

RESPONSE TO CBER COMMUNICATION REGARDING CLINICAL TOPICS (IR 13) RECEIVED ON DECEMBER 09, 2020

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 1:

From November 11,2020 data-cut, please provide an overview table of participants who reported an immediate adverse event within 30 minutes of vaccination at the study site after each dose (Injection 1, Injection 2) and overall.

Sponsor Response:

As requested, an overview table of participants who reported an immediate adverse event within 30 minutes of vaccination after each dose (Injection 1, Injection 2) and overall is provided, based on 11-NOV-2020 data snapshot.

Frequency of participants with immediate adverse events occurring within 30 minutes following each dose and overall, Safety Set

Adverse events (AE)	Vaccine Group Dose 1 N ¹ =15184 n (%)	Placebo Group Dose 1 N ¹ =15165 n (%)	Vaccine Group Dose 2 N ² =13985 n (%)	Placebo Group Dose 2 N ² =13913 n (%)	Vaccine Group Any Dose N ³ =15184 n (%)	Placebo Group Any Dose N ³ =15165 n (%)
Any	60 (0.4)	62 (0.4)	33 (0.2)	27 (0.2)	88 (0.6)	85 (0.6)
Serious	0	0	0	0	0	0
Death	0	0	0	0	0	0
Leading to vaccine discontinuation	0	1 (<0.1)	0	0	0	1 (<0.1)
Severe	4 (<0.1)	9 (<0.1)	3 (<0.1)	0	7 (<0.1)	9 (<0.1)
Medically-attended	9 (<0.1)	9 (<0.1)	0	3 (<0.1)	9 (<0.1)	12 (<0.1)
Related	15 (<0.1)	17 (0.1)	12 (<0.1)	8 (<0.1)	26 (0.2)	25 (0.2)
Related serious	0	0	0	0	0	0
Related severe	1 (<0.1)	1 (<0.1)	1 (<0.1)	0	2 (<0.1)	1 (<0.1)

Adverse events (AE)	Vaccine Group Dose 1 N¹=15184 n (%)	Placebo Group Dose 1 N¹=15165 n (%)	Vaccine Group Dose 2 N²=13985 n (%)	Placebo Group Dose 2 N²=13913 n (%)	Vaccine Group Any Dose N³=15184 n (%)	Placebo Group Any Dose N³=15165 n (%)
Related medically-attended	3 (<0.1)	5 (<0.1)	0	1 (<0.1)	3 (<0.1)	6 (<0.1)

¹N= Number of participants in Safety Set who received dose 1

²N=: Number of participants in Safety Set who received dose 2

³N= Number of participants in Safety Set who received at least one dose

n= Number of participants who reported AEs in specified category

Source: Ad-hoc Table IR13.1.1, Ad-hoc Table IR13.1.2, Ad-hoc Table IR13.1.3 ([Module 5.3.5.1](#))

ITEM 2:

Please provide a separate table that summarizes the reported AEs (by PT, any/severe) that occurred within the 30 minutes following each vaccination dose and overall (in descending order of frequency).

Sponsor Response:

The requested table is provided based on 11-NOV-2020 data snapshot.

Incidence of participants with adverse events occurring within 30 minutes following each dose and overall (in at least 3 participants), by preferred term, any/severe, Safety Set

Preferred Term (at least one reported)	Vaccine Group Dose 1 N¹=15184 n (%)	Placebo Group Dose 1 N¹=15165 n (%)	Vaccine Group Dose 2 N²=13985 n (%)	Placebo Group Dose 2 N²=13913 n (%)	Vaccine Group Any Dose N³=15184 n (%)	Placebo Group Any Dose N³=15165 n (%)
Any	60 (0.4)	62 (0.4)	33 (0.2)	27 (0.2)	88 (0.6)	85 (0.6)
Severe	4 (<0.1)	9 (<0.1)	3 (<0.1)	0	7 (<0.1)	9 (<0.1)
Hypertension	12 (<0.1)	14 (<0.1)	5 (<0.1)	6 (<0.1)	15 (<0.1)	19 (0.1)
Severe	2 (<0.1)	4 (<0.1)	1 (<0.1)	0	3 (<0.1)	4 (<0.1)
Tachypnoea	13 (<0.1)	16 (0.1)	0	0	13 (<0.1)	16 (0.1)
Severe	0	0	0	0	0	0
Blood pressure increased	3 (<0.1)	3 (<0.1)	4 (<0.1)	0	7 (<0.1)	3 (<0.1)
Severe	1 (<0.1)	1 (<0.1)	1 (<0.1)	0	2 (<0.1)	1 (<0.1)

Preferred Term (at least one reported)	Vaccine Group Dose 1 N ¹ =15184 n (%)	Placebo Group Dose 1 N ¹ =15165 n (%)	Vaccine Group Dose 2 N ² =13985 n (%)	Placebo Group Dose 2 N ² =13913 n (%)	Vaccine Group Any Dose N ³ =15184 n (%)	Placebo Group Any Dose N ³ =15165 n (%)
Dizziness	3 (<0.1)	5 (<0.1)	5 (<0.1)	3 (<0.1)	7 (<0.1)	8 (<0.1)
Severe	0	0	0	0	0	0
Bradycardia	4 (<0.1)	5 (<0.1)	3 (<0.1)	4 (<0.1)	6 (<0.1)	8 (<0.1)
Severe	1 (<0.1)	2 (<0.1)	0	0	1 (<0.1)	2 (<0.1)
Arthralgia	3 (<0.1)	0	1 (<0.1)	0	4 (<0.1)	0
Severe	0	0	0	0	0	0
Fatigue	3 (<0.1)	0	0	1 (<0.1)	3 (<0.1)	1 (<0.1)
Severe	0	0	0	0	0	0
Injection site pain	2 (<0.1)	4 (<0.1)	1 (<0.1)	1 (<0.1)	3 (<0.1)	5 (<0.1)
Severe	0	0	0	0	0	0
Tachycardia	2 (<0.1)	2 (<0.1)	1 (<0.1)	0	3 (<0.1)	2 (<0.1)
Severe	0	0	0	0	0	0
Dysgeusia	0	2 (<0.1)	2 (<0.1)	1 (<0.1)	2 (<0.1)	3 (<0.1)
Severe	0	0	0	0	0	0
Presyncope	2 (<0.1)	3 (<0.1)	0	0	2 (<0.1)	3 (<0.1)
Severe	0	0	0	0	0	0

The preferred terms are presented in descending order for any events in vaccine group any dose column.

¹N: Number of participants in Safety Set who received dose 1

²N: Number of participants in Safety Set who received dose 2

³N: Number of participants in Safety Set who received at least one dose

n: Number of participants who reported AEs in specified category

Source: Ad-hoc Table IR13.2.1, Ad-hoc Table IR13.2.2, Ad-hoc Table IR13.2.3 ([Module 5.3.5.1](#))

ITEM 3:

Please direct us to the TFLs that include unsolicited AEs reported within the 30 minutes post-vaccination time. Please direct us to the flag/variable in the appropriate dataset in which these events can be identified.

Sponsor Response:

The TFLs for unsolicited AEs reported within the 30 minutes post-vaccination time were not included in the submitted package for EUA. [Ad hoc analyses](#) have been performed and the tables are included in Module 5.3.5.1 of this submission. These tables support Items 1 and 2.

The specification of using the ADAE dataset and variables to identify the unsolicited AEs reported within 30 minutes post vaccination is as follows:

From ADaM.ADAE

Select all records where ASTAGE="Vaccination stage"

Use TR01SDTM as Dose Reference Datetime if ADAE.MDOSREF="Vaccination 1"

Use DOS2DTM as Dose Reference Datetime if ADAE.MDOSREF="Vaccination 2"

Select all records where $0 \leq (\text{ASTDTM} - \text{DOSE Reference Date Time})/60 \leq 30$