Efficacy & Safety of BNT162b2 booster - C4591031 2 month interim analysis

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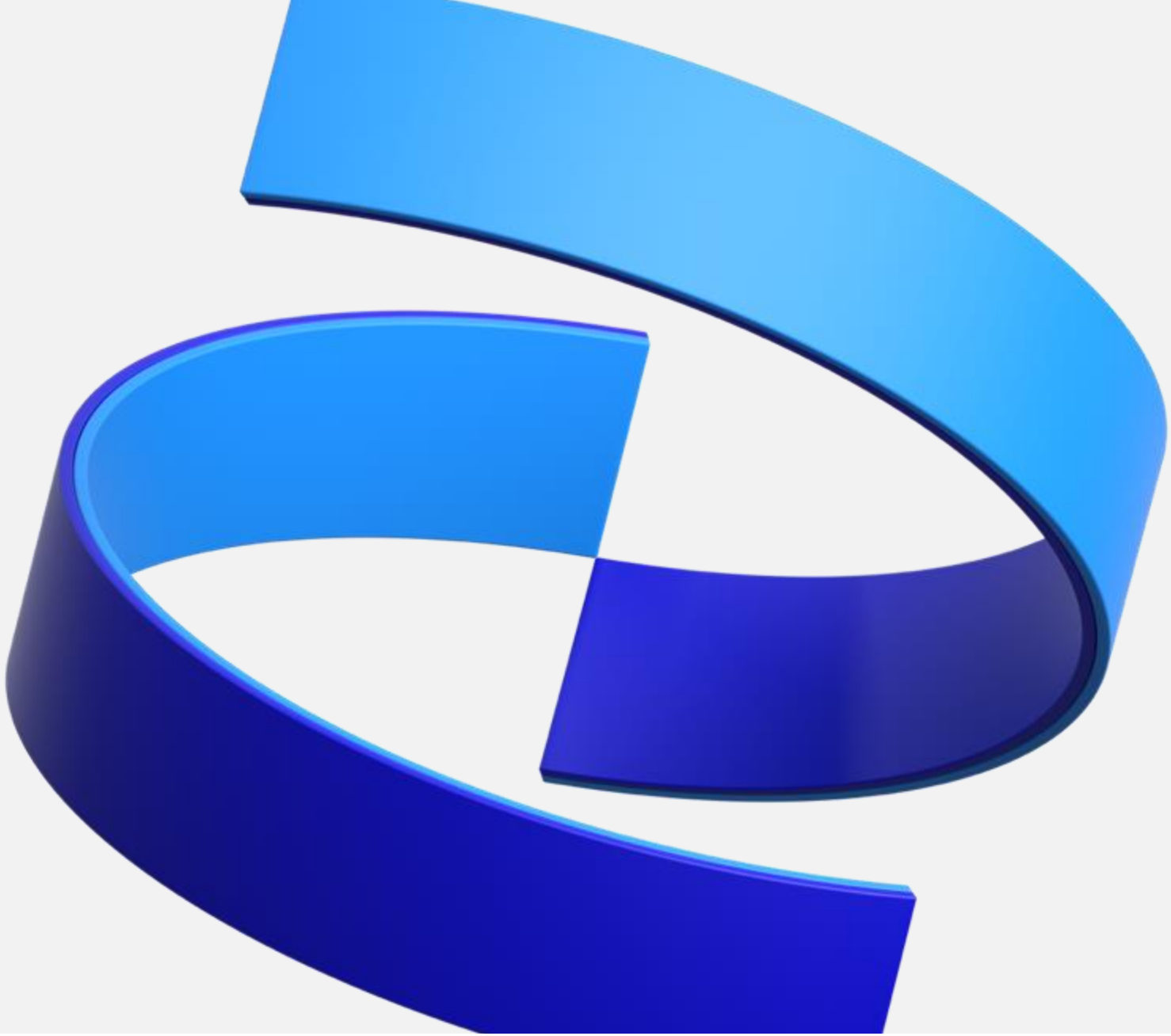


Study Design C4591031

- Recruited approximately 10,000 participants ≥16 years of age who completed a 2 dose primary series of BNT162b2 30 µg in Study C4591001
- Randomized at a 1:1 ratio into Study C4591031 to receive either
  - a booster dose of BNT162b2 30 µg or a placebo dose at least 6 months after the second dose.
- Randomization was stratified by age, such that approximately 60% of participants enrolled would be ≥16 to 55 years of age and approximately 40% of participants >55 years of age.
- Assessments include safety evaluations of adverse events and COVID-19 case surveillance for booster efficacy estimation after the booster dose.
  - Reactogenicity data were not collected in this study but booster reactogenicity was reported from study 1001

Demographic characteristics (Safety population) 1/2

Representative participants enrolled from the landmark C4591001 study

		BNT162b2 (30 µg) (N=5081) n (%)	Placebo (N=5044) n (%)	Total (N=10125) n (%)
Sex	Male	2457 (48.4)	2518 (49.9)	4975 (49.1)
	Female	2624 (51.6)	2526 (50.1)	5150 (50.9)
Race	White	3997 (78.7)	4002 (79.3)	7999 (79.0)
	Black or African American	472 (9.3)	460 (9.1)	932 (9.2)
	American Indian or Alaska native	86 (1.7)	91 (1.8)	177 (1.7)
	Asian	288 (5.7)	269 (5.3)	557 (5.5)
	Native Hawaiian or other Pacific Islander	8 (0.2)	11 (0.2)	19 (0.2)
	Multiracial	207 (4.1)	196 (3.9)	403 (4.0)
	Not reported	23 (0.5)	15 (0.3)	38 (0.4)
Ethnicity	Hispanic/Latino	760 (15.0)	748 (14.8)	1508 (14.9)
	Non-Hispanic/non-Latino	4309 (84.8)	4288 (85.0)	8597 (84.9)
	Not reported	12 (0.2)	8 (0.2)	20 (0.2)
Country	Brazil	580 (11.4)	584 (11.6)	1164 (11.5)
	South Africa	134 (2.6)	134 (2.7)	268 (2.6)
	USA	4367 (85.9)	4326 (85.8)	8693 (85.9)

Demographic characteristics (Safety population) 2/2

Representative participants enrolled from the landmark C4591001 study

		BNT162b2 (30 µg) (N=5081) n (%)	Placebo (N=5044) n (%)	Total (N=10125) n (%)
Age group (at vaccination)	16-55 Years	2823 (55.6)	2797 (55.5)	5620 (55.5)
	>55 Years	2258 (44.4)	2247 (44.5)	4505 (44.5)
	16-17 Years	46 (0.9)	44 (0.9)	90 (0.9)
	18-55 Years	2777 (54.7)	2753 (54.6)	5530 (54.6)
	56-64 Years	1083 (21.3)	1059 (21.0)	2142 (21.2)
	65+ Years	1175 (23.1)	1188 (23.6)	2363 (23.3)
Age at vaccination (years)	Mean (SD)	51.8 (15.24)	51.7 (15.33)	51.7 (15.28)
	Median	53.0	53.0	53.0
	Min, max	(16, 86)	(16, 87)	(16, 87)
Baseline SARS-CoV-2 status	Positive	284 (5.6)	261 (5.2)	545 (5.4)
	Negative	4789 (94.3)	4775 (94.7)	9564 (94.5)
	Unknown	8 (0.2)	8 (0.2)	16 (0.2)

Vaccine administration timing (All randomized)

Majority of booster doses administered 10-12 months after dose 2

	BNT162b2 (30 µg) (N=5088) n (%)	Placebo (N=5048) n (%)
Randomized	5088 (100.0)	5048 (100.0)
Not vaccinated	6 (0.1)	5 (0.1)
Received booster vaccination	5082 (99.9)	5043 (99.9)
Time from Dose 2 of BNT162b2 (received in Study C4591001) to booster vaccination:		
<6 Months	14 (0.3)	6 (0.1)
≥6 Months to <8 Months	752 (14.8)	732 (14.5)
≥8 Months to <10 Months	819 (16.1)	833 (16.5)
≥10 Months to <12 Months	3321 (65.3)	3298 (65.3)
≥12 Months	176 (3.5)	174 (3.4)
Mean (SD)	10.1 (1.62)	10.2 (1.59)
Median	10.8	10.7
Min, max	(5.0, 12.6)	(5.0, 12.8)

Blinded follow-up time after booster vaccination (Safety population)

Prespecified analysis 2 months after last participant enrolled

	BNT162b2 (30 µg) (N=5081) n (%)	Placebo (N=5044) n (%)	Total (N=10125) n (%)
Participants (%) with length of blinded follow-up of:			
<2 Months	**99 (1.9)**	**204 (4.0)**	**303 (3.0)**
≥2 Months to <4 Months	**4982 (98.1)**	**4840 (96.0)**	**9822 (97.0)**
Mean (SD)	**2.5 (0.29)**	**2.5 (0.35)**	**2.5 (0.32)**
Median	**2.5**	**2.5**	**2.5**
Min, max	**(0.4, 3.5)**	**(0.3, 3.5)**	**(0.3, 3.5)**

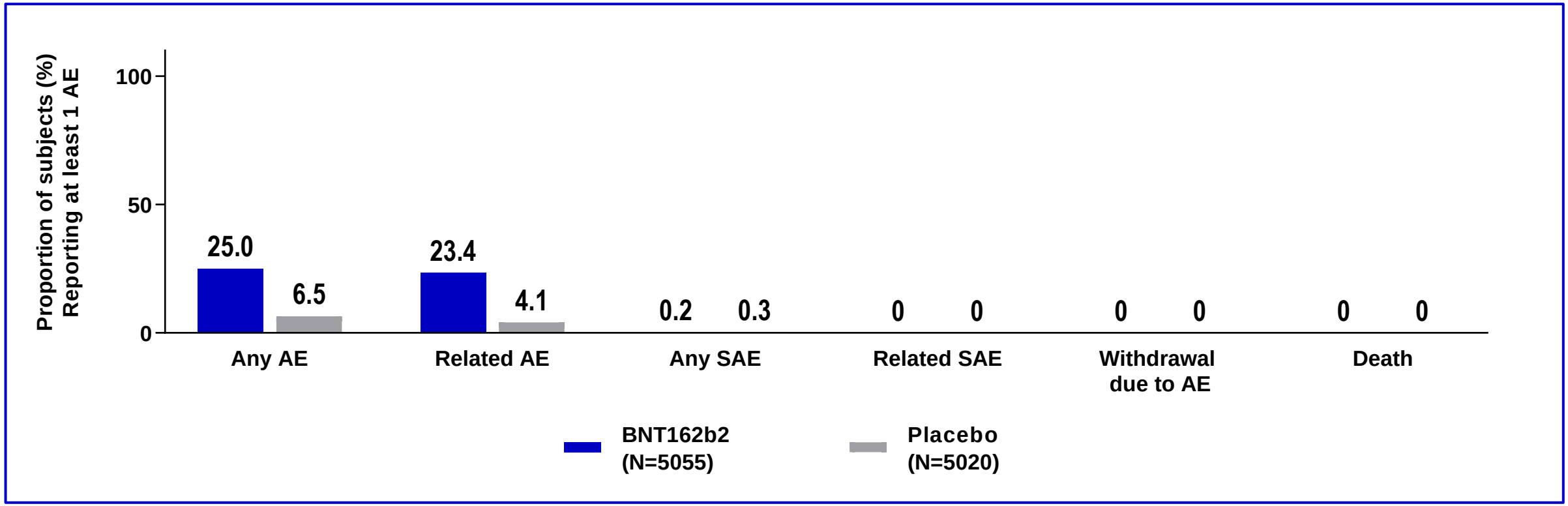
Safety

Summary of Reactogenicity of a Booster Dose ≥ Grade 3

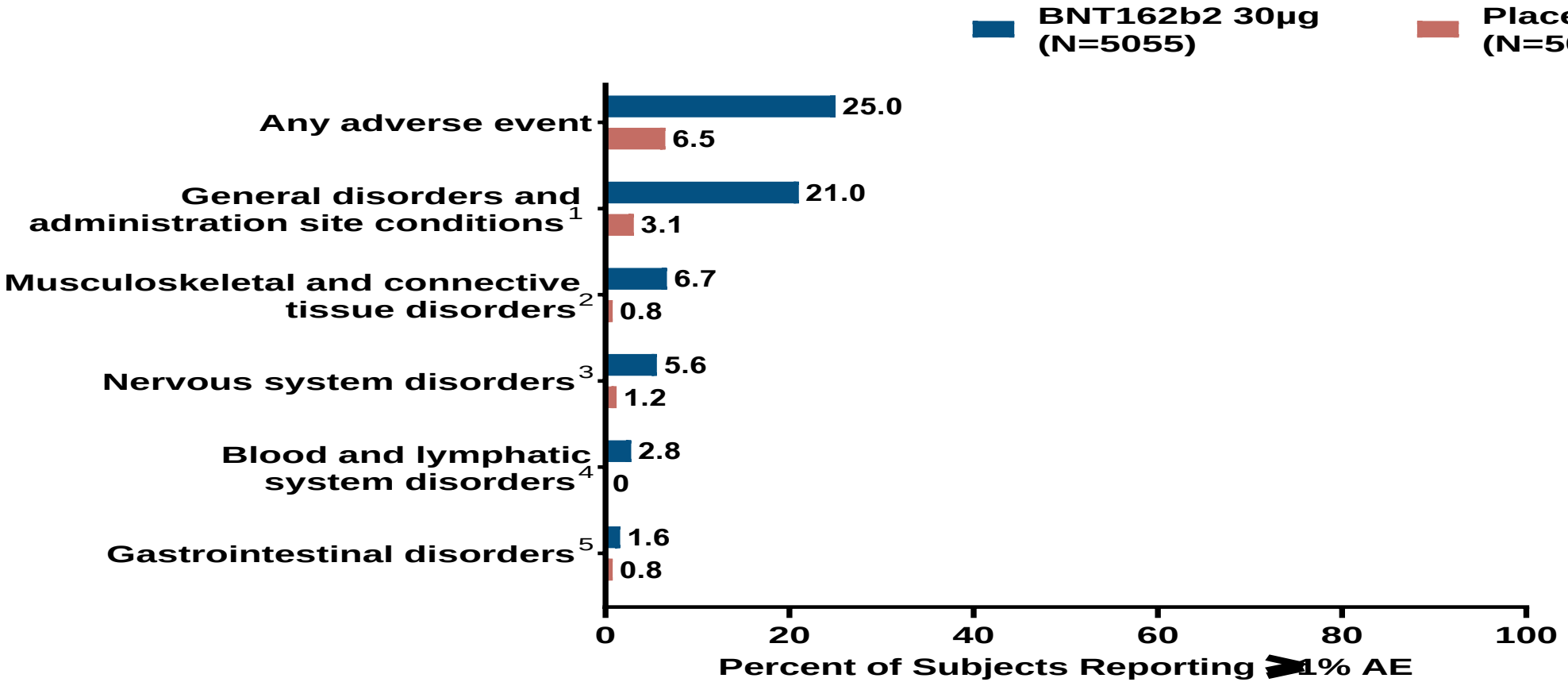
			BNT162b2 (30 µg) N=289	
			n	% (95%CI)
Any ≥ grade 3 reactogenicity event			19	6.6% (4.0, 10.1)
Local reactions	All		2	0.7% (0.1, 2.5)
		Injection site pain	1	0.3% (0.0, 1.9)
		Injection site redness	0	0% (0.0, 1.3)
		Injection site swelling	1	0.3% (0.0, 1.9
Systemic events	All		17	5.9% (3.5, 9.3)
		Fever	1	0.3% (0.0, 1.9)
		Vomiting	0	0% (0.0, 1.3)
		Diarrhea	0	0% (0.0, 1.3)
		Headache	3	1% (0.2, 3.0)
		Fatigue	13	4.5% (2.4, 7.6)
		Chills	3	1% (0.2, 3.0)
		Muscle pain	4	1.4% (0.4, 3.5)
		Joint pain	1	0.3% (0.0, 1.9)

Overall adverse events from booster dose to 1 month after booster dose

AEs more frequent in BNT162b2 group due to already known events



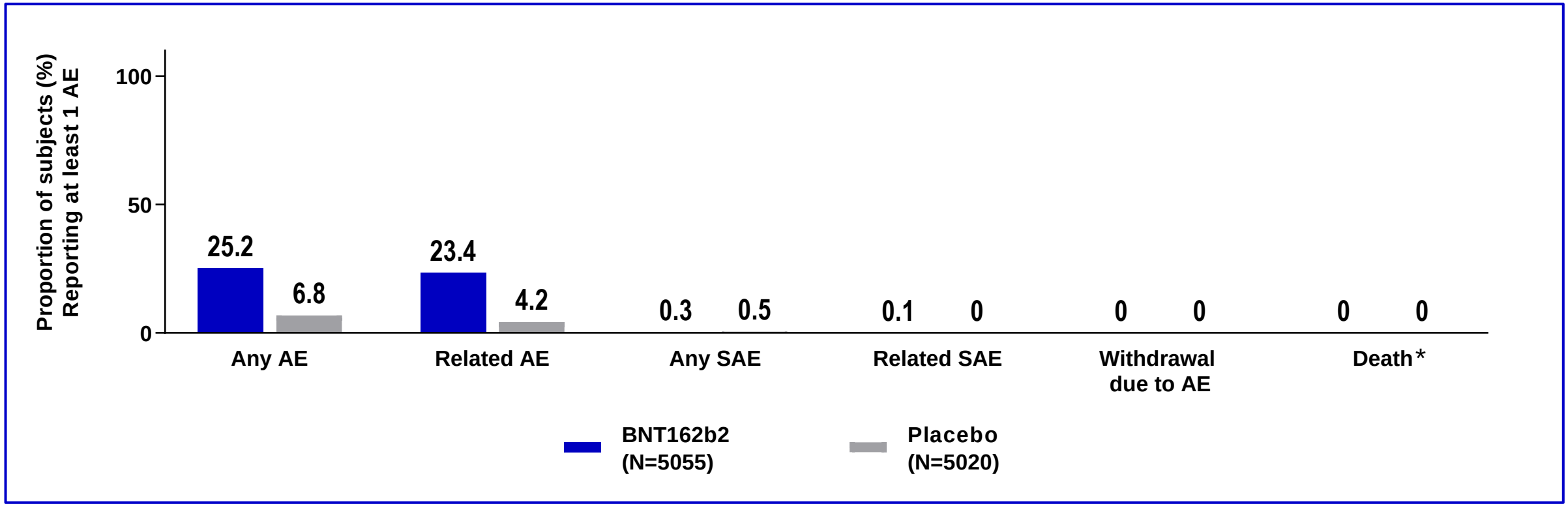
Adverse Events ≥1% by System Organ Class From Booster Vaccination to 1 Month Post Booster Dose – Blinded Follow-up Period



1. Predominantly reflect local reactions at the injection site and systemic reactions of fever, fatigue and chills
2. Predominantly reflects myalgia and arthralgia
3. Predominantly reflects headache
4. Lymphadenopathy = 2.7% (compared to 0.4% after the second dose from Study C4591001)
5. Predominantly reflects nausea and diarrhea

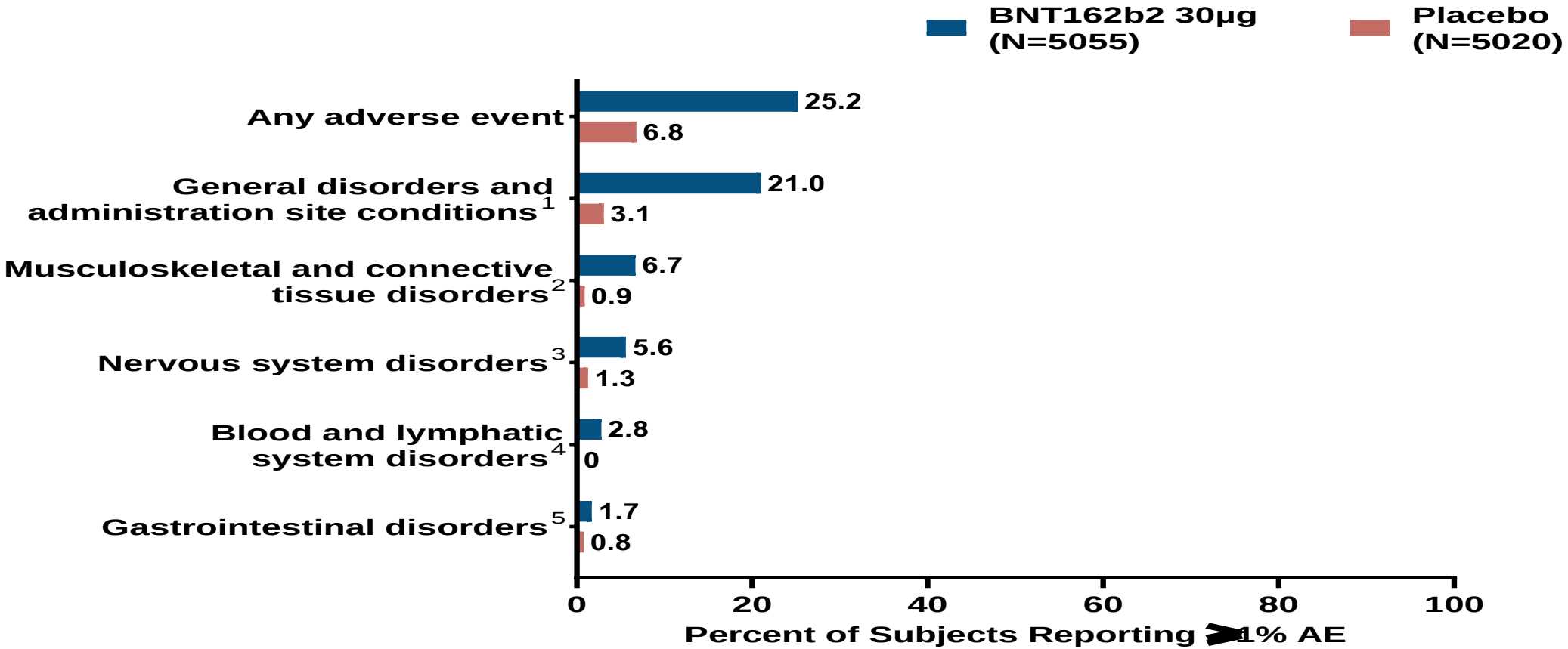
Overall adverse events from booster dose to cut-off date (5-Oct-2021) (Safety population)

Very few additional AEs identified beyond 1 month after booster



* 1 non-related death occurred 53 days after a placebo injection

Adverse Events ≥1% by System Organ Class From Booster Vaccination to Cutoff Date– Blinded Follow-up Period



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Serious Adverse Events By System Organ Class from Booster Vaccination to Cutoff Date– Blinded Follow-up Period

	BNT162b2 (N=5055) n (%)	Placebo (N=5020) n (%)
Any event	16 (0.3)	24 (0.5)
Cardiac disorders	2 (0.0)	3 (0.0)
Gastrointestinal disorders	1 (0.0)	0
General disorders and administration site conditions	0	2 (0.0)
Infections and infestations	4 (0.1)	4 (0.1)
Injury, poisoning and procedural complications	1 (0.0)	2 (0.0)
Investigations	2 (0.0)	0
Musculoskeletal and connective tissue disorders	1 (0.0)	1 (0.0)
Neoplasms benign, malignant and unspecified	2 (0.0)	5 (0.1)
Nervous system disorders	3 (0.1)	2 (0.0)
Pregnancy, puerperium and perinatal conditions	0	1 (0.0)
Psychiatric disorders	1 (0.0)	0
Renal and urinary disorders	1 (0.0)	0
Reproductive system and breast disorders	0	1 (0.0)
Respiratory, thoracic and mediastinal disorders	0	6 (0.1)
Vascular disorders	0	1 (0.0)

Related Serious Adverse Events from Booster Vaccination to Cutoff Date

BNT162b2 recipients:

- Young adult male with PMH of postural orthostatic tachycardia syndrome and orthostatic hypotension, developed tachycardia 8 days after booster vaccination, was moderate in nature and resolved 2 days later.

- Female > 55 years with Gilbert's syndrome developed moderate hepatic enzyme increase (transient elevated liver enzymes) that occurred 5 days after booster vaccination and resolved 37 days later. She started taking Tylenol (500mg q 6 PRN) for diverticulitis that started 2 days before the booster dose.

- 18-55 y/o female developed mild hepatic enzyme increase (transient elevated liver enzymes) that occurred 49 days after booster vaccination and was ongoing at the time of data cut off. Now thought to be secondary to atorvastatin.

Placebo recipients:

- > 55 year old female with DM, HTN, obesity, prior smoking, supraventricular tachycardia (SVT), and heart failure developed acute myocardial infarction (acute non-ST elevation MI) that occurred 9 days after placebo, was life threatening in nature and resolved 4 days later

- Young adult male with SVT, developed chest pain of unknown origin that occurred 6 days after placebo, was severe in nature and resolved without treatment 1 day later. Troponin & ECG normal.

Efficacy

Relative Vaccine efficacy during blinded follow-up period

Booster dose was highly effective against symptomatic COVID-19

Subjects WITHOUT Evidence of Infection Prior to 7 days after Dose 2

	BNT162b2 (30 µg) N=4695		Placebo N=4671			
Efficacy Endpoint	**n**	**Surveillance Time (n)**	**n**	**Surveillance Time (n)**	**RVE (%)**	**(95% CI)**
First COVID-19 occurrence from ≥7 days after booster vaccination to <2 months after booster vaccination	**6**	**0.823 (4659)**	**123**	**0.792 (4614)**	**95.3**	**(89.5,98.3)**

Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint
RVE = relative vaccine efficacy of the BNT162b2 booster group relative to the placebo group (nonbooster)

Vaccine efficacy during blinded follow-up period (Evaluable efficacy population)

Booster dose was highly effective against symptomatic COVID-19

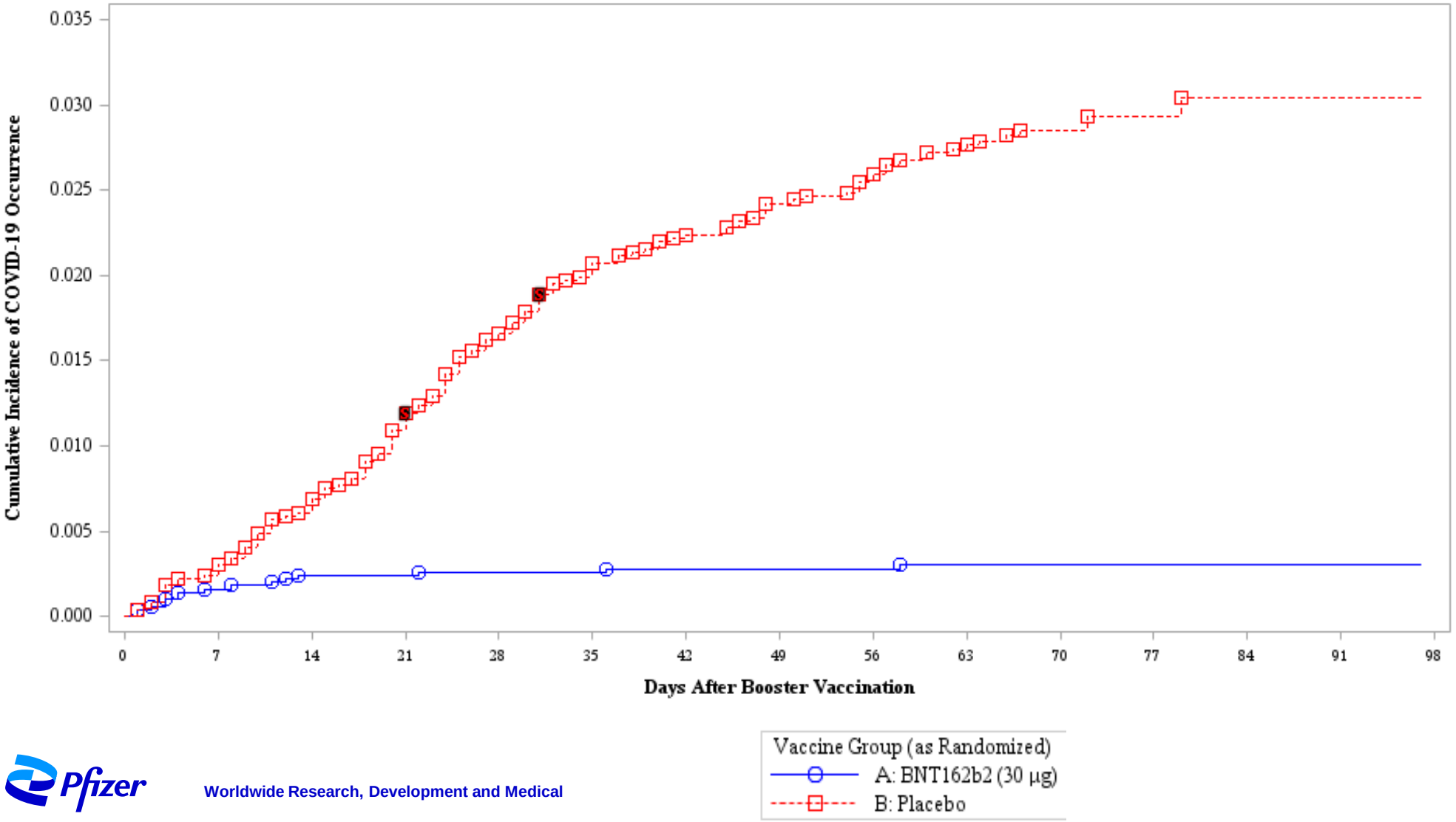
Subjects WITH or WITHOUT Evidence of Infection Prior to 7 days after Dose 2

	BNT162b2 (30 µg) N=4993		Placebo N=4952			
Efficacy Endpoint	**n**	**Surveillance Time (n)**	**n**	**Surveillance Time (n)**	**RVE (%)**	**(95% CI)**
First COVID-19 occurrence from ≥7 days after booster vaccination to <2 months after booster vaccination	**7**	**0.871 (4934)**	**124**	**0.835 (4863)**	**94.6**	**(88.5, 97.9)**

Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint
RVE = relative vaccine efficacy of the BNT162b2 booster group relative to the placebo group (nonbooster)

Cumulative Incidence Curve for First COVID-19 Occurrence After Booster Vaccination – All Available Efficacy Population

Curves diverge rapidly, starting even before 7 days after booster



Note the 2 severe cases met the FDA definition only, based only on SpO2 <93%. They were not hospitalized

Vaccine efficacy during blinded follow-up period by Subgroup Evaluable Efficacy Population Without Evidence of Infection Prior to 7 Days after Booster Vaccination

		BNT162b2 (30 µg) N=4,695 n	Placebo N=4,671 n	RVE (%)	(95% CI)
Overall		**6**	**123**	**95.3**	**(89.5, 98.3))**
Age	**16-55 years of age**	**3**	**81**	**96.5**	**(89.3, 99.3)**
	>55 years of age	**3**	**42**	**93.1**	**(78.4, 98.6)**
Sex	**Male**	**4**	**70**	**94.3**	**(84.8, 98.5)**
	Female	**2**	**53**	**96.5**	**(86.7, 99.6)**
Race	**White**	**5**	**100**	**95.2**	**(88.4, 98.5)**
	Black or African American	**0**	**13**	**100.0**	**(68.0, 100.0)**
	American Indian or Alaska	**0**	**4**	**100.0**	**(-59.2, 100.0)**
	Asian	**1**	**3**	**69.4**	**(-280.7, 99.4)**
	Multiracial	**0**	**2**	**100.0**	**(-395.3, 100.0)**
Ethnicity	**Hispanic/Latino**	**1**	**19**	**94.8**	**(67.5, 99.9)**
	Non-Hispanic/Non-Latino	**5**	**104**	**95.4**	**(88.9, 98.5)**

Vaccine efficacy during blinded follow-up period by Subgroup
Evaluable Efficacy Population
Without Evidence of Infection Prior to 7 Days after Booster Vaccination

		BNT162b2 (30 µg) N=4,695 n	Placebo N=4,671 n	RVE (%)	(95% CI)
Overall		**6**	**123**	**95.3**	**(89.5, 98.3))**
Country	**Brazil**	**0**	**4**	**100.0**	**(-52.7, 100.0)**
	South Africa	**0**	**2**	**100.0**	**(-554.9, 100.0)**
	US	**6**	**117**	**95.1**	**(89.1, 98.2)**
Comorbidity	**No comorbidity**	**1**	**59**	**98.4**	**(90.7, 100.0)**
	Any comorbidity*	**5**	**64**	**92.4**	**(81.2, 97.6)**
	Any malignancy	**1**	**4**	**78.6**	**(-116.4, 99.6)**
	Cardiovascular	**2**	**1**	**-57.3**	**(-9181.8, 91.8)**
	Chronic pulmonary disease	**1**	**16**	**93.4**	**(57.8, 99.8)**
	Diabetes	**1**	**17**	**94.3**	**(63.3, 99.9)**
	Obese (≥30.0 kg/m^2)	**2**	**52**	**96.2**	**(85.7, 99.6)**
Hypertension		**3**	**33**	**91.1**	**(71.7, 98.3)**
Diabetes		**1**	**17**	**94.3**	**(63.3, 99.9)**

* Participants who had at least 1 Charlson Comorbidity Index, or a BMI ≥30.0 kg/m2

Conclusions

- High relative efficacy in the boosted group compared to the unboosted group from 7 days after the boost in those without evidence of prior SARS-CoV-2 infection was 95.6%
- None of the protocol-defined cases of COVID-19 in the unboosted (placebo) group resulted in hospitalization
- 2 cases of severe COVID-19 occurred in the placebo group (based only on SpO2 <93%).
- Multiple subgroup analyses showed efficacy was consistent irrespective of age, sex, race, ethnicity, comorbid conditions
- The adverse events observed were consistent with those seen in previous studies with no safety signal identified; no cases of myocarditis or pericarditis were observed
  - Lymphadenopathy = 2.7% compared to 0.4% after the second dose from Study C4591001
- These data strongly support that a booster dose of BNT162b2 administered in individuals 18 years of age and older, ≥6 months (mean ~10 months) after the second dose, improves the protection against symptomatic COVID-19