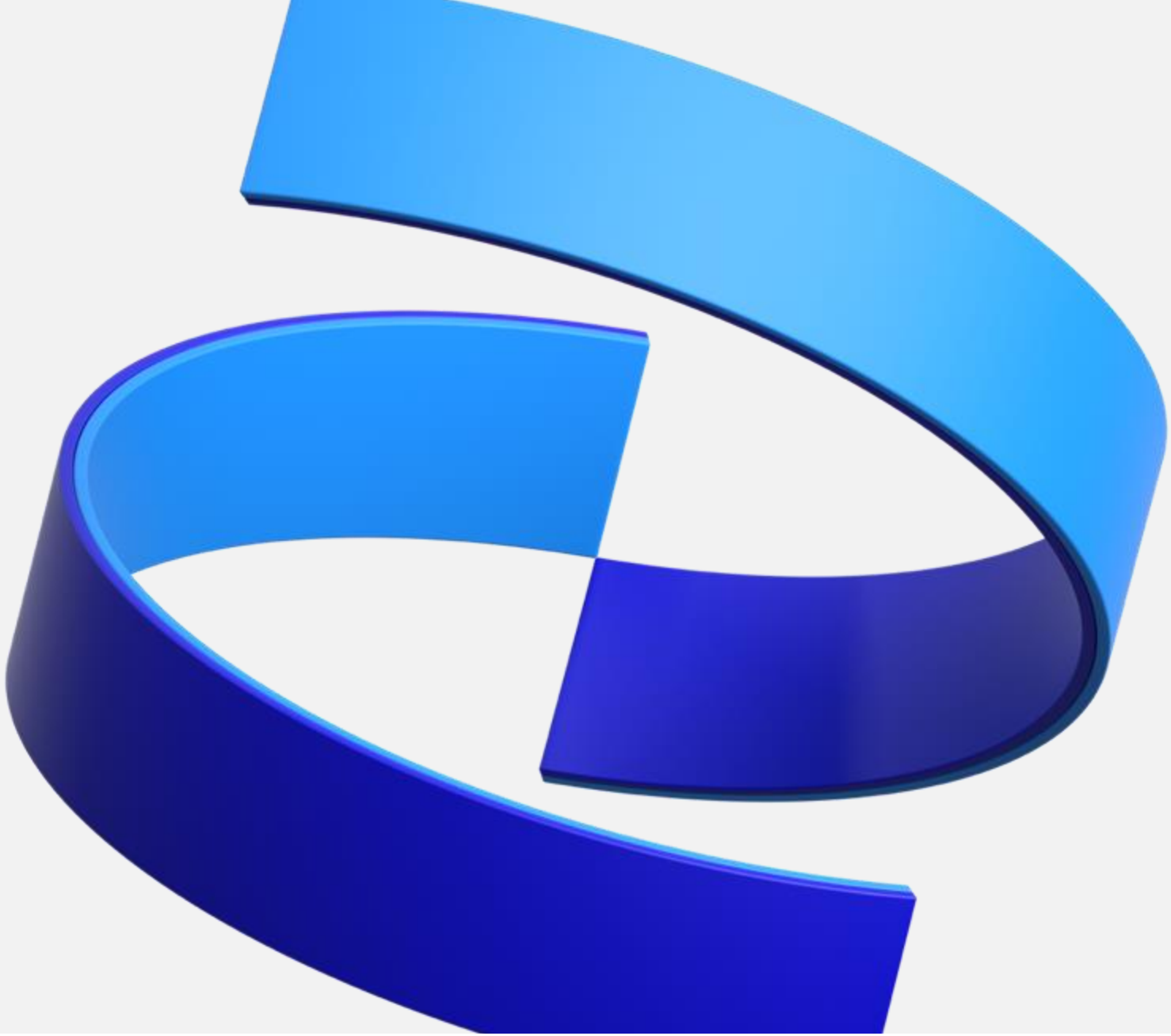
COVID-19 Vaccine BNT162b2

Safety, Immunogenicity, and Efficacy in Subjects 12–15-years-old

Presentation to ACIP
12 May 2021

John L. Perez, MD, MBA, MA



Inclusion of adolescents <16 yrs of age

- C4591001 was initially an adult study
- Once acceptable tolerance in adults was established within the original study the protocol was amended to allow inclusion of subjects 16-17 years of age and subsequently 12-15 years of age at the same dose and schedule as adults, without further dose-finding.
- The purpose was to generate data to understand whether people 12-15 years of age could be included in pandemic COVID-19 immunisation programmes
- Data is from dose 1 to 1 month post dose 2 (12-15- and 16–25-year-olds); and from dose 1 to data cut-off point (13 March 2021) – 12–15-year-olds
  - Data from subjects 16-25 years of age were used for the safety comparisons and immunobridging purposes

Phase 2/3 Safety Schema – Started 27 July, 2020

Vaccination period | **Follow-up period**

21 days apart

Up to 2 years

Active surveillance
for potential COVID-19 symptoms **TRIGGERING**
telehealth or in-person visit and nasal swab

7 days

7 days

Reactogenicity in subsets for 16 and above; all 12-15 year olds

One month post dose 2

Non-serious AE: all participants

Six months post dose 2

Serious AE: all participants

Deaths: all participants

Through study

- All 12-15 year olds had e-diaries to capture solicited events (N=2260)
- A random subset of 16-25 year olds had e-diaries (N=1097)
- Prior history of symptomatic COVID-19/MIS-C were excluded

Demography for 12-15 and 16-25 year olds (Safety population)

		BNT162b2		Placebo	
		12-15 Years (N=1131) n (%)	16-25 Years (N=1867) n (%)	12-15 Years (N=1129) n (%)	16-25 Years (N=1903) n (%)
Sex	Male	567 (50.1)	921 (49.3)	585 (51.8)	882 (46.3)
	Female	564 (49.9)	946 (50.7)	544 (48.2)	1021 (53.7)
Race	White	971 (85.9)	1443 (77.3)	962 (85.2)	1510 (79.3)
	Black or African American	52 (4.6)	189 (10.1)	57 (5.0)	179 (9.4)
	American Indian or Alaska native	4 (0.4)	32 (1.7)	3 (0.3)	18 (0.9)
	Asian	72 (6.4)	108 (5.8)	71 (6.3)	108 (5.7)
	Native Hawaiian or other Pacific Islander	3 (0.3)	10 (0.5)	0	3 (0.2)
	Multiracial	23 (2.0)	76 (4.1)	29 (2.6)	74 (3.9)
	Not reported	6 (0.5)	9 (0.5)	7 (0.6)	11 (0.6)
Racial desig.	Japanese	5 (0.4)	3 (0.2)	2 (0.2	6 (0.3)
Ethnicity	Hispanic/Latino	132 (11.7)	604 (32.4)	130 (11.5)	575 (30.2)
	Non-Hispanic/non-Latino	997 (88.2)	1259 (67.4)	996 (88.2)	1322 (69.5)
	Not reported	2 (0.2)	4 (0.2)	3 (0.3)	6 (0.3)
Country	USA	1131 (100.0)	1333 (71.4)	1129 (100.0)	1364 (71.7)
	Others*	0	534 (28.6)	0	539 (28.3)

*Argentina, Brazil, Germany, South Africa, Turkey

Note: All 12-15 year olds from the US; ~72% of 16-25 year olds from the US

Reactogenicity in 12-15 year olds and 16-25 year olds

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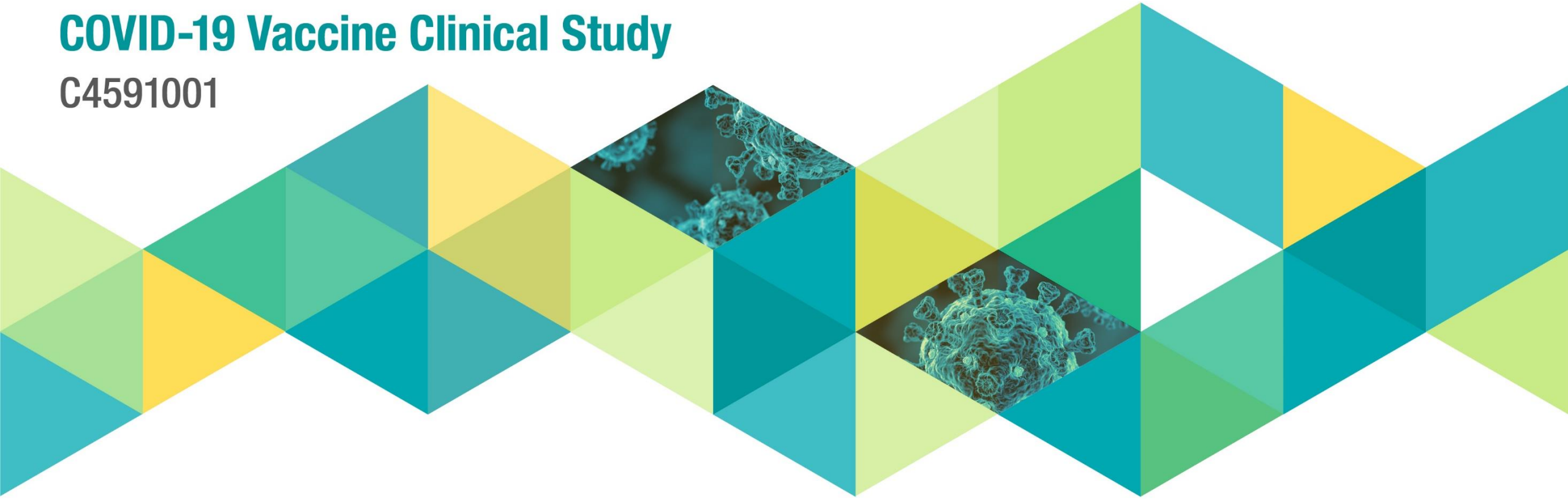
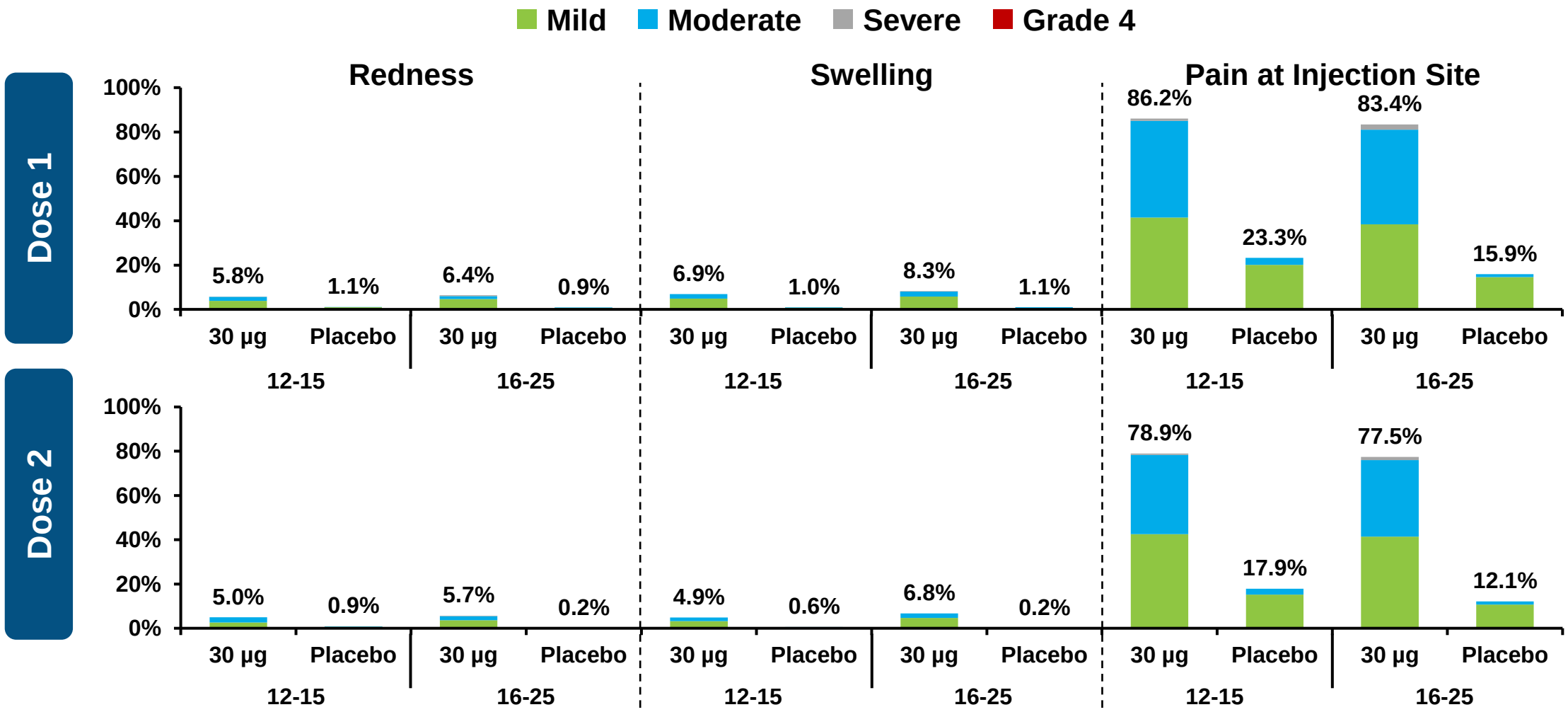
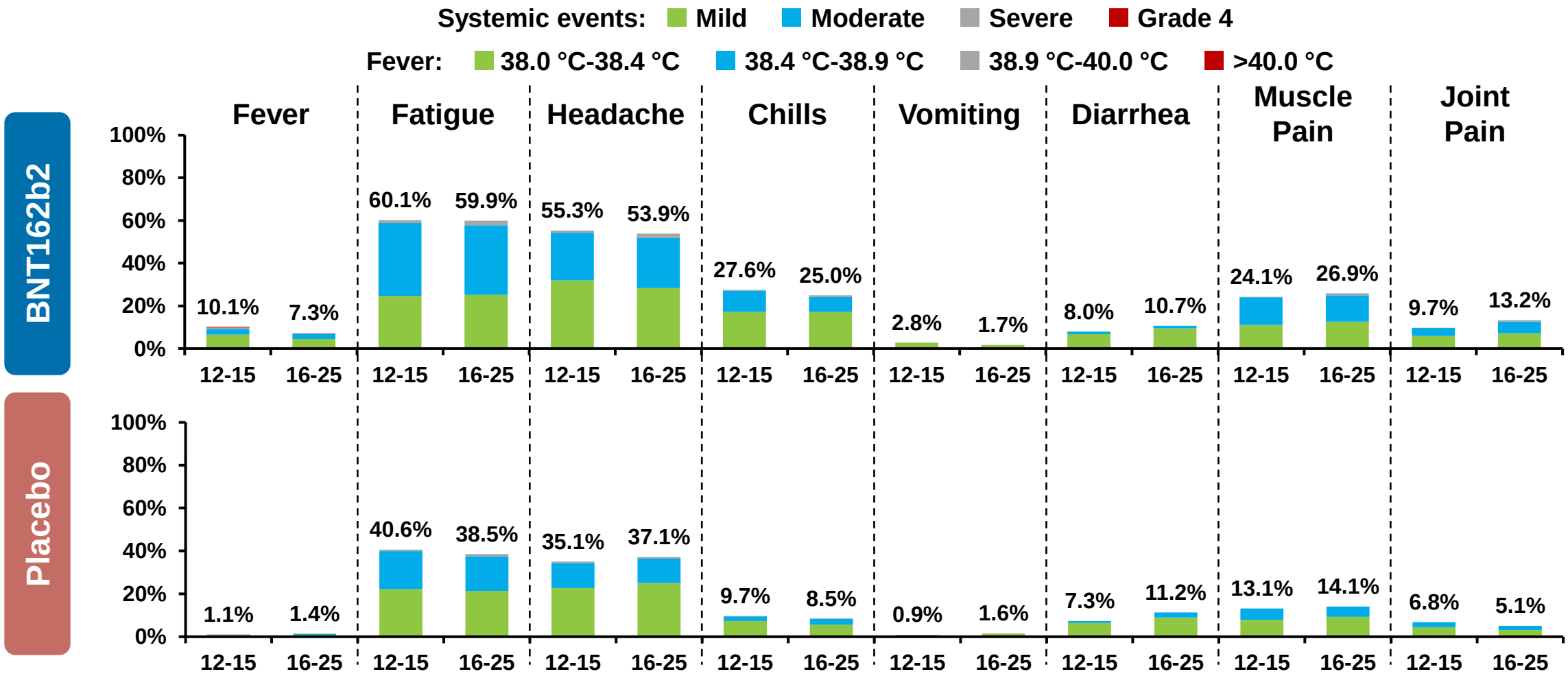


Subjects Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose in 12-15 and 16-25 Year Olds



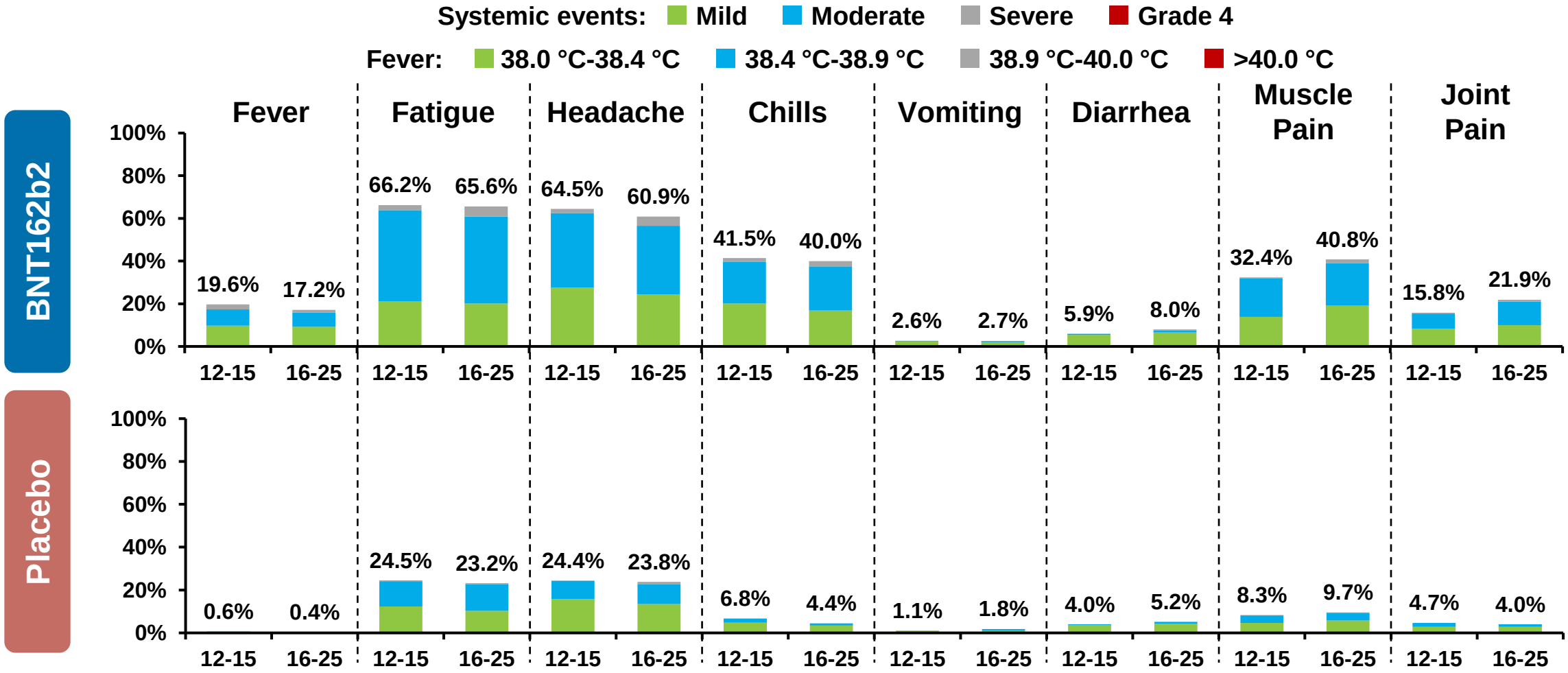
Redness and sweeling severity definition: Mild= >2-5cm, Moderate= >5-10 cm; Severe= >10 cm; Grade 4= necrosis
Pain at injection site severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Dose 1: 12-15 yrs N=2254; 16-25 yrs N=1084 Dose 2: 12-15 yrs N=2175 16-25 yrs N=984

Subjects Reporting Systemic Events, by Maximum Severity, Within 7 Days After **Dose 1** in 12-15 and 16-25 Year Olds



Fatigue, headache, chills, muscle pain, joint pain severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Vomiting severity definition: Mild=1-2 time in 24h; Moderate=>2times in 24h; Severe=Requires IV hydration; Grade 4=ER visit or hospitalization
Diarrhea severity definition: Mild=2-3 times in 24h; Moderate=4-5 times in 24h; Severe=6 or more times in 24h; Grade 4=ER visit or hospitalization
Dose 1; 12-15 yrs N=2254; 16-25 yrs N=1084

Subjects Reporting Systemic Events, by Maximum Severity, Within 7 Days After **Dose 2** in 12-15 and 16-25 Year Olds



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Dose 2: 12-15 yrs N=2175 16-25 yrs N=984

Conclusions: Local reactions and systemic events Phase 3 within 7 days of each dose – 12-15 yr olds (N=2254)

- Local reactions were predominantly pain at the injection site – more prominent after the first dose
  - Mostly mild to moderate

- Systemic events were predominantly fatigue, headaches, chills and muscle pain as well as fever and joint pain – more prominent after the second dose
  - Mostly mild to moderate

Adverse events in Phase 3 – 12-15 year olds and 16-25 year olds

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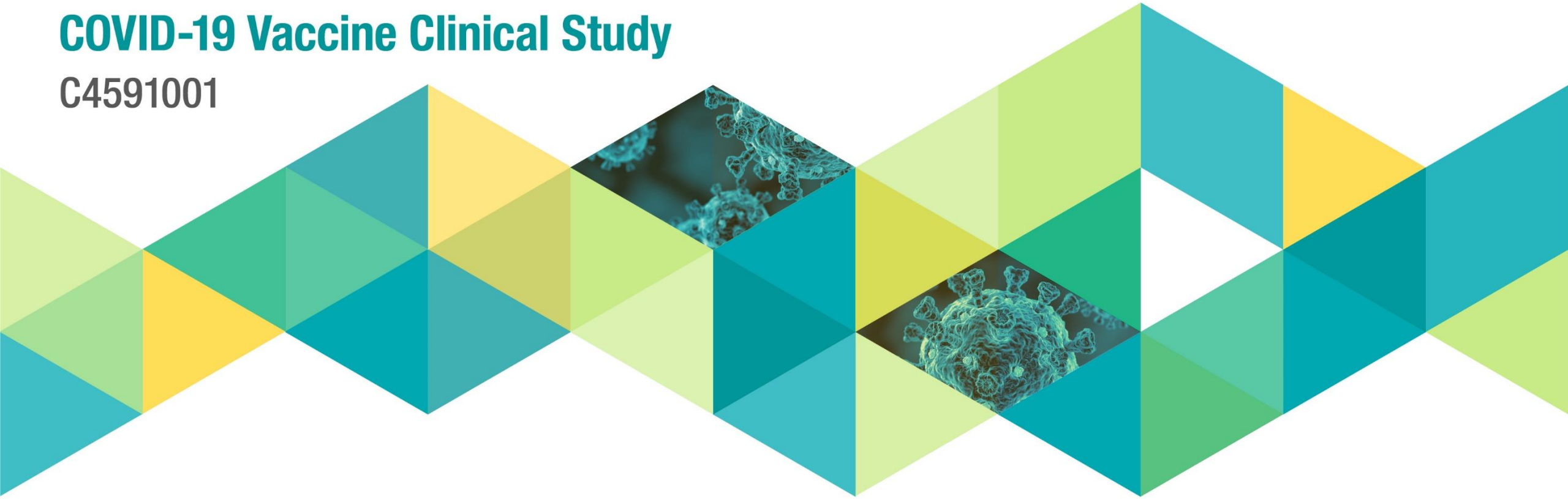
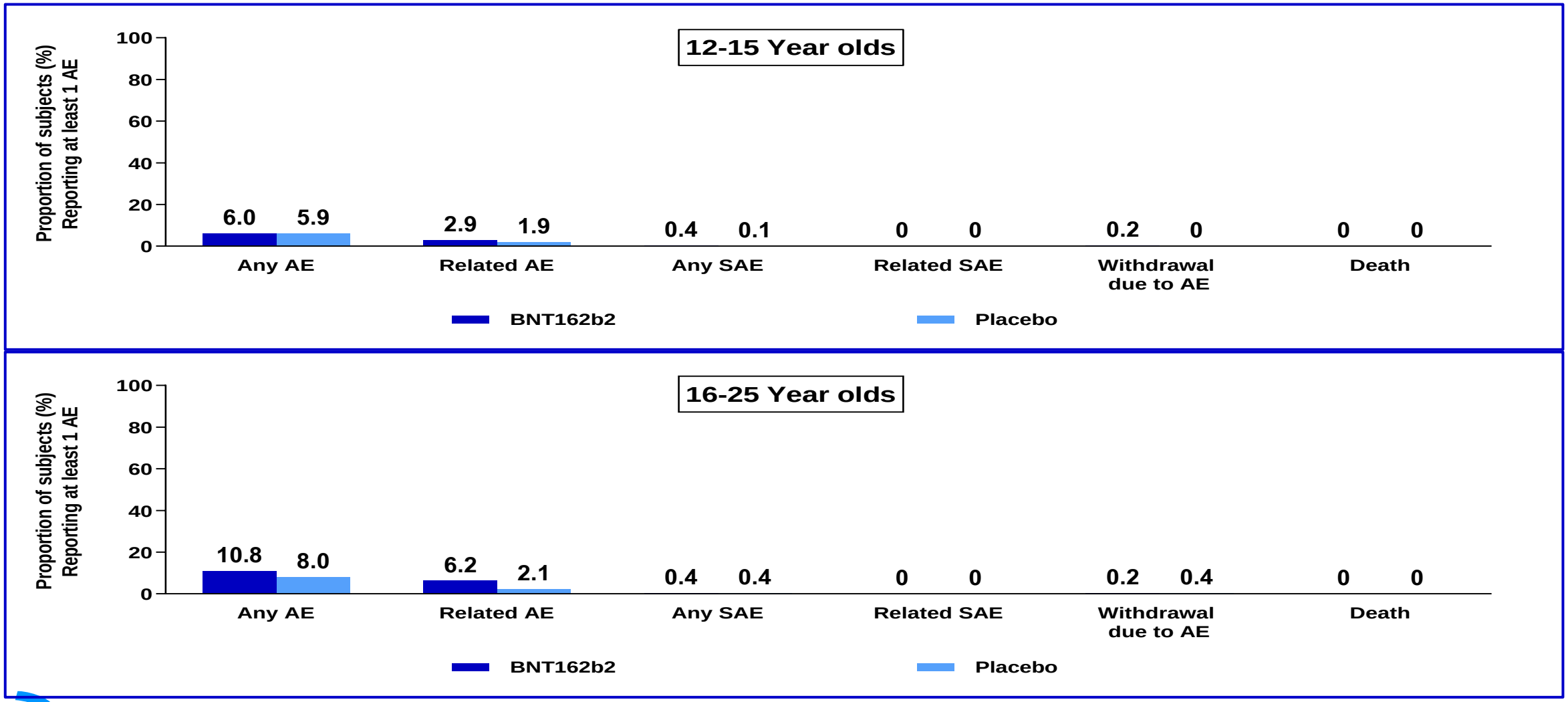
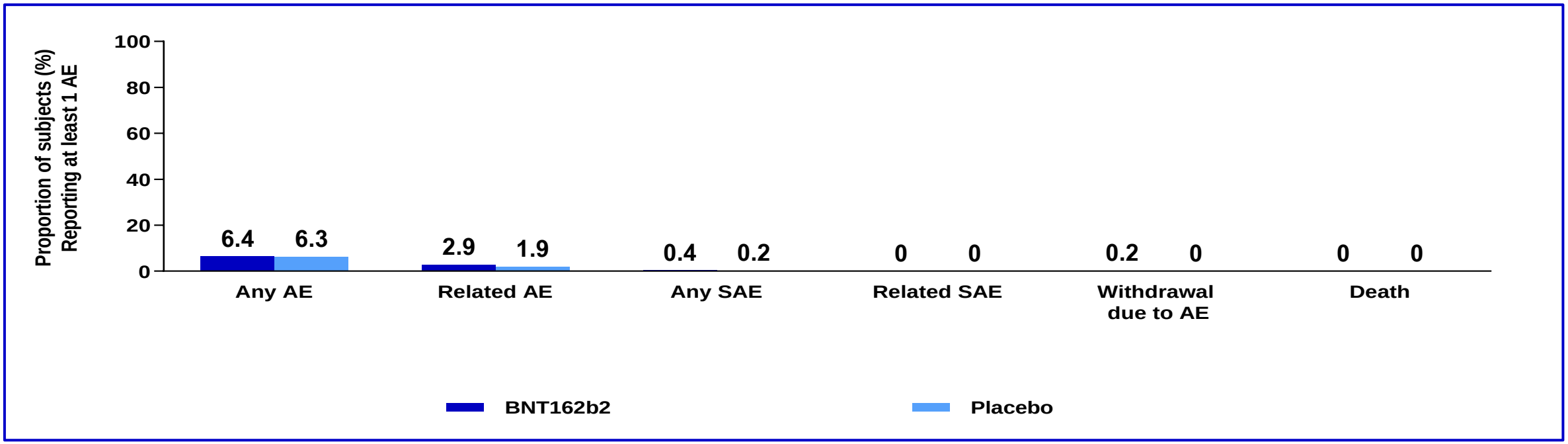


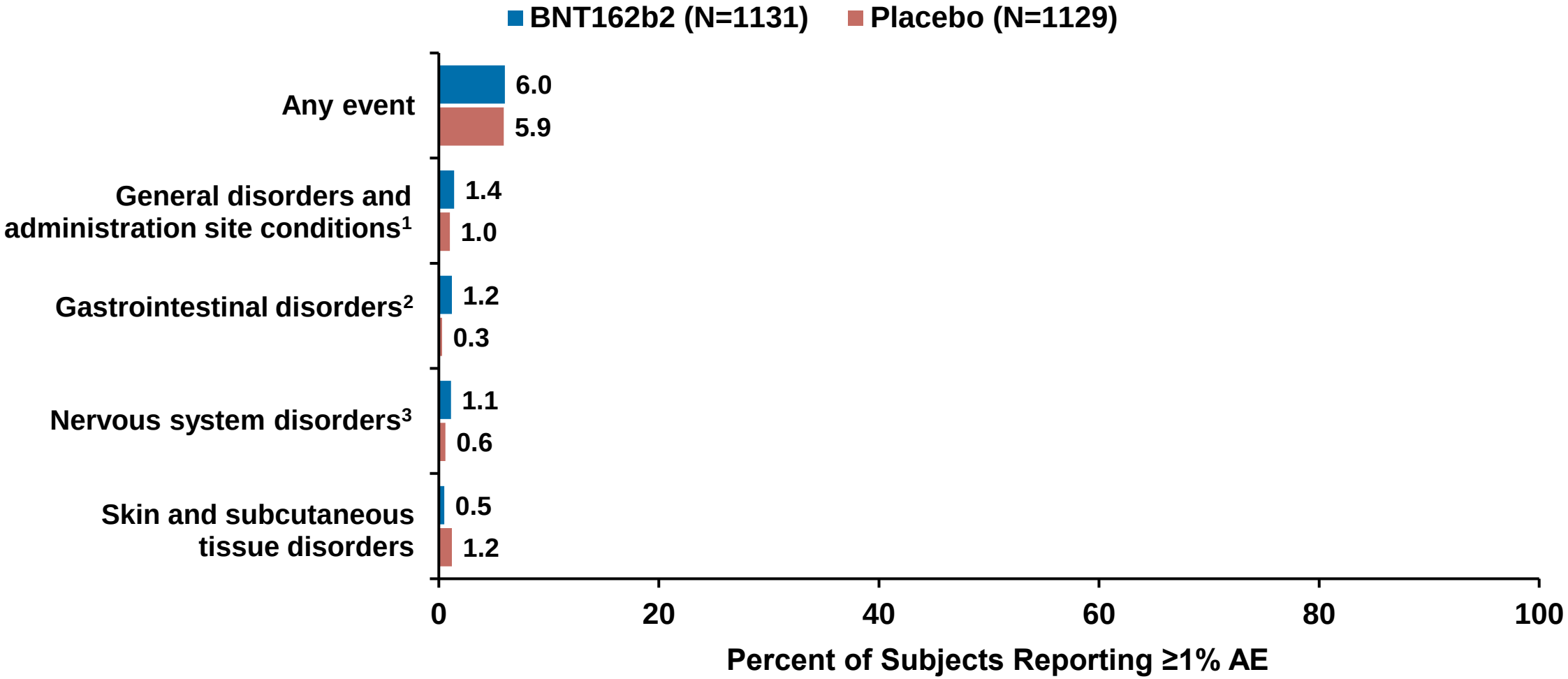
Overall Adverse Events from Dose 1 to 1 Month Post Dose 2
12-15 (N=2260) and 16-25 (Reactogenicity subset N=1097) year olds



Overall Adverse Events from Dose 1 to Data Cut-off Date (13Mar2021) 12-15 year olds (N=2260)

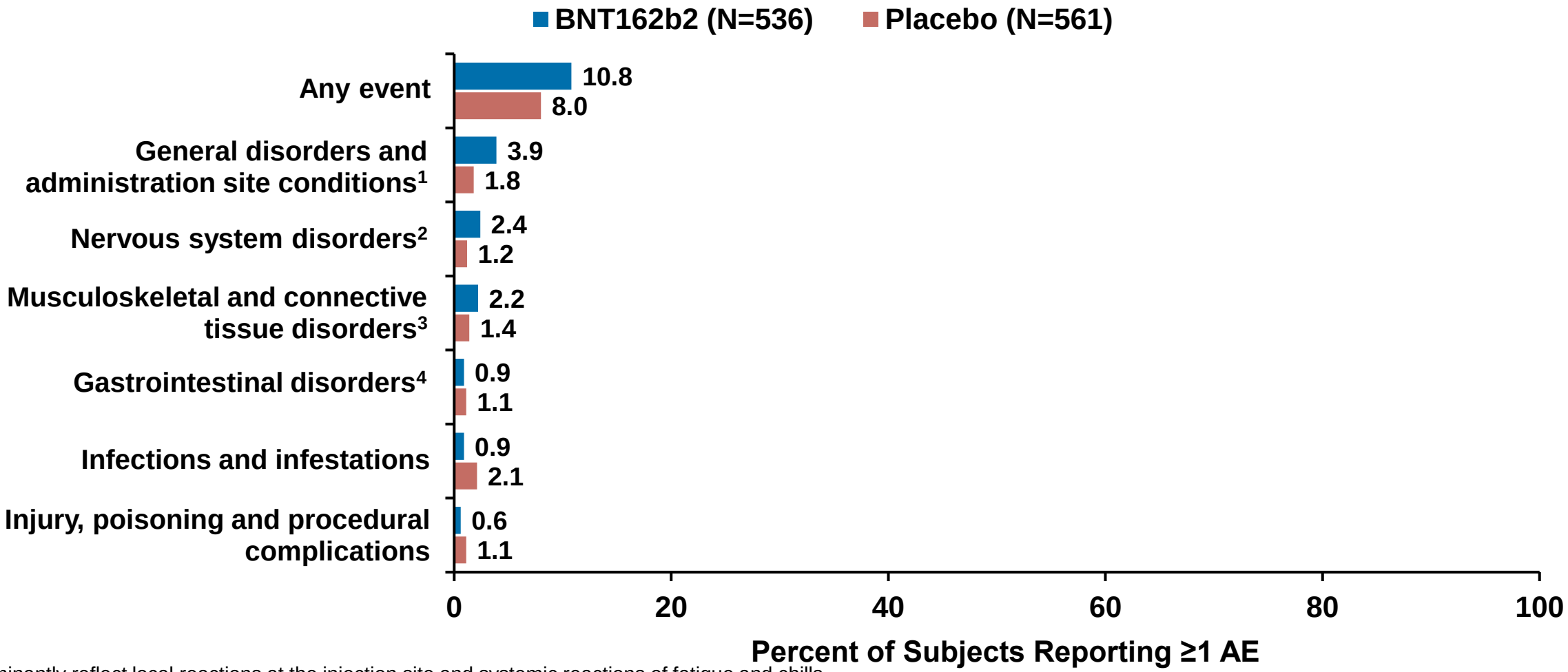


Adverse Events ≥1.0% by System Organ Class for 12-15 year olds 1 Month Post Dose 2



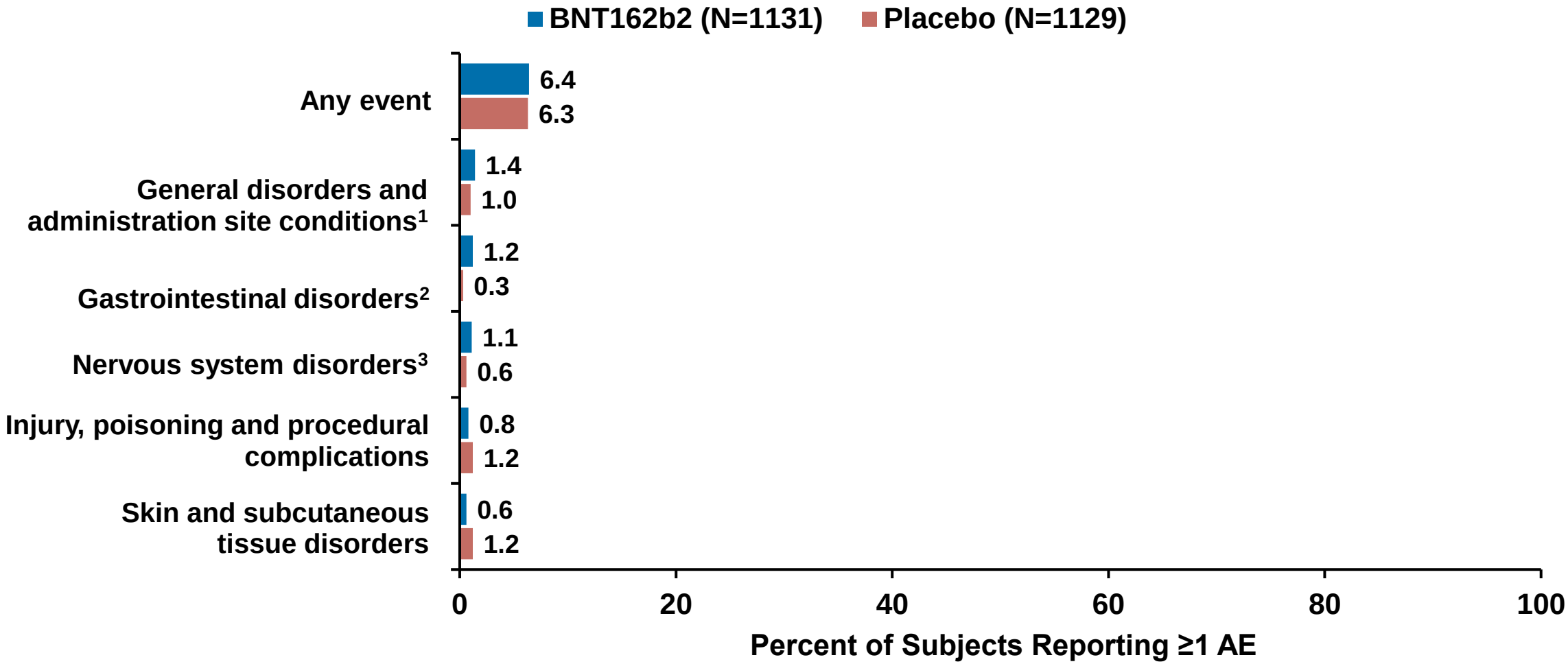
1. Predominantly reflect local reactions at the injection site and systemic reactions of fever and fatigue
2. Predominantly reflect nausea and diarrhea
3. Predominantly reflects Headache

Adverse Events ≥1.0% by System Organ Class for 16-25 year olds 1 Month Post Dose 2



1. Predominantly reflect local reactions at the injection site and systemic reactions of fatigue and chills
2. Predominantly reflects Headache
3.. Predominantly reflect myalgias and arthralgia's as part of systemic events
4. Predominantly reflects Nausea and Vomiting

Adverse Events ≥1.0% by System Organ Class for 12-15 year olds from Dose 1 to Data Cut-off Date (13 Mar 2021)



1. Predominantly reflect local reactions at the injection site and systemic reactions of fever and fatigue
2. Predominantly reflect nausea and diarrhea
3. Predominantly reflects Headache

Lymphadenopathy in 12-15 Year Olds

- 9 cases (0.8%) in BNT162b2 and 2 cases placebo (0.2%)
  - 7 (0.6%) were related to vaccination; 1 (0.1%) in the placebo group
  - Primarily Left axillary or Left cervical
  - Onset within 2-10 days after vaccination
  - Duration 1-10 days where reported (others were ongoing at the time of the data cutoff date).
- In adults (16-55 years of age), 52 participants (0.4%) in the BNT162b2 group and 2 participants (0.0%) in the placebo group had lymphadenopathy events reported up to the unblinding date and assessed by the investigator as related to study intervention.
  - The majority of these events occurred in the arm and neck region, were reported within 2-4 days after vaccination (usually after Dose 2), and typically resolved within approximately 1 week.

Serious Adverse Events by SOC/PT from Dose 1 to Data Cut-off Date 12-15 year olds

System Organ Class/PT	BNT162b2 (30 µg) (N=1131)		Placebo (N=1129)	
	n	%	n	%
ANY EVENT	5	0.4	2	0.1
GASTROINTESTINAL DISORDERS	1	0.1	0	0
*Abdominal pain	1	0.1	0	0
*Constipation	1	0.1	0	0
INFECTIONS AND INFESTATIONS	0	0	2	0.2
#Appendicitis	0	0	2	0.2
#Focal peritonitis	0	0	1	0.1
NERVOUS SYSTEM DISORDERS	1	0.1	0	0
*Neuralgia	1	0.1	0	0
PSYCHIATRIC DISORDERS	4	0.4	0	0
Depression	3	0.3	0	0
Anxiety	1	0.1	0	0
Suicidal ideation	1	0.1	0	0

*Abdominal pain, constipation and neuralgia were in the same participant

#Appendicitis and focal peritonitis were in the same participant

Deaths: 12–15-year-olds

- No deaths

Efficacy and Immunogenicity

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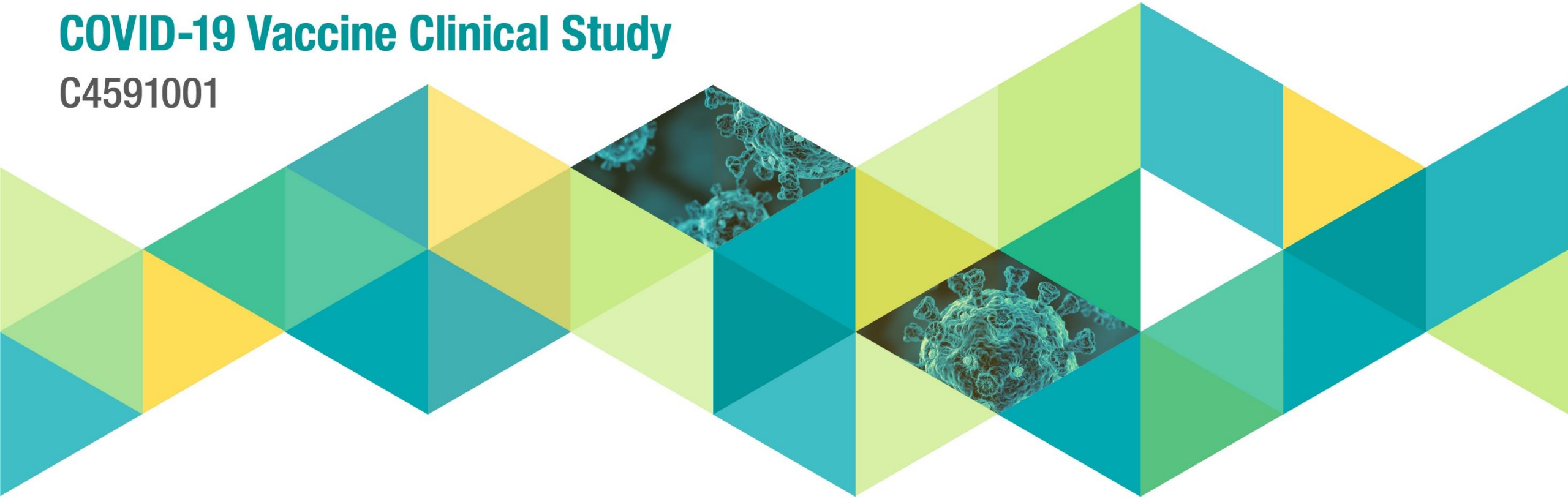
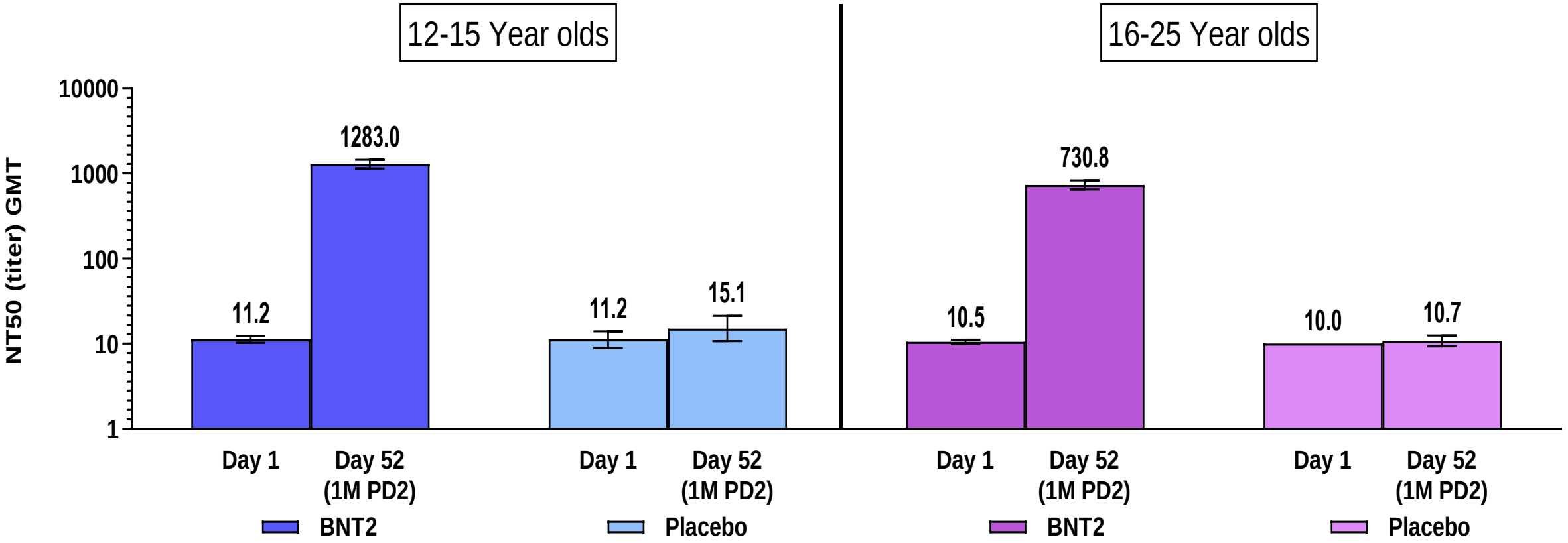


Follow-up Time After Dose 2: 12-15 year olds – Safety Population

Total exposure from Dose 2 to cut-off date	BNT162b2 (30 µg) (N=1131) n[b](%)	Placebo (N=1129) n (%)	Total (N=2260) n (%)
< 1 Month	13 (1.1)	25 (2.2)	38 (1.7)
≥1 Month to < 2 months	458 (40.5)	456 (40.4)	914 (40.4)
≥2 Months to <3 months	612 (54.1)	599 (53.1)	1211 (53.6)
≥3 Months	48 (4.2)	49 (4.3)	97 (4.3)

Note: 98.3% of subjects had at least 1 month of follow-up time

Geometric Mean Titers: SARS-CoV-2 Neutralization Assay – NT50* – Subjects 12-15 and 16-25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population (All subjects)



*NT50 = 50% neutralizing titers

Noninferiority Between 12-15 and 16-25 years Of Age Was Met Geometric Mean Ratio (GMR) in Neutralization Titers

(Without prior infection)

		BNT162b2 (30 µg)					
		12-15 year		16-25 years		12-15/16-25 years	
Assay	Dosing/ Sampling Time Point	n	GMT (95% CI)	n	GMT (95% CI)	GMR (95% CI)	Met NI (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)	2 / 1 Month	190	1239.5 (1095.5, 1402.5)	170	705.1 (621.4, 800.2)	1.76 (1.47, 2.10)	Y

- Noninferiority is declared if the lower bound of the 95% confidence interval is > 0.67
- LBCI for GMR >1 indicating a statistically greater response in 12-15 that 16-25 year olds

First COVID-19 Occurrence From 7 Days After Dose 2

Subjects 12-15 Years of Age – Evaluable Efficacy Population

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

	BNT162b2 (30 µg) N=1005		Placebo N=978			
Efficacy Endpoint	**n**	**Surveillance Time (n)**	**n**	**Surveillance Time (n)**	**VE (%)**	**(95% CI)**
First COVID-19 occurrence ≥7 days after Dose 2	**0**	**0.154 (1001)**	**16**	**0.147 (972)**	**100.0**	**(75.3, 100.0)**

- There were no severe COVID-19 cases

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint.
The analysis is descriptive; no hypothesis test

First COVID-19 Occurrence From 7 Days After Dose 2

Subjects 12-15 Years of Age – Evaluable Efficacy Population

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

	BNT162b2 (30 µg) N=1119		Placebo N=1110			
Efficacy Endpoint	**n**	**Surveillance Time (n)**	**n**	**Surveillance Time (n)**	**VE (%)**	**(95% CI)**
First COVID-19 occurrence ≥7 days after Dose 2	**0**	**0.170 (1109)**	**18**	**0.163 (1094)**	**100.0**	**(78.1, 100.0)**

- There were no severe COVID-19 cases

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint.
The analysis is descriptive; no hypothesis test

Overall safety conclusions for 12-15 year olds in the Phase 2/3 analysis

- **Reactogenicity: BNT162b2 was well tolerated in subjects 12-15 years old and showed a similar pattern to that seen in 16-25 year olds**
  - Pain at the injection site, fatigue, headaches, chills, joint pain and muscle pain were the most predominant as well as fever
  - Increased systemic events after dose 2 was similar to that seen with 16-25 year olds

- **Adverse events overall were relatively few**
  - Highest incidence was in the General Disorders and Administration Site Conditions, reflecting local and systemic reactogenicity events
  - Lymphadenopathy was identified as related to vaccination
  - There were no related SAEs
  - No deaths were reported

Immunogenicity & Efficacy Conclusions for 12-15 year olds in the Phase 2/3 analysis

- Immune response to Pfizer-BioNTech COVID-19 Vaccine in SARS-CoV-2 50% neutralizing titers in adolescents 12-15 years of age was noninferior to (and in fact exceeded) the immune response in young adults 16-25 years of age, which provides immunobridging for adolescents in pivotal Study C4591001.

- In the adolescent group, efficacy analyses based on cases reported from at least 7 days after Dose 2 through the data cutoff date, the observed VE was **100%** (95% CI: 75.3%, 100%) for individuals without evidence of prior SARS-CoV-2 infection before and during vaccination regimen, and **100%** (2-sided 95% CI: 78.1%, 100%) for those with or without evidence of prior SARS-CoV-2 infection before and during vaccination regimen.

- No severe cases were reported in the 12-15 years of age group as of the date cutoff date.

- Overall, these immunogenicity and efficacy data strongly support BNT162b2 use in adolescents 12-15 years of age.