

RESPONSE TO CBER COMMUNICATION REGARDING SENSITIVITY ANALYSES RECEIVED ON NOVEMBER 25, 2020

The Sponsor acknowledges CBER's communication regarding sensitivity analyses for study site 393.

This document provides the Sponsor's responses to CBER's requests (in **Bold**).

Item 1:

After inspection of study site 393 (Dr. Neil Sheth, Glendale, AZ) by FDA's Bioresearch Monitoring team, a Form FDA 483 was issued. Given the concern for data integrity at this study site, please conduct a sensitivity analysis for the primary efficacy endpoint (overall and by the protocol specified age and risk subgroups) excluding all data from this study site. This should be done both for the interim analysis (Nov 11 snapshot) as well as for the final analysis.

Sponsor Response:

As requested, the following sensitivity analyses of the primary efficacy endpoint (COVID-19 starting 14 days after the 2nd injection) were performed excluding all data from study site 393 based on the adjudication committee assessments using Per-Protocol Set using the data snapshot occurred on 11-Nov-2020:

- Sensitivity analysis of vaccine efficacy of mRNA-1273 to prevent COVID-19 based on adjudication committee assessments starting 14 days after second injection excluding site 393 data
- Subgroup analysis of vaccine efficacy of mRNA-1273 to prevent COVID-19 based on adjudication committee assessments starting 14 days after second injection by age group (≥ 18 and < 65 years, ≥ 65 years) excluding site 393 data
- Subgroup analysis of vaccine efficacy of mRNA-1273 to prevent COVID-19 based on adjudication committee assessments starting 14 days after second injection by age and health risk for severe COVID-19 (≥ 18 and < 65 years and no risk, ≥ 18 and < 65 years and at risk, ≥ 65 years) excluding site 393 data

There was one COVID-19 case starting 14 days after the 2nd injection based on the adjudication committee assessment in participants enrolled at site 393. The results are summarized in the [table](#) below. The sensitivity analyses results excluding all data from site 393 are consistent with the primary analysis and subgroup analysis of the primary efficacy endpoint in both the Data Snapshot #1 (11 Nov 2020) and DS#2 (23 Nov 2020) timepoints.

Table 1: Primary and Sensitivity analyses excluding data from Site 393: Primary Efficacy Endpoint: COVID-19 starting 14 days after the 2nd dose – Per-Protocol Set (11 Nov 2020 Cut Off Date)

	mRNA-1273 Cases n (%)	Placebo Cases n (%)	Vaccine Efficacy (VE) % (95% CI)*
Primary Analyses: COVID-19 starting 14 days after 2nd injection per adjudication committee assessment			
All subjects	5 / 13934 (<0.1)	90 / 13883 (0.6)	94.5% (86.5%, 97.8%)
In Age subgroups			
18 to <65 years	5 / 10407 (<0.1)	75 / 10384 (0.7)	93.4% (83.7%, 97.3%)
65 years and older	0 / 3527	15 / 3499 (0.4)	100%
In Age and health risk for severe COVID-19 (used as stratification factor for randomization)			
18 and <65 and not at risk	4 / 8309 (<0.1)	57 / 8323 (0.7)	93.0% (80.8%, 97.5%)
18 and <65 and at risk	1 / 2098 (<0.1)	18 / 2061 (0.9)	94.6% (59.4%, 99.3%)
≥65	0 / 3527	15 / 3499 (0.4)	100%
Sensitivity Analyses excluding data from Site 393: Primary efficacy endpoint: COVID-19 starting 14 days after 2nd injection per adjudication committee assessment			
All subjects	5 / 13831 (<0.1)	89 / 13777 (0.6)	94.4% (86.3%, 97.7%)
In Age subgroups			
18 to <65 years	5 / 10341 (<0.1)	74 / 10309 (0.7)	93.3% (83.5%, 97.3%)
65 years and older	0 / 3490	15 / 3468 (0.4)	100%
In Age and health risk for severe COVID-19 (used as stratification factor for randomization)			
18 and <65 and not at risk	4 / 8256 (<0.1)	56 / 8263 (0.7)	92.9% (80.5%, 97.4%)
18 and <65 and at risk	1 / 2085 (<0.1)	18 / 2046 (0.9)	94.6% (59.4%, 99.3%)
≥65	0 / 3490	15 / 3468 (0.4)	100%

*VE and 95% Confidence Interval (CI) from the stratified Cox proportional hazard model