Synopsis

Title of Study: A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older

Investigator(s): This was a multicenter study.

Study Center(s): This study was conducted at 99 study sites in the United States.

Publication(s) (Reference): Refer to the mRNA-1273-P301 Part A clinical study report (CSR) for relevant publications describing Part A results. No publications reporting Part B data have been submitted.

Study Period (Years): 27 Jul 2020 (First participant first visit-Part A)

Dec 2020 (First participant decision visit)

26 Mar 2021 (data cutoff date)

Drug Development Phase: 3

Background and Rationale: On 18 Dec 2020, the US FDA granted emergency use authorization (EUA) for the mRNA-1273 vaccine for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 18 years of age and older. This was the second EUA for COVID-19 vaccines after the EUA granted for the Pfizer-BioNTech vaccine on 11 Dec 2020. Following EUA approval of COVID-19 vaccines, there was a substantial increase in withdrawals of EUA-eligible participants who opted to be immunized with authorized vaccines, given that all participants in this study had to meet the inclusion criterion for increased risk of COVID-19 disease based on circumstances or geography. To preserve the remaining participants in the study while still enabling them to be vaccinated against SARS-CoV-2, the clinical protocol for this study was subsequently amended to adapt the study design to a 2-part Phase 3 study: Part A and Part B. Part A, the Blinded Phase was a randomized, stratified, observer-blind, placebo-controlled study to evaluate the efficacy, safety, and immunogenicity of mRNA-1273 SARS-CoV-2 vaccine compared to placebo in adults 18 years of age and older who have no known history of SARS-CoV-2 infection but

whose occupation or location and living circumstances put them at increased risk of acquiring COVID-19 and/or SARS-CoV-2 infection.

Given that the primary efficacy endpoint for mRNA-1273 against COVID-19 was met per the protocol-defined interim analysis (IA), Part B, the Open-Label Observational Phase was designed to offer participants who received placebo in Part A of this study and who met EUA eligibility an option to request 2 doses of mRNA-1273 vaccine and remain on study. After the EUA was granted for COVID-19 vaccines, and prior to the mRNA-1273 P301 protocol amendment, which allowed unblinding, there were several hundred participants who unblinded early or discontinued the study to receive vaccine under EUA. Part B was prompted by the EUA and permitted all ongoing study participants to (a) be informed of the availability and eligibility criteria of any COVID-19 vaccine made available under EUA and (b) the option to offer all ongoing study participants who request unblinding an opportunity to schedule a participant decision visit (PDV) to know their original group assignment (placebo vs. mRNA-1273 vaccine). All participants in Part A were to proceed to Part B, starting with a PDV, at which time participants were given the option to be unblinded to their original group assignment.

The results of Part A (database lock was performed on 04 May 2021 and includes data for each individual participant up to early unblinding, study discontinuation, the Part B PDV, or data cutoff date [26 Mar 2021], whichever was earlier) are presented in the Part A CSR.

The purpose of this addendum is to present data (descriptive summaries) from the Open-Label Observational Phase (Part B) of the study based on the database lock on 04 May 2021 and includes safety (unsolicited adverse events [AEs], serious adverse events [SAEs], medically-attended AEs [MAAEs], and AEs leading to discontinuation) and efficacy (case counts) data from early unblinding or the Part B PDV to the data cutoff date (26 Mar 2021). Part A (Blinded Phase, randomization to early unblinding or PDV) of the study provides a median of 148 days of follow-up. Part B (Open-Label Observational Phase, early unblinding or PDV to data cutoff date) of the study provides additional follow-up of a median of 67 days. The total median follow-up period was 7.6 months from randomization or 6.5 months after Dose 2 across Part A and Part B up to database lock for the analysis, aligned with published regulatory guidance regarding the necessary data package for the evaluation of COVID-19 vaccines.

Objectives: The study objectives and endpoints for this study are presented in the final randomized blinded phase (Part A) CSR.

Methodology: Study mRNA-1273-P301 has two parts: Part A, the Blinded Phase and Part B, the Open-Label Observational Phase.

Part A was a randomized, stratified, observer-blind, placebo-controlled evaluation of the efficacy, safety, and immunogenicity of mRNA-1273 SARS CoV-2 vaccine compared to placebo in adults 18 years of age or older. A total of 30,415 participants were randomly assigned to receive doses of either 100 µg of mRNA-1273 vaccine or placebo in a 1:1 randomization ratio. Given that the primary efficacy endpoint for mRNA-1273 against COVID-19 was met per the protocol-defined IA, Part B, the Open-Label Observational Phase of this study, was designed to offer participants who received placebo in Part A of this study and who met EUA eligibility an option to request open-label mRNA-1273. All participants in Part A were to proceed to Part B, starting with a PDV, at which time participants were given the option to be unblinded to their original group assignment. At the initiation of Part B, site personnel who were blinded during Part A were unblinded at the participant level at the PDV.

This CSR addendum provides the safety and efficacy results of Part B from early unblinding or the PDV through data cutoff date (26 Mar 2021).

Participants who requested to not be unblinded, who requested to be unblinded but received mRNA-1273 in Part A, and who requested to be unblinded and received placebo in Part A and chose to remain on placebo were to continue the original study schedule of events (SoE).

Participants who were unblinded, received placebo in Part A, were EUA eligible, and requested to receive mRNA-1273 were planned to have the following additional clinic visits as shown the Supplemental SoE (mRNA-1273-P301 Clinical Study Protocol Table 21 [Appendix 16.1.1]).

- Open-label Dose 1 (OL-D1): occurred at the PDV or at a scheduled subsequent visit.
- Open-label Dose 2 (OL-D29): occurred 28 days after Dose 1 on OL-D1.
- Open-label Clinic Visit (OL-D57): occurred 1 month after Dose 2 on OL-D29.
- Participants were to continue to comply with the original study SoE (mRNA-1273-P301 Clinical Study Protocol Table 16, Table 17, Table 18, and Table 19) as applicable.

Participants who were unblinded, received only 1 dose of mRNA-1273 in Part A, were EUA eligible, and requested to receive mRNA-1273 were planned to have the following additional clinic visits as shown in the Modified Supplemental SoE (mRNA-1273-P301 Clinical Study Protocol Table 22 [Appendix 16.1.1]).

- Their second dose on OL-D1: occurred at the PDV or at a scheduled subsequent visit.
- Open-label Clinic Visit (OL-D29): occurred 1 month after Dose 2 on OL-D1.

Participants receiving only 1 dose of mRNA-1273 in Part A were eligible to receive the second dose of mRNA-1273 under the following circumstances:

- They had a dosing error in Part A of the study that resulted in 1 dose of mRNA-1273 and 1 dose of placebo being administered.
- They did not have an AE that contraindicated the second dose of mRNA-1273 in Part A of the study.
- They did not withdraw consent in Part A of the study.
- They did not complete their second dose in Part A of the study for reasons other than the above.

All participants are expected to complete 24 months of follow-up after the second injection; study participants who entered the Supplemental or Modified Supplemental SoE did so in addition to their original SoE. Accordingly, all study participants are planned to complete the full study follow-up to 24 months after the second injection in Part A (mRNA-1273 or placebo).

Efficacy endpoints included COVID-19 cases, severe COVID-19 cases, COVID-19 cases using the secondary definition of COVID-19, cases of SARS-CoV-2 infection regardless of symptomatology and severity, and cases of asymptomatic SARS-CoV-2 infection.

Safety assessments included unsolicited AEs, MAAEs, SAEs, AEs leading to discontinuation from injection and/or study participation, pregnancy and accompanying outcomes, and concomitant medications and non-study vaccinations.

Number of Subjects (Planned and Analyzed): Approximately 30,000 participants were planned to receive doses of either 100 µg of mRNA-1273 vaccine or placebo in a 1:1 randomization ratio in Part A.

In Part A, a total of 30,415 participants were randomized: 15,206 in the placebo group and 15,209 in the mRNA-1273 group.

A total of 28,964 participants started Part B. Of these, 14,618 participants received mRNA-1273 in Part A (referred as mRNA-1273 group); 1698 participants received placebo in Part A and chose to remain in the placebo group; 12,648 participants received placebo in Part A and chose to receive mRNA-1273 in Part B (referred as placebo–mRNA-1273 group).

Diagnosis and Main Criteria for Inclusion and Exclusion: Refer to the Part A CSR for the inclusion and exclusion criteria for the study.

Test Product, Dose and Mode of Administration, Batch Number(s): In Part B, participants who were unblinded, received placebo in Part A, and requested to receive mRNA-1273, were administered an 0.5 mL intramuscular (IM) injection containing 100 µg of mRNA-1273 (Lot Numbers: 7006121001, 7006320002, 7006320003, 7006320005, 7006320006, 7006320008, 7006320010, 7007421001, 7007421002) into the deltoid muscle on a 2-dose injection schedule on Open Label Day 1 and Day 29.

Participants who were unblinded, received only 1 dose of mRNA-1273 in Part A, and requested to receive mRNA-1273 were administered a single dose of 0.5 mL IM injection containing 100 µg of mRNA-1273 (Lot Numbers: 7006121001, 7006320002, 7006320003, 7006320005, 7006320006, 7006320008, 7006320010, 7007421001, 7007421002) into the deltoid muscle on Open Label Day 1.

Control Product, Dose and Mode of Administration, Batch Number(s): Placebo; participants who requested to be unblinded in Part B and received placebo in Part A and chose to remain on placebo. These participants had received placebo (0.9% sodium chloride) as an 0.5 mL IM injection into the deltoid muscle on an identical schedule as mRNA-1273 during Part A of the study only, and they did not receive any additional placebo injections.

Duration of Treatment: Two doses of mRNA-1273 28 days apart (Day 1 and Day 29) for participants who were unblinded, received placebo in Part A, and requested to receive mRNA-1273 in Part B. A single dose on Day 1 for participants who were unblinded, received only 1 dose of mRNA-1273 in Part A, and requested to receive mRNA-1273 in Part B.

Estimands and Intercurrent Events: Refer to the Part A CSR for estimands and intercurrent events.

Statistical Methods: The following analysis periods and treatment groups were used for efficacy analyses for Part B:

Part B Group	Per-Protocol Set Sample Size	Description	Part B Analysis Period for Efficacy
mRNA-1273	14,287	Participants randomized to mRNA-1273 in Part A	From PDV/early unblinding to the earlier of 2 potential dates: data cutoff date for efficacy (26 Mar 2021) or the last observed in study date, where last observed was defined as the earliest of the following possibilities: study discontinuation, study completion, or death.
Placebo	2104	Participants randomized to placebo in Part A and did not receive mRNA-1273 in Part B	

The following analysis period and treatment groups were used for safety analyses for Part B:

Part B Group	Safety Set Sample Size	Description	Part B Analysis Period for Safety
mRNA-1273	15,184	Participants received at least 1 dose of mRNA-1273 in Part A	From PDV/early unblinding to the earlier of 2 dates: the data cutoff date for safety (26 Mar 2021) or the date last observed in the study. If a participant received mRNA-1273 in Part B, from the first date of study vaccine in Part B to the earlier of 2 dates: data cutoff date for safety (26 Mar 2021) or the date last observed in the study. Last observed was defined as the earliest of the following possibilities: study discontinuation, study completion, or death.
Placebo	2514	Participants only received Placebo in Part A and did not receive mRNA-1273 in Part B	From PDV/early unblinding to the earlier of 2 dates: data cutoff date for safety (26 Mar 2021) or the date last observed in study. Last observed was defined as the earliest of the following possibilities: study discontinuation, study completion, or death.
Placebo-mRNA-1273	12,648	Participants only received Placebo in Part A and received mRNA-1273 in Part B	From first dose of mRNA-1273 in Part B to earlier of 2 dates: data cutoff date for safety (26 Mar 2021) or the date last observed in the study. Last observed was defined as the earliest of the following possibilities: study discontinuation, study completion, or death.

Summary of Results:

Subject Disposition: A total of 28,964 participants started Part B (participants who had PDV or early unblinding). Of these, 14,618 participants received mRNA-1273 in Part A (referred as mRNA-1273 group); 1698 participants received placebo in Part A and chose to remain in the placebo group; 12,648 participants received placebo in Part A and chose to receive mRNA-1273 in Part B (referred as placebo–mRNA-1273 group) and received at least 1 dose of the vaccine.

Of 12,648 participants in the placebo-mRNA-1273 group, 19 participants discontinued the study vaccine.

There were 195 participants who received 1 dose of mRNA-1273 during Part A and received the second dose of mRNA-1273 in Part B in the Safety Set.

A total of 1698/30,346 (5.6%) participants discontinued the study in Part B; 290/15,184 (1.9%) participants in the mRNA-1273 group, 1357/2514 (54.0%) participants in the placebo group, and 51/12,648 (0.4%) participants in the placebo-mRNA-1273 group. The most common reasons for study discontinuations were protocol deviations, withdrawal of consent by participant, and other reasons.

Efficacy

The purpose of this CSR addendum is to provide the efficacy results of Part B based on the median follow-up of 67 days. For the purpose of this CSR addendum, efficacy results are provided for mRNA-1273 and placebo group in text and in summary tables (case counts and incidence rate). For the placebo-mRNA-1273 group, incidence rates are not reported as this group had a relative short duration of follow-up after the second dose of mRNA-1273 in Part B, therefore, efficacy results for the placebo-mRNA-1273 group are not described in this CSR addendum.

For efficacy analyses in Part B, participants at risk were defined as participants who started the open-label phase before or on the efficacy data cutoff date, had no prior SARS-CoV-2 infection (defined by positive postbaseline RT-PCR or Elecsys results) and were not a COVID-19 case up to PDV or early unblinding, whichever was earlier.

Primary endpoint:
In the mRNA-1273 group, of 13,704 participants at risk, 19 (0.1%) adjudicated COVID-19

cases were detected in the per-protocol (PP) Set during the Part B of the study. The corresponding incidence rate for the mRNA-1273 group remained low (7.961 cases per 1000 person-years; 95% confidence interval [CI]: 4.793, 12.432). The results in Part B are consistent with Part A, where the incidence rate in the mRNA-1273 group was 9.599 cases per 1000 person-years (95% CI: 7.231, 12.494) which confirms the persistence of efficacy in the mRNA-1273 group. In the placebo group, of 1,175 participants at risk, 3 (0.3%) adjudicated COVID-19 cases were detected. The incidence rate for the placebo group was 77.378 cases per 1000 person-years; (95% CI: 15.957, 226.131), which was 10-fold higher than in the mRNA-1273 group.

	Part A final analysis (Median follow-up from randomization to early unblinding or PDV: 148 days)		**Part B (Median follow-up from early unblinding or PDV to data cutoff: 67 days)**		
	mRNA-1273 (N=14287)	**Placebo (N=14164)**	**mRNA-1273 (N=14287)**	**Placebo (N=2104)**	**Placebo-mRNA-1273 (N=12060)**
Number of subjects at risk[a]	–	–	13704	1175	11234
Number of subjects with COVID-19* n (%)[b]	55 (0.4)	744 (5.3)	19 (0.1)	3 (0.3)	56 (0.5)
Before first injection of mRNA-1273 in open-label phase	–	–	–	–	17 (0.2)
Between first injection and second injection of mRNA-1273 in open-label phase	–	–	–	–	37 (0.3)
After second injection of mRNA-1273 in open-label phase	–	–	–	–	2 (<0.1)
Number of subjects censored, n (%)[b]	14232 (99.6)	13420 (94.7)	13685 (99.9)	1172 (99.7)	11178 (99.5)
Person-years[c]	5729.9	5445.2	2386.6	38.8	–
Incidence rate per 1,000 person-years (95% CI)[d]	9.599 (7.231, 12.494)	136.633 (126.991, 146.814)	7.961 (4.793, 12.432)	77.378 (15.957, 226.131)	–

Abbreviations: CI = confidence intervals; COVID-19 = coronavirus disease 2019; PDV = participant decision visit; RT-PCR = reverse transcription polymerase chain reaction

* With the censoring rules for efficacy analyses. COVID-19 case is based on eligible symptoms and positive RT-PCR within 14 days. If a subject had positive RT-PCR at scheduled visits without eligible symptoms within 14 days, or positive Elecsys at scheduled visits prior to becoming a COVID-19 case, the subject is censored at the date with positive RT-PCR or Elecsys.

a. Subjects at risk are defined as subjects who started the open-label phase before or on efficacy data cutoff date, had no prior SARS-CoV-2 infection (defined by positive postbaseline RT-PCR or Elecsys results) and were not a disease COVID-19 case up to PDV or early unblinding, whichever is earlier.

b. Percentages in Part B are based on number of subjects at risk.

[c.] Person-years is defined as the total years from randomization date (Part A) or PDV/early unblinding date (Part B) to the date of COVID-19, the date of earliest positive RT-PCR or Elecsys at scheduled visits, last date of study participation, or efficacy data cutoff date, whichever is earlier.

[d.] Incidence rate is defined as the number of subjects with an event divided by the number of subjects at risk and adjusted by person-years (total time at risk) in each treatment group. The 95% CI is calculated using the exact method (Poisson distribution) and adjusted by person-years.

Secondary endpoints:

Severe COVID-19: The number of severe COVID-19 cases in Part B were too low in the PP Set for any meaningful comparison.

Secondary Definition of COVID-19: In the mRNA-1273 group, of 13,704 participants at risk, 39 (0.3%) COVID-19 cases using the secondary definition for COVID-19 in the PP set were detected. The incidence rate in Part B was 16.357 cases per 1000 person-years; (95% CI: 11.631, 22.360). The results are consistent with Part A (10.124 cases per 1000 person-years; 95% CI: 7.688, 13.088) and supported the persistence of efficacy of mRNA-1273. In the placebo group, of 1,175 participants at risk, 4 (0.3%) COVID-19 cases using the secondary definition for COVID-19 in the PP set were detected. The incidence rate in Part B was 103.713 cases per 1000 person-years; (95% CI: 28.258, 265.546), and the incidence rate in Part A was 148.525 cases per 1000 person-years; (95% CI: 138.453, 159.136).

The RT-PCR results and anti-nucleocapsid bAb as measured by Elecsys assay at PDV were included in the analyses of SARS-CoV-2 infection regardless of symptomatology and severity and asymptomatic infection in Part A CSR. No further analyses are provided for the open-label phase.

Safety

The safety assessments included unsolicited AEs MAAEs, SAEs, and AEs leading to withdrawal from study vaccine and/or study from early unblinding or PDV to data cutoff date.

The purpose of this CSR addendum is to provide additional safety follow-up data based on median follow-up of 67 days in Part B for those remaining in the original randomized groups (mRNA-1273 and placebo groups) beyond early unblinding or the PDV up to the data cutoff date (26 Mar 2021), which yielded a total observation period of 7.6 months from randomization or 6.5 months after Dose 2 across Part A and Part B. In addition, data from the placebo group participants who were vaccinated with mRNA-1273 (placebo-mRNA-1273

group) in Part B were collected to further expand the safety evaluation of mRNA-1273 from this newly vaccinated group.

Overall, no new safety concerns were identified in Part B.

Unsolicited treatment-emergent AEs (TEAEs)

In the mRNA-1273 group, 1729/15,184 (11.4%) participants experienced 2557 TEAEs in the Safety Set. Of these, 22/15,184 (0.1%) participants experienced TEAEs related to the study vaccine. No unsolicited TEAE (preferred term [PT]) occurred in ≥1% of participants. No unexpected findings or new trend appeared in unsolicited TEAEs in the mRNA-1273 group.

In the placebo group, 41/2514 (1.6%) participants experienced 66 TEAEs in the Safety Set. No participants had TEAEs considered related to the study vaccine. No unsolicited TEAE (PT) occurred in ≥1% of participants.

In the placebo-mRNA-1273 group, 2446/12,648 (19.3%) participants experienced 4814 TEAEs in the Safety Set. Of these, 758/12,648 (6.0%) participants experienced TEAEs related to study vaccine. The most common unsolicited TEAEs (at least 1% of participants) were injection site pain (451 [3.6%] participants), headache (233 [1.8%] participants), fatigue (211 [1.7%] participants), pain (175 [1.4%] participants), pyrexia (167 [1.3%] participants), chills (136 [1.1%] participants), and hypertension (129 [1.0%] participants). The commonly reported events were generally consistent with reactogenicity and the unsolicited adverse events reported within the 28-day follow-up period after vaccination in the mRNA-1273 group observed in Part A.

Deaths

As of the data cutoff date of this CSR addendum, 12 participants died in Part B.

A total of 8/15,184 (<0.1%) participants in the mRNA-1273 group died (median time from PDV: 46.5 days) during Part B: cardiac TEAEs in 3 participants (cardiac arrest, myocardial infarction, and acute myocardial infarction in 1 participant each); head injury in 1 participant; pulmonary embolism, gastrointestinal hemorrhage, and pulseless electrical activity in 1 participant; cerebrovascular accident in 1 participant; and sudden death (unknown cause) for 1 participant. One participant experienced an SAE of pulmonary mass before PDV (during Part A) and died during Part B.

In the placebo group, 1/2514 (<0.1%) participant (age 84 years) died 9 days after the PDV due to ventricular arrhythmia.

A total of 3/12,648 (<0.1%) participants in the placebo–mRNA-1273 group died (median time from PDV: 54 days) during Part B: congestive cardiac failure, gastrointestinal hemorrhage, and anticoagulation drug level above therapeutic range in 1 participant; accidental drug overdose in 1 participant; and cerebrovascular accident in 1 participant.

None of the participants died due to COVID-19. None of the deaths was considered related to the study vaccine.

SAEs

In the mRNA-1273 group, 141/15,184 (0.9%) participants reported 181 SAEs. All individual SAEs (PT) were reported in <0.1% of participants. No SAEs were considered related to the study vaccine. Overall, no new safety concern was identified.

In the placebo group, 7/2514 (0.3%) participants reported 8 SAEs. No SAEs were considered related to the study vaccine.

In the placebo-mRNA-1273 group, 148/12,648 (1.2%) participants reported 190 SAEs. All individual SAEs (PT) were reported in <0.1% of participants. Serious AEs considered by the investigator to be related to the study vaccine were reported in 4 participants: paraesthesia, muscular weakness, spontaneous abortion, and autoimmune thyroiditis. All events resolved within 2 days except autoimmune thyroiditis which was ongoing at the time of data cutoff. In addition, 1 participant experienced an SAE (considered as related to the study vaccine by the investigator) of pericardial effusion in Part B before data cutoff but was reported by site after the database lock.

Unsolicited TEAEs leading to discontinuation from the study vaccine and the study

The participant incidence of TEAEs leading to study discontinuation was low (7/15,184 participants in the mRNA-1273 group, 1/2514 participant in the placebo group, and 4/12,648 participants in the placebo–mRNA-1273 group); none of the events was considered related to study vaccine by the investigator.

In the placebo–mRNA-1273 group, 12/12,648 (<0.1%) participants discontinued the study vaccine due to TEAEs. Of these 12 participants, 4 participants discontinued the vaccine because of nonserious TEAEs that were considered by the investigator to be vaccine-related.

One participant discontinued the vaccine because of Grade 1 chills. The participant experienced the event 34 days after receiving the first dose. The event resolved after 2 days.

One participant discontinued the vaccine because of Grade 2 urticaria. The participant experienced the event 1 day after receiving the first dose. The event resolved after 3 days.

One participant discontinued the vaccine because of Grade 3 parotitis. The participant experienced the event 11 days after receiving the first dose. The event was ongoing at the time of data cutoff.

One participant (64-year-old) discontinued the vaccine because of Grade 2 unilateral deafness. The participant experienced the event 5 days after receiving the first dose of mRNA-1273 in Part B. The event was resolving at the time of data cutoff.

MAAEs

In the mRNA-1273 group, 1457/15,184 (9.6%) participants experienced 2067 MAAEs. Of these, 9 (<0.1%) participants experienced MAAEs related to the study vaccine. All MAAEs (PT) were reported in <1% of participants. The most common MAAEs (≥ 0.4% of participants) were hypertension (69/15,184 [0.5%] participants), urinary tract infection (65/15,184 [0.4%] participants), and COVID-19 (32/15,184 [0.2%] participants). Overall, no new safety concern was identified related to MAAEs.

In the placebo group, 37/2514 (1.5%) participants experienced 51 MAAEs. All MAAEs (PT) were reported in ≤0.1% of participants.

In the placebo–mRNA-1273 group, 1509/12,648 (11.9%) participants experienced 2202 MAAEs. Of these, 74 (0.6%) participants experienced MAAEs related to the study vaccine. All MAAEs (PT) were reported in <1% of participants. The most common MAAEs (≥ 0.4% of participants) were hypertension (98/12,648 [0.8%] participants) and urinary tract infection (59/12,648 [0.5%] participants), and COVID-19 (51/12,648 [0.4%] participants).

Pregnancies

According to the safety database, a total of 37 pregnancies were reported (19 in the placebo-mRNA-1273 group and 18 in the mRNA-1273 group) during Part B of the study. Of the outcomes known as of 04 May 2021, 4 participants (3 in the placebo-mRNA-1273 group and 1 in the mRNA-1273 group) experienced spontaneous abortion; of these, the event in 1 participant in the placebo–mRNA-1273 group was considered related to the study vaccine by the investigator.

One participant in the placebo-mRNA-1273 group underwent elective termination of pregnancy; there were no reported pregnancy complications for this participant.

Conclusions: In conclusion, efficacy of mRNA-1273 to prevent COVID-19 persisted in Part B. The safety profile of mRNA-1273 remained acceptable, similar to that observed in Part A, and no new safety concerns were noted. The benefit/risk profile of mRNA-1273 remains strongly favorable through 6.5 months median follow-up after Dose 2.

Original Report Date (Part A CSR): 05 Aug 2021

Report Addendum Date: 05 Aug 2021