

**RESPONSE TO CBER COMMUNICATION REGARDING CLINICAL TOPICS (IR 19)
RECEIVED ON DECEMBER 14, 2020**

The Sponsor acknowledges CBER's communication regarding Clinical topics (IR 19).

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

ITEM 1:

Please fill in the following table:

COVID-19 (based on RT-PCR and eligible symptoms) starting from randomization in the Full Analysis Set by time period (DS1, 11-Nov-2020), please include efficacy rates with 95% CI in each row.

	Vaccine Group N= n1/n2 (person-years)	Placebo Group N= n1/n2 (person-	VE (%) (95% CI)
First COVID-19 occurrence after dose 1			
Any time after dose 1 to before dose 2			
Any time after dose 2			

Sponsor Response:

For the secondary efficacy objective, to evaluate the efficacy of mRNA-1273 to prevent COVID-19 in all study participants, regardless of evidence of prior SARS-CoV-2 infection, a planned sensitivity analysis is to evaluate vaccine efficacy with cases starting from randomization. For this secondary efficacy objective, the analysis population is the Full Analysis Set (FAS) that includes randomized subjects who received at least one dose of IP, regardless of baseline SARS-CoV-2 status. Subjects are included in the group to which they were randomized.

In addition to the planned sensitivity analysis of COVID-19 starting from randomization, regardless of prior SARS-CoV-2 infection, in FAS, as requested, below is the exploratory analyses of vaccine efficacy of COVID-19 by time period in the FAS Set based on DS1, 11-Nov-2020.

In the ad-hoc exploratory analyses by time period, VE and 95% CI are based on the exact method conditional on the total number of cases adjusting for person-years using the Poisson distribution. All cases received dose 1 on the date of randomization. Analyses for each time period were

performed separately. In each of the analyses, for the time period, only cases with onset/confirmation date of COVID-19 in that time period are considered cases; subjects who are not at risk for the time period, either a case or censored at a time point that is prior to the time period of interest, are excluded from the analysis. Subjects who did not receive dose 2 and are COVID-19 cases are included (as cases) in the time period of ‘Any time after dose 1 to before dose 2’. For those subjects who are at risk for the time period and not a case during the time period, their follow-up time are truncated at the end of the time period.

Exploratory Analysis of COVID-19 (based on RT-PCR and eligible symptoms) from randomization by Time Period – FAS

	Vaccine Group N=15180 n1/n2 incidence rate/1000 person-years (person-years)	Placebo Group N=15170 n1/n2 incidence rate/1000 person-years (person-years)	VE (%) (95% CI)*
First COVID-19 occurrence after dose 1	21 7.1 (2947.5)	173 59.0 (2932.2)	87.9% (81.0%, 92.7%)
Any time after dose 1 to before dose 2	14 11.3 (1237.6)	46 37.0 (1242.1)	69.5% (43.5%, 84.5%)
Any time after dose 2**	7 / 13857 2.5 (2823.9)	127 / 13792 (2801.8)	94.5% (88.4%, 97.8%)

Surveillance time in person years for given endpoint across all subjects within each group at risk for the endpoint

n1: number of cases; n2: number of subjects at risk for the time period

* VE is calculated as 1-ratio of incidence rates (mRNA-1273/Placebo). The 95% CI of VE is calculated using the exact method conditional upon the total number of cases, adjusting for person-years

**Subjects who were not at risk (cases or censored at prior time period) are excluded from this analysis