BNT162b2 (COMIRNATY)

BLA STN 125742/0

Response to 09 August 2021 CBER Information Request Regarding Sequencing Data

August 2021

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1. INTRODUCTION

Reference is made to BLA STN 125742/0 for the Pfizer-BioNTech COVID-19 Vaccine for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals ≥16 years of age.

The purpose of this document is to respond to CBER's Information Request (IR) communicated from Captain Michael Smith, PhD (CBER) to Elisa Harkins Tull (Pfizer Inc.) via email on 09 August 2021, with questions regarding Study C4591001 and sequencing data. CBER has requested a response by 12 August 2021.

CBER's comments/requests in ***bold italics*** are followed by the Sponsor's responses below.

2. CBER REQUESTS

The review team has the below clinical questions for you regarding study C4591001. Please respond as soon as possible and no later than Thursday, August 12, 2021.

2.1. CBER Request 1

One subject in the vaccine group, (Site No: 1252, Subject No: 12521010): 80-year-old white, non-Hispanic male who received two doses of BNT162b2 (17 Aug 2020 and 08 September 2020), died from COVID pneumonia.

If available, please provide sequencing data for the virus isolated from this patient.

Response

Subject number 12521010 was not a confirmed COVID-19 case per protocol due to lack of central lab or eligible local PCR test result. The diagnosis of COVID-19 pneumonia was based on a local COVID-19 test, which was not one of the approved assays specified in the study. Additionally, the test was done locally, and hence the sponsor did not have access to the specimen and is unable to perform the sequencing analysis.

2.2. CBER Request 2

If there is available genomic sequencing data for any other COVID-19 case, especially those with fatal outcomes, and those from HIV positive subjects, please submit that information.

Response

All available genomic sequencing data were included in SDTM dataset XB and ADaM dataset ADXB of the eSUB package submitted on 07 June 2021, which included cases from the efficacy and safety analysis cut-off date of 13 March 2021. There was no sequencing data available for HIV positive subjects. A total of 3 subjects who died during the study had

sequencing data (Table 1); 1 of these 3 subjects had sequencing done on swab taken after unblinding.

Table 1. eff.16.2.8.6.1 Listing of Subjects with Fatal Outcome and SARS-CoV-2 Variants for COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1027 10271191 (USA/NORTH CAROLINA/68/F)	Placebo	Dose 2/103*	12JAN2021	13FEB2021	Neg/Neg/Neg	Fever	Pos/, 13JAN2021, B.1.2
						New or increased cough	
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Vomiting	
C4591001 1088 10881126 (USA/NORTH CAROLINA/65/M)	Placebo	Dose 2/68	29NOV2020	01DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 30NOV2020, B.1.2

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Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1231 12315324 (ARG/58/F)	Placebo	Dose 2/99	25DEC2020	31JAN2021	Neg/Neg/Neg	Fever	Pos/, 26DEC2020, B.1.1.291
						New or increased cough	
						Chills	

Abbreviations: ARG = Argentina; NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein–binding; Neg = negative; Pos = positive; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: HIV-positive subjects are included in this listing but not included in the analyses of the overall study objectives.
Note: * = COVID-19 occurrence after subject was unblinded.
a. Relative Day (Rel Day) = date of first symptom - date of last dose before first symptom + 1.
b. SARS-CoV-2 NAAT results from the local lab are based on the Cepheid Xpert® Xpress SARS-CoV-2 test, Roche cobas® SARS-CoV-2 real-time RT-PCR test (EUA200009/A001), or Abbott RealTime SARS-CoV-2 assay (EUA200023/A001) only.
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