BNT162b2 (COMIRNATY)

BLA STN 125742/0

Response to CBER Comment Regarding Analyses for Safety for the Two Age Groups

August 2021

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1. INTRODUCTION

Reference is made to BLA STN 125742/0 for COVID-19 mRNA Vaccine (COMIRNATY), for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals ≥16 years of age and to CBER's 29 July 2021 Information Request received via email from Laura Gottschalk, PhD, CBER, OVRR regarding safety for the following age groups: 1) 16 through 55 years, 2) 56 years and older.

CBER's request in ***bold italics*** is followed by Pfizer/BioNTech's response below.

2. REQUESTS

2.1. CBER Request

Our review of the information provided in your BLA STN 125742/0 for COMIRNATY (COVID-19 Vaccine, mRNA), for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older, is ongoing. We have the following request for additional information:

Please submit the analyses as presented in Table 7 (page 116) of the Summary of Clinical Safety for the following age groups: 1) 16 through 55 years, 2) 56 years and older.

Response

Table 7 in the Summary of Clinical Safety presents the incident rates of at least 1 adverse event from dose 1 to unblinding date in the Phase 2/3 Subjects ≥16 Years of Age (Safety Population). The corresponding analyses for the two requested age groups were presented in Tables 14.106 and 14.107 located in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Section 14, which are also provided in this response (Table 1 and Table 2).

Table 1. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Age Group – Phase 2/3 Subjects ≥16 Years of Age – Safety Population
Age Group: 16-55 Years

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=12995, TE[b]=49.7)			Placebo (N[a]=13026, TE[b]=49.1)		
Adverse Event	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])
Any event	4396	88.4	(85.8, 91.0)	2136	43.5	(41.7, 45.4)
Related[f]	3484	70.0	(67.7, 72.4)	884	18.0	(16.8, 19.2)
Severe	193	3.9	(3.4, 4.5)	124	2.5	(2.1, 3.0)
Life-threatening	13	0.3	(0.1, 0.4)	20	0.4	(0.2, 0.6)
Any serious adverse event	103	2.1	(1.7, 2.5)	117	2.4	(2.0, 2.9)
Related[f]	3	0.1	(0.0, 0.2)	1	0.0	(0.0, 0.1)
Severe	56	1.1	(0.9, 1.5)	75	1.5	(1.2, 1.9)
Life-threatening	13	0.3	(0.1, 0.4)	20	0.4	(0.2, 0.6)
Any adverse event leading to withdrawal	22	0.4	(0.3, 0.7)	28	0.6	(0.4, 0.8)
Related[f]	9	0.2	(0.1, 0.3)	8	0.2	(0.1, 0.3)
Severe	5	0.1	(0.0, 0.2)	6	0.1	(0.0, 0.3)
Life-threatening	3	0.1	(0.0, 0.2)	5	0.1	(0.0, 0.2)
Death	3	0.1	(0.0, 0.2)	4	0.1	(0.0, 0.2)

a. N = number of subjects in the specified group.
b. TE = total exposure time in 100 person-years across all subjects in the specified group. Exposure time for a subject is the time from Dose 1 to the end of blinded follow-up. This value is the denominator for the incidence rate calculation.
c. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
d. Incidence rate (IR) is calculated as number of subjects reporting the event/total exposure time in 100 person-years (PY) across all subjects in the specified group.
e. 2-sided CI based on Poisson distribution.
f. Assessed by the investigator as related to investigational product.

Table 1. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Age Group – Phase 2/3 Subjects ≥16 Years of Age – Safety Population
Age Group: 16-55 Years

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=12995, TE[b]=49.7)			Placebo (N[a]=13026, TE[b]=49.1)		
Adverse Event	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])

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Table 2. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Age Group – Phase 2/3 Subjects ≥16 Years of Age – Safety Population
Age Group: >55 Years

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=8931, TE[b]=33.7)			Placebo (N[a]=8895, TE[b]=33.1)		
Adverse Event	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])
Any event	2551	75.7	(72.8, 78.7)	1432	43.3	(41.1, 45.6)
Related[f]	1762	52.3	(49.9, 54.8)	429	13.0	(11.8, 14.3)
Severe	163	4.8	(4.1, 5.6)	132	4.0	(3.3, 4.7)
Life-threatening	35	1.0	(0.7, 1.4)	34	1.0	(0.7, 1.4)
Any serious adverse event	165	4.9	(4.2, 5.7)	151	4.6	(3.9, 5.4)
Related[f]	1	0.0	(0.0, 0.2)	0	0.0	(0.0, 0.1)
Severe	92	2.7	(2.2, 3.3)	81	2.4	(1.9, 3.0)

Table 2. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Age Group – Phase 2/3 Subjects ≥16 Years of Age – Safety Population
Age Group: >55 Years

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=8931, TE[b]=33.7)			Placebo (N[a]=8895, TE[b]=33.1)		
Adverse Event	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])
Life-threatening	35	1.0	(0.7, 1.4)	34	1.0	(0.7, 1.4)
Any adverse event leading to withdrawal	23	0.7	(0.4, 1.0)	23	0.7	(0.4, 1.0)
Related[f]	4	0.1	(0.0, 0.3)	4	0.1	(0.0, 0.3)
Severe	5	0.1	(0.0, 0.3)	6	0.2	(0.1, 0.4)
Life-threatening	12	0.4	(0.2, 0.6)	11	0.3	(0.2, 0.6)
Death	12	0.4	(0.2, 0.6)	10	0.3	(0.1, 0.6)

a. N = number of subjects in the specified group.
b. TE = total exposure time in 100 person-years across all subjects in the specified group. Exposure time for a subject is the time from Dose 1 to the end of blinded follow-up. This value is the denominator for the incidence rate calculation.
c. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
d. Incidence rate (IR) is calculated as number of subjects reporting the event/total exposure time in 100 person-years (PY) across all subjects in the specified group.
e. 2-sided CI based on Poisson distribution.
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3. REFERENCES

None