

RESPONSE TO CBER COMMUNICATION REGARDING CLINICAL RECEIVED ON DECEMBER 02, 2020

The Sponsor acknowledges CBER's communication regarding Clinical topics.

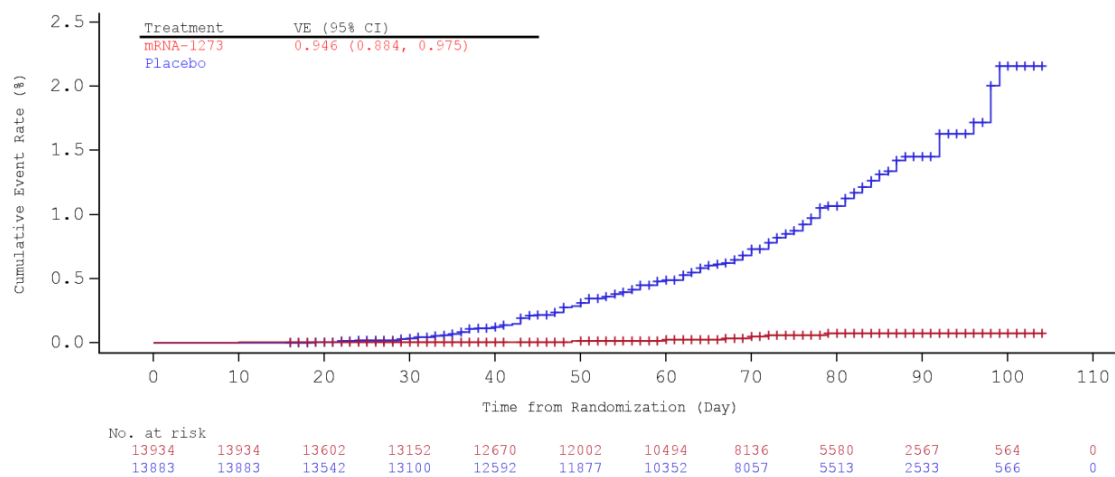
This document provides the Sponsor's responses to CBER's requests (in **Bold**).

Item 1:

Please provide a cumulative incidence curve of first COVID-19 occurrence starting after Dose 1.

Sponsor Response:

Cumulative incidence curve of first COVID-19 starting from randomization based on the Per-Protocol Set is provided. This figure also accompanies Table 14.2.2.1.2.5.1 Sensitivity Analysis of Vaccine Efficacy of mRNA-1273 to Prevent COVID-19 Starting After Randomization Per-Protocol Set, that was submitted to CBER. Of note, for all the cases, the randomization date and the date of Dose 1 are all the same.



Source: Figure 14.2.2.1.2.5.1.3 Kaplan-Meier Estimates of Time to First Occurrence of COVID-19 Starting After Randomization - Per-Protocol Set

Item 2:

Please fill in the following table:

Reasons for exclusion from Per Protocol Set	Vaccine Group N=	Placebo Group N=	Total N=
Subjects excluded from PP Set	xx (%)	xx (%)	xx (%)

Baseline SARS-CoV-2 status was positive or not known*	xx (%)	xx (%)	xx (%)
Did not receive second dose of IP	xx (%)	xx (%)	xx (%)
Discontinued study or study vaccine without receiving the second dose	xx (%)	xx (%)	xx (%)
Received IP other than what the subject was randomized to	xx (%)	xx (%)	xx (%))
Received vaccine out of window	xx (%)	xx (%)	xx (%)
Major protocol deviation**	xx (%)	xx (%)	xx (%)
add additional lines for other reasons as needed	xx (%)	xx (%)	xx (%)

***: defined as positive PCR at baseline, and/or positive serological results for anti-N protein antibodies; or missing or unknown baseline status**

****:** please provide a list of major protocol violations by study arm

Sponsor Response:

Please see below for the requested table using the Randomized Set, subjects are included in the group they were randomized to. A subject may be excluded from the Per-protocol Set due to multiple reasons listed below, in that situation, the subject is listed under the category appeared earliest in the table.

Reasons for exclusion from Per Protocol Set	Vaccine Group N= 15208	Placebo Group N= 15210	Total N= 30418
Subjects excluded from PP Set	1274 (8.4%)	1327 (8.7%)	2601 (8.6%)
Randomized but not received any IP	28 (0.2%)	40 (0.3%)	68 (0.2%)
Baseline SARS-CoV-2 status was positive or not known*	868 (5.7%)	800 (5.3%)	1668 (5.5%)
Received IP other than what the subject was randomized to	5 (<0.1%)	7 (<0.1%)	12 (<0.1%)
Discontinued study or study vaccine without receiving the second dose	136 (0.9%)	203 (1.3%)	339 (1.1%)

Did not receive second dose of IP	144 (0.9%)	155 (1.0%)	299 (1.0%)
Received vaccine out of window	81 (0.5%)	98 (0.6%)	179 (0.6%)
Major protocol deviation**	12 (<0.1%)	24 (0.2%)	36 (0.1%)

* Defined as positive PCR at baseline, and/or positive serological results for anti-N protein antibodies; or missing or unknown baseline status

**Major protocol deviations other than the categories listed earlier in the table:

- Inclusion criteria not met, but subject randomized
- Exclusion criteria met, but subject randomized
- Study treatment impacted by a temperature excursion which was not reported or approved or which was disapproved for further use
- Prohibited concomitant medication or vaccine received by subject

Item 3:

For the Safety Set population, please provide the number and percentage of participants across study groups with each of the protocol-defined high-risk conditions (chronic lung disease, significant cardiac disease, severe obesity, Diabetes (Type 1, Type 2, or gestational), liver disease, and Human Immunodeficiency Virus infection. Please include this information as additional rows in the ‘Demographic Characteristics’ table for the Safety Set requested by CBER on 12/1/2020.

Sponsor Response:

A summary of demographics and baseline characteristics table (Table 14.1.3.2.2) based on the Safety Set was created in response to EUA IR_001. As requested, summary of each of the protocol-defined risk of severe COVID-19 is provided below using the table for the Safety Set requested by CBER on 12/1/2020. Subjects with each of the protocol-defined risk of severe COVID-19 are generally balanced between the two groups.

Table 1: Demographic characteristics – Safety Set (Source: Table 14.1.3.2.2)

	Vaccine Group (N=15184) n (%)	Placebo Group (N=15165) n (%)	Total (N=30350) n (%)
Subjects with any protocol-defined risk for Severe COVID-19	3360 (22.1)	3382 (22.3)	6742 (22.2)
Subjects without protocol-defined risk for Severe COVID-19	11824 (77.9)	11783 (77.7)	23608 (77.8)

Subjects with Chronic Lung Disease	707 (4.7)	741 (4.9)	1448 (4.8)
Subjects with Significant Cardiac Disease	742 (4.9)	741 (4.9)	1483 (4.9)
Subjects with Severe Obesity	986 (6.5)	978 (6.4)	1964 (6.5)
Subjects with Diabetes	1427 (9.4)	1431 (9.4)	2858 (9.4)
Subjects with Liver Disease	100 (0.7)	96 (0.6)	196 (0.6)
Subjects with Human Immunodeficiency Virus Infection	90 (0.6)	86 (0.6)	176 (0.6)