591001_IA_P3_2MFD2/adce_f001_re_max_age_p3

Following both Dose 1 and Dose 2, use of antipyretic/pain medication was slightly less frequent in the older age group (19.9% vs 37.7%) than in the younger age group (27.8% vs 45.0%) after both doses, and medication use increased in both age groups after Dose 2 as compared with after Dose 1.

After the first and second dose , majority of systemic events were mild or moderate in severity across both age groups. Systemic events across age groups after Dose 1 of BNT162b2 were generally lower in frequency than after Dose 2: fever (2.7% vs 13.6%), fatigue (41.5% vs 55.5%), headache (34.5% vs 46.1%), chills (10.6% vs 29.6%), muscle pain (18.0% vs 33.5%), and joint pain (9.9% vs 20.5). diarrhoea and vomiting frequencies were generally similar. The frequency of any severe systemic event after Dose 1 was ≤0.9%. After Dose 2, severe systemic events had frequencies of ≤2% with the exception after Dose 2 of fatigue (3.8%) and headache (2.0%).

High fever (>38.9°C to 40.0°C) was reported in the BNT162b2 group after Dose 1 for 0.2% and after Dose 2 for 0.8% (placebo group after Dose 1 for 0.1% and after Dose 2 for 0.1%). Grade 4 fever (>40.0°C) was reported for 2 subjects in each of the BNT162b2 and placebo groups. One participant in the younger BNT162b2 group reported fever of 41.2°C only on Day 2 after Dose 2 and was afebrile for all other days of the reporting period. One other subject in the older BNT162b2 group reported fever that reached a high temperature of 40.7°C only on Day 4 after Dose 1 and was afebrile for all other days of the reporting period.

8.3.1.4. Unsolicited (non-serious) AEs (SOCs and PTs)

Among the 37,586 participants with a median of 2 months of safety follow-up after Dose 2, most AEs reported up to 1 month after Dose 2 were reactogenicity, in system organ class (SOCs) of:

- general disorders and administration site conditions (18.6% BNT162b2 vs 3.9% placebo)
- musculoskeletal and connective tissue disorders (7.3% BNT162b2 vs 2.0% placebo)