

RESPONSE TO CBER COMMUNICATION REGARDING CLINICAL TOPICS (IR 13)
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The Sponsor acknowledges CBER's communication regarding Clinical topics (IR 13).

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

ITEM 4:

For the table provided with response to Item 4 of document "EUT RTQ IR#8 Items 3-5", please also provide VE estimate and 95% CI.

	Vaccine Group (N=996) Case n (%)	Placebo Group (N=1079) Case n (%)	VE (95% CI)
Number of subjects with severe COVID-19 starting after randomization, n (%)	2 (0.2)	4 (0.4)	Please fill in

Sponsor Response:

Please see below for the requested vaccine efficacy and its 95% confidence interval for the exploratory analysis of Severe COVID-19 in subjects who were in the modified intent-to-treat (mITT) set and only received one dose at IA1 (DS1, 11-Nov-2020).

Please note this is an exploratory adhoc analysis in a non-randomized subset.

	Vaccine Group (N=996) Case n (%)	Placebo Group (N=1079) Case n (%)	VE (95% CI)
Number of subjects with severe COVID-19 starting after randomization, n (%)	2 (0.2)	4 (0.4)	42.6% (-300.8%, 94.8%)*

* VE and the 95% CI is based the exact method conditional upon the total number of cases, adjusting for person-years.

The summary of these 6 subjects were provided in EUA SN009 are copied here for your convenience:

- Subject US3162078 (49 year old white Hispanic male, does not have health risk for developing severe COVID-19) randomized to and received mRNA-1273 on 07-Aug, discontinued study vaccination due to SARS-CoV-2 or positive COVID-19, started to report symptoms on 19-Aug, positive RT-PCR on 19-Aug, had O₂ saturation of 93% on 29-Aug. The AE was considered recovered/resolved on 3 Sept.
- Subject US3532279 (66 years old white not-Hispanic female, does not have health risk for developing severe COVID-19) randomized to and received mRNA-1273 on 10-Sep, started to report symptoms on 04-Aug, had positive RT-PCR on 08-Aug, and O₂ saturation of 80% on 10-Oct. The AE was considered recovered/resolved on 21 Oct.
- Subject US3252638 (41 years old white Hispanic female, with severe obesity) randomized to and received Placebo on 07-Oct, started to report symptoms on 24-Oct, had positive RT-PCR on 28-Oct, O₂ Saturation of 92% on 07-Nov. The AE was considered recovered/resolved on 24 Nov.
- Subject US3322006 (50 years old black not-Hispanic female, with severe obesity) randomized to and received Placebo on 17-Aug, discontinued study vaccination due to SARS-CoV-2 or positive COVID-19, started to report symptoms on 14-Sep, had positive RT-PCR on 14-Sep, had O₂ saturation of 92% on 17-Sep. The AE was considered recovered/resolved on 6 Oct.
- Subject US3942079 (42 years old white not-Hispanic male, with severe obesity, hypertension) randomized to and received Placebo on 08-Sep, discontinued study vaccination due to SARS-CoV-2 or positive COVID-19, started to report symptoms on 24-Sep, positive RT-PCR on 24-Sep, had lowest O₂ saturation of 85% on 29-Sep. The AE was considered recovered/resolved on 16 Oct.
- Subject US3952033 (52 years old white not-Hispanic female, with severe obesity) randomized to and received Placebo on 02-Sep, discontinued study vaccination due to SARS-CoV-2 or positive COVID-19, started to report symptoms on 03-Oct, had positive RT-PCR on 08-Oct, had lowest O₂ saturation of 89% on 09-Oct. Temperature was 103.7F on 10 Oct. The AE was considered recovered/resolved on 25 Oct.