



Clinical trial results:

A Phase 2/3, Randomized, Observer-Blind, Placebo-Controlled Study to Evaluate the Safety, Reactogenicity, and Effectiveness of mRNA-1273 SARS-CoV-2 Vaccine in Healthy Adolescents 12 to <18 Years of Age Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2023-000382-14 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 12 July 2024 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 26 January 2025 |
| First version publication date | 26 January 2025 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | mRNA-1273-P203 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04649151 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | ModernaTX, Inc. |
| Sponsor organisation address | 325 Binney Street, Cambridge, MA, United States, 02142 |
| Public contact | Moderna Clinical Trials Support Center, ModernaTX, Inc., +1 877-777-7187, clinicaltrials@modernatx.com |
| Scientific contact | Moderna Clinical Trials Support Center, ModernaTX, Inc., +1 877-777-7187, clinicaltrials@modernatx.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-002893-PIP01-20 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 23 July 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 June 2024 |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 July 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The study was designed to primarily evaluate the safety, reactogenicity, and effectiveness of mRNA-1273 vaccine administered as primary series and a booster dose (BD) to an adolescent population. The study also evaluated the safety and immunogenicity of an mRNA-1273.222 vaccine against the SARS-CoV- 2 omicron variant.

Protection of trial subjects:

This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki, and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines, applicable International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, and other applicable laws and regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 09 December 2020 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 12 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | United States: 3994 |
| Country: Number of subjects enrolled | Dominican Republic: 334 |
| Worldwide total number of subjects | 4328 |
| EEA total number of subjects | 0 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |

| | |
|---------------------------|------|
| Adolescents (12-17 years) | 4328 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study included Part 1A as the Blinded Phase with participants remaining blinded until the initiation of Part 1B (open-label cross-over phase), and Parts 1C-1, 1C-2, 2, and 3 as open-label. A comparison to the mRNA-1273-P301 (P301) (NCT04470427) study's efficacy data was performed on a subgroup of P301 study participants aged 18-25 (N=296).

Period 1

| | |
|------------------------------|---------------------------------------|
| Period 1 title | Parts 1, 2, and 3 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Monitor |

Blinding implementation details:

Part 1A was observer-blind. Participants remained blinded until the initiation of Part 1B (open-label cross-over phase). Parts 1C-1, 1C-2, 2, and 3 were open-label.

Arms

| | |
|------------------------------|---------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Part 1A: mRNA-1273 100 µg |

Arm description:

Participants received 2 doses of 100 micrograms (µg) mRNA-1273 by intramuscular (IM) injection (Day 1 and Day 29).

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | mRNA-1273 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Sterile concentrate |
| Routes of administration | Intramuscular use |

Dosage and administration details:

mRNA-1273 was administered per dose and schedule specified in the arm description.

| | |
|------------------|------------------|
| Arm title | Part 1A: Placebo |
|------------------|------------------|

Arm description:

Participants received 2 doses of placebo matched to mRNA-1273 100 µg by IM injection (Day 1 and Day 29).

| | |
|--|---------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Sterile concentrate |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Placebo matched to mRNA-1273 was administered per schedule specified in the arm description.

| | |
|------------------|-------------------------------|
| Arm title | Part 1C-2: mRNA-1273 50 µg BD |
|------------------|-------------------------------|

Arm description:

Participants who completed primary COVID-19 vaccination series with a non-Moderna vaccine under emergency use authorization (EUA), received a single BD of 50 µg mRNA-1273 IM injection on BD Day 1.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|---|-----------------------------|
| Investigational medicinal product name | mRNA-1273 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Sterile concentrate |
| Routes of administration | Intramuscular use |
| Dosage and administration details: mRNA-1273 was administered per dose and schedule specified in the arm description. | |
| Arm title | Part 2: mRNA-1273 50 µg |
| Arm description: Participants received 2 doses of 50 µg mRNA-1273 by IM injection (Day 1 and Day 29). | |
| Arm type | Experimental |
| Investigational medicinal product name | mRNA-1273 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Sterile concentrate |
| Routes of administration | Intramuscular use |
| Dosage and administration details: mRNA-1273 was administered per dose and schedule specified in the arm description. | |
| Arm title | Part 3: mRNA-1273.222 50 µg |
| Arm description: Participants received 1 dose of mRNA-1273.222 50 µg by IM injection (Day 1). Some participants may have received a second dose of mRNA-1273.222 50 µg at approximately 6 months after the first dose (Day 181). | |
| Arm type | Experimental |
| Investigational medicinal product name | mRNA-1273.222 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Sterile concentrate |
| Routes of administration | Intramuscular use |
| Dosage and administration details: mRNA-1273.222 was administered per dose and schedule specified in the arm description. | |

| Number of subjects in period 1 | Part 1A: mRNA-1273 100 µg | Part 1A: Placebo | Part 1C-2: mRNA-1273 50 µg BD |
|---|---------------------------|-------------------|-------------------------------|
| Started | 2490 | 1243 | 155 |
| Part 1: 1st Injection | 2486 | 1240 | 0 ^[1] |
| Part 2: 1st Injection | 0 ^[2] | 0 ^[3] | 0 ^[4] |
| Part 1: 2nd Injection | 2480 | 1222 | 0 ^[5] |
| Part 2: 2nd Injection | 0 ^[6] | 0 ^[7] | 0 ^[8] |
| Part 1C-2: BD | 0 ^[9] | 0 ^[10] | 155 |
| Part 3: 1 Dose | 0 ^[11] | 0 ^[12] | 0 ^[13] |
| Part 3: 2 Doses | 0 ^[14] | 0 ^[15] | 0 ^[16] |
| Safety Analysis Set | 2486 | 1240 | 155 |
| Solicited Safety Set | 2485 | 1240 | 125 ^[17] |
| Per-Protocol (PP) Immunogenicity Subset | 340 ^[18] | 0 ^[19] | 136 ^[20] |

| | | | |
|---|----------------------|-------------------|-------------------|
| PP Set for Efficacy | 2142 ^[21] | 1044 | 0 ^[22] |
| Part 2 BD | 0 ^[23] | 0 ^[24] | 0 ^[25] |
| PP Immunogenicity SARS-CoV-2 Positive | 0 ^[26] | 0 ^[27] | 0 ^[28] |
| Completed | 2246 | 279 | 143 |
| Not completed | 244 | 964 | 12 |
| Physician decision | 2 | - | - |
| Consent withdrawn by subject | 112 | 88 | 2 |
| Protocol Deviation | 2 | 2 | - |
| Adverse event, non-fatal | 1 | - | - |
| Death | - | - | - |
| Pregnancy | - | - | - |
| Other than specified | 21 | 229 | - |
| Received another COVID-19 vaccine under EUA | 39 | 630 | - |
| Lost to follow-up | 67 | 15 | 10 |

| Number of subjects in period 1 | Part 2: mRNA-1273 50 µg | Part 3: mRNA- 1273.222 50 µg |
|---|----------------------------|---------------------------------|
| Started | 52 | 388 |
| Part 1: 1st Injection | 0 ^[29] | 0 ^[30] |
| Part 2: 1st Injection | 52 | 0 ^[31] |
| Part 1: 2nd Injection | 0 ^[32] | 0 ^[33] |
| Part 2: 2nd Injection | 50 | 0 ^[34] |
| Part 1C-2: BD | 0 ^[35] | 0 ^[36] |
| Part 3: 1 Dose | 0 ^[37] | 388 |
| Part 3: 2 Doses | 0 ^[38] | 335 ^[39] |
| Safety Analysis Set | 52 | 388 |
| Solicited Safety Set | 52 | 387 |
| Per-Protocol (PP) Immunogenicity Subset | 46 | 373 |
| PP Set for Efficacy | 0 ^[40] | 0 ^[41] |
| Part 2 BD | 19 ^[42] | 0 ^[43] |
| PP Immunogenicity SARS-CoV-2 Positive | 44 | 372 |
| Completed | 41 | 358 |
| Not completed | 11 | 30 |
| Physician decision | 1 | 1 |
| Consent withdrawn by subject | 7 | 15 |
| Protocol Deviation | - | - |
| Adverse event, non-fatal | - | - |
| Death | - | 1 |
| Pregnancy | - | 3 |
| Other than specified | - | 4 |

| | | |
|---|---|---|
| Received another COVID-19 vaccine under EUA | - | - |
| Lost to follow-up | 3 | 6 |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

[11] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

[12] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

[13] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

Period 2

| | |
|------------------------------|----------------|
| Period 2 title | Part 1C-1 BD |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|-------------------------------|
| Arm title | Part 1C-1: mRNA-1273 50 µg BD |
|------------------|-------------------------------|

Arm description:

Participants received mRNA-1273 100 µg in blinded or cross-over phase (Parts 1A or 1B) and then a single BD of 50 µg mRNA-1273 IM injection on BD Day 1 in Part 1 C-1.

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | mRNA-1273 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Sterile concentrate |
| Routes of administration | Intramuscular use |

Dosage and administration details:

mRNA-1273 was administered per dose and schedule specified in the arm description.

| Number of subjects in period 2^[44] | Part 1C-1: mRNA-1273 50 µg BD |
|--|-------------------------------|
| Started | 1408 |
| Safety Set | 1408 |
| Solicited Safety Set | 1351 |
| PPIS | 331 ^[45] |
| PP Immunogenicity SARS-CoV-2 Negative | 267 ^[46] |
| Completed | 1136 |
| Not completed | 272 |
| Physician decision | 3 |
| Consent withdrawn by subject | 123 |
| Protocol Deviation | 2 |
| Other than specified | 4 |
| Received another COVID-19 vaccine under EUA | 17 |
| Lost to follow-up | 123 |

Notes:

[44] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who started in Part 1 received BD in Part 1C-1.

[45] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

[46] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Value indicates the number of applicable participants for the milestone and dose group.

Period 3

| | |
|------------------------------|-------------------------|
| Period 3 title | Part 1B Crossover Phase |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|----------------------------|
| Arm title | Part 1 B: mRNA-1273 100 µg |
|-----------|----------------------------|

Arm description:

Participants previously received 2 doses of placebo in the blinded phase and then received crossover vaccination with 100 µg of mRNA-1273.

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | mRNA-1273 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Sterile concentrate |
| Routes of administration | Intramuscular use |

Dosage and administration details:

mRNA-1273 was administered per dose and schedule specified in the arm description.

| Number of subjects in period 3 ^[47] | Part 1 B: mRNA-1273 100 µg |
|--|----------------------------|
| Started | 96 |
| Received First Injection on Day 1 | 96 |
| Received Second Injection on Day 29 | 93 |
| Safety Set | 96 |
| Completed | 93 |
| Not completed | 3 |
| Adverse event, non-fatal | 1 |
| Other than specified | 1 |
| Lost to follow-up | 1 |

Notes:

[47] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who received placebo in Part 1 crossed over to Part 1B

Baseline characteristics

Reporting groups

| | |
|---|-------------------------------|
| Reporting group title | Part 1A: mRNA-1273 100 µg |
| Reporting group description: | |
| Participants received 2 doses of 100 micrograms (µg) mRNA-1273 by intramuscular (IM) injection (Day 1 and Day 29). | |
| Reporting group title | Part 1A: Placebo |
| Reporting group description: | |
| Participants received 2 doses of placebo matched to mRNA-1273 100 µg by IM injection (Day 1 and Day 29). | |
| Reporting group title | Part 1C-2: mRNA-1273 50 µg BD |
| Reporting group description: | |
| Participants who completed primary COVID-19 vaccination series with a non-Moderna vaccine under emergency use authorization (EUA), received a single BD of 50 µg mRNA-1273 IM injection on BD Day 1. | |
| Reporting group title | Part 2: mRNA-1273 50 µg |
| Reporting group description: | |
| Participants received 2 doses of 50 µg mRNA-1273 by IM injection (Day 1 and Day 29). | |
| Reporting group title | Part 3: mRNA-1273.222 50 µg |
| Reporting group description: | |
| Participants received 1 dose of mRNA-1273.222 50 µg by IM injection (Day 1). Some participants may have received a second dose of mRNA-1273.222 50 µg at approximately 6 months after the first dose (Day 181). | |

| Reporting group values | Part 1A: mRNA-1273 100 µg | Part 1A: Placebo | Part 1C-2: mRNA-1273 50 µg BD |
|--|---------------------------|------------------|-------------------------------|
| Number of subjects | 2490 | 1243 | 155 |
| Age Categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 2490 | 1243 | 155 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 1206 | 607 | 78 |
| Male | 1284 | 636 | 77 |

| Reporting group values | Part 2: mRNA-1273 50 µg | Part 3: mRNA-1273.222 50 µg | Total |
|------------------------|-------------------------|-----------------------------|-------|
| Number of subjects | 52 | 388 | 4328 |
| Age Categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |

| | | | |
|--|----|-----|------|
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 52 | 388 | 4328 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 26 | 185 | 2102 |
| Male | 26 | 203 | 2226 |

Subject analysis sets

| | |
|---|---|
| Subject analysis set title | Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 µg |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Participants (young adults; 18-25 years of age) received 100 µg mRNA-1273 on a 2 injection schedule in Study mRNA-1273-P301 (P301). | |
| Subject analysis set title | Part 2: mRNA-1273 50 µg First Injection |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received 1 dose of 50 µg mRNA-1273 by IM injection (Day 1). | |
| Subject analysis set title | Part 2: mRNA-1273 50 µg Second Injection |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received 2nd dose of 50 µg mRNA-1273 by IM injection (Day 29). | |
| Subject analysis set title | Part 2: mRNA-1273 50 µg BD |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received open-label mRNA-1273 50 µg in Part 2 and then a single BD of 50 µg mRNA-1273 IM injection on BD Day 1 in Part 2. | |
| Subject analysis set title | Part 3: mRNA-1273.222 50 µg 1 Dose |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received 1 dose of mRNA-1273.222 50 µg by IM injection (Day 1). | |
| Subject analysis set title | Part 1A: mRNA-1273 100 µg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received at least 1 dose of the 2-dose series of 100 µg mRNA-1273 by IM injection (Day 1 and Day 29). | |
| Subject analysis set title | Part 1A: Placebo |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received at least 1 dose of the 2-dose series of placebo matched to mRNA-1273 100 µg by IM injection (Day 1 and Day 29). | |
| Subject analysis set title | Part 1B: mRNA-1273 100 µg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants previously received 2 doses of placebo in the blinded phase and then received crossover vaccination with 100 µg of mRNA-1273. | |

| | |
|---|-------------------------------|
| Subject analysis set title | Part 1C-1: mRNA-1273 50 µg BD |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received mRNA-1273 100 µg in blinded or cross-over phase (Parts 1A or 1B) and then a single BD of 50 µg mRNA-1273 IM injection on BD Day 1 in Part 1 C-1. | |
| Subject analysis set title | Part 1C-2: mRNA-1273 50 µg BD |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants who completed primary COVID-19 vaccination series with a non-Moderna vaccine under EUA, received a single BD of 50 µg mRNA-1273 IM injection on BD Day 1 | |
| Subject analysis set title | Part 2: mRNA-1273 50 µg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received at least 1 dose of the 2-dose series of 50 µg mRNA-1273 by IM injection (Day 1 and Day 29). | |

| Reporting group values | Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 µg | Part 2: mRNA-1273 50 µg First Injection | Part 2: mRNA-1273 50 µg Second Injection |
|--|---|---|--|
| Number of subjects | 296 | 52 | 50 |
| Age Categorical Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 296 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Gender Categorical Units: Subjects | | | |
| Female | 153 | | |
| Male | 143 | | |

| Reporting group values | Part 2: mRNA-1273 50 µg BD | Part 3: mRNA-1273.222 50 µg 1 Dose | Part 1A: mRNA-1273 100 µg |
|--|----------------------------|------------------------------------|---------------------------|
| Number of subjects | 19 | 388 | 2486 |
| Age Categorical Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |

| | | | |
|--------------------|--|--|--|
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |

| Reporting group values | Part 1A: Placebo | Part 1B: mRNA-1273 100 µg | Part 1C-1: mRNA- 1273 50 µg BD |
|---|------------------|------------------------------|-----------------------------------|
| Number of subjects | 1240 | 96 | 1408 |
| Age Categorical | | | |
| Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |

| Reporting group values | Part 1C-2: mRNA- 1273 50 µg BD | Part 2: mRNA-1273 50 µg | |
|---|-----------------------------------|----------------------------|--|
| Number of subjects | 155 | 52 | |
| Age Categorical | | | |
| Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Part 1A: mRNA-1273 100 µg |
| Reporting group description: Participants received 2 doses of 100 micrograms (µg) mRNA-1273 by intramuscular (IM) injection (Day 1 and Day 29). | |
| Reporting group title | Part 1A: Placebo |
| Reporting group description: Participants received 2 doses of placebo matched to mRNA-1273 100 µg by IM injection (Day 1 and Day 29). | |
| Reporting group title | Part 1C-2: mRNA-1273 50 µg BD |
| Reporting group description: Participants who completed primary COVID-19 vaccination series with a non-Moderna vaccine under emergency use authorization (EUA), received a single BD of 50 µg mRNA-1273 IM injection on BD Day 1. | |
| Reporting group title | Part 2: mRNA-1273 50 µg |
| Reporting group description: Participants received 2 doses of 50 µg mRNA-1273 by IM injection (Day 1 and Day 29). | |
| Reporting group title | Part 3: mRNA-1273.222 50 µg |
| Reporting group description: Participants received 1 dose of mRNA-1273.222 50 µg by IM injection (Day 1). Some participants may have received a second dose of mRNA-1273.222 50 µg at approximately 6 months after the first dose (Day 181). | |
| Reporting group title | Part 1C-1: mRNA-1273 50 µg BD |
| Reporting group description: Participants received mRNA-1273 100 µg in blinded or cross-over phase (Parts 1A or 1B) and then a single BD of 50 µg mRNA-1273 IM injection on BD Day 1 in Part 1 C-1. | |
| Reporting group title | Part 1 B: mRNA-1273 100 µg |
| Reporting group description: Participants previously received 2 doses of placebo in the blinded phase and then received crossover vaccination with 100 µg of mRNA-1273. | |
| Subject analysis set title | Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 µg |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Participants (young adults; 18-25 years of age) received 100 µg mRNA-1273 on a 2 injection schedule in Study mRNA-1273-P301 (P301). | |
| Subject analysis set title | Part 2: mRNA-1273 50 µg First Injection |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received 1 dose of 50 µg mRNA-1273 by IM injection (Day 1). | |
| Subject analysis set title | Part 2: mRNA-1273 50 µg Second Injection |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received 2nd dose of 50 µg mRNA-1273 by IM injection (Day 29). | |
| Subject analysis set title | Part 2: mRNA-1273 50 µg BD |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received open-label mRNA-1273 50 µg in Part 2 and then a single BD of 50 µg mRNA-1273 IM injection on BD Day 1 in Part 2. | |
| Subject analysis set title | Part 3: mRNA-1273.222 50 µg 1 Dose |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received 1 dose of mRNA-1273.222 50 µg by IM injection (Day 1). | |

| | |
|---|-------------------------------|
| Subject analysis set title | Part 1A: mRNA-1273 100 µg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received at least 1 dose of the 2-dose series of 100 µg mRNA-1273 by IM injection (Day 1 and Day 29). | |
| Subject analysis set title | Part 1A: Placebo |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received at least 1 dose of the 2-dose series of placebo matched to mRNA-1273 100 µg by IM injection (Day 1 and Day 29). | |
| Subject analysis set title | Part 1B: mRNA-1273 100 µg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants previously received 2 doses of placebo in the blinded phase and then received crossover vaccination with 100 µg of mRNA-1273. | |
| Subject analysis set title | Part 1C-1: mRNA-1273 50 µg BD |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received mRNA-1273 100 µg in blinded or cross-over phase (Parts 1A or 1B) and then a single BD of 50 µg mRNA-1273 IM injection on BD Day 1 in Part 1 C-1. | |
| Subject analysis set title | Part 1C-2: mRNA-1273 50 µg BD |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants who completed primary COVID-19 vaccination series with a non-Moderna vaccine under EUA, received a single BD of 50 µg mRNA-1273 IM injection on BD Day 1 | |
| Subject analysis set title | Part 2: mRNA-1273 50 µg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received at least 1 dose of the 2-dose series of 50 µg mRNA-1273 by IM injection (Day 1 and Day 29). | |

Primary: Number of Participants With Solicited Local and Systemic Adverse Reactions (ARs)

| | |
|---|--|
| End point title | Number of Participants With Solicited Local and Systemic Adverse Reactions (ARs) ^{[1][2]} |
| End point description: Solicited ARs (local and systemic) were collected in an electronic diary (eDiary). Local ARs included injection site pain, injection site erythema (redness), injection site swelling/induration (hardness), and axillary (underarm) swelling or tenderness ipsilateral to the side of injection. Systemic ARs included fever, headache, fatigue, myalgia, arthralgia, nausea/vomiting, and chills. Solicited ARs considered causally related to injection were graded 1-4 (per Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials); lower score indicated lower severity, and higher score indicated greater severity. Solicited Safety Set included participants who received at least 1 dose of study drug and contributed any solicited AR data. Investigator reviewed if the solicited AR was recorded as an adverse event (AE). A Summary of serious AEs (SAEs) and nonserious AEs ("Other"), regardless of causality, is located in the AE section. | |
| End point type | Primary |
| End point timeframe: 7 days post-vaccination | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| End point values | Part 1A: mRNA-1273 100 µg | Part 1C-1: mRNA-1273 50 µg BD | Part 1A: Placebo | Part 1C-2: mRNA-1273 50 µg BD |
|-----------------------------|---------------------------------|-------------------------------------|---------------------|-------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2485 | 1351 | 1240 | 125 |
| Units: participants | | | | |
| Grade 1 | 586 | 627 | 585 | 42 |
| Grade 2 | 1250 | 501 | 293 | 48 |
| Grade 3 | 627 | 150 | 59 | 9 |
| Grade 4 | 3 | 0 | 1 | 0 |
| Any Solicited AR | 2466 | 1278 | 938 | 99 |

| End point values | Part 2: mRNA- 1273 50 µg First Injection | Part 2: mRNA- 1273 50 µg Second Injection | Part 2: mRNA- 1273 50 µg BD | Part 3: mRNA- 1273.222 50 µg 1 Dose |
|-----------------------------|--|--|--------------------------------|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 52 | 46 | 19 | 387 |
| Units: participants | | | | |
| Grade 1 | 25 | 18 | 7 | 145 |
| Grade 2 | 16 | 9 | 0 | 62 |
| Grade 3 | 1 | 3 | 1 | 25 |
| Grade 4 | 0 | 0 | 0 | 1 |
| Any Solicited AR | 42 | 30 | 8 | 233 |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Unsolicited AEs

| | |
|-----------------|---|
| End point title | Number of Participants With Unsolicited AEs ^[3] ^[4] |
|-----------------|---|

End point description:

An AE was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. Any abnormal laboratory test result or other safety assessment, including one that worsened from baseline and was considered clinically significant by the Investigator was recorded as an AE.

Non-serious SARs persisting beyond 7 days, leading to discontinuation, or medically attended were defined as AEs in Part 1/2 but not in Part 3. COVID-19/SARS-CoV-2 infections were AEs in Part1/2 but were considered clinical events for efficacy in Part 3 and not AEs.

A Summary of SAEs and nonserious AEs ("Other"), regardless of causality, is located in the AE section.

Safety Set: participants who received at least 1 dose of study drug.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to 28 days post-vaccination

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| End point values | Part 1A: mRNA-1273 100 µg | Part 1C-1: mRNA-1273 50 µg BD | Part 1A: Placebo | Part 1C-2: mRNA-1273 50 µg BD |
|-----------------------------|---------------------------------|-------------------------------------|---------------------|-------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2486 | 1405 | 1240 | 155 |
| Units: participants | 582 | 209 | 237 | 19 |

| End point values | Part 2: mRNA- 1273 50 µg | Part 2: mRNA- 1273 50 µg BD | Part 3: mRNA- 1273.222 50 µg 1 Dose | |
|-----------------------------|-----------------------------|--------------------------------|---|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 52 | 19 | 388 | |
| Units: participants | 10 | 2 | 52 | |

Statistical analyses

No statistical analyses for this end point

Primary: Part 1A Seroresponse Rate (SRR) for Serum Pseudovirus nAb ID50 in Study P203 Vaccine Recipients at Day 57 Compared With Those From Young Adult (18 to 25 Years of Age) Vaccine Recipients (Day 57) in Study P301

| | |
|-----------------|---|
| End point title | Part 1A Seroresponse Rate (SRR) for Serum Pseudovirus nAb ID50 in Study P203 Vaccine Recipients at Day 57 Compared With Those From Young Adult (18 to 25 Years of Age) Vaccine Recipients (Day 57) in Study P301 ^[5] |
|-----------------|---|

End point description:

Percentage of participants with seroresponse for pseudovirus nAb ID50 measured using PsVNA assay are reported. Seroresponse was defined as a change from below the LLOQ to equal above 4*LLOQ, or at least a 4-fold rise if baseline is equal to or above the LLOQ. P301 mRNA-1273 group included young adults (≥18 and ≤25 years) who received 2 doses of mRNA-1273 in P301 Part A and who were baseline SARS-CoV-2 negative in P301 Part A.

PPIS: all randomized participants who received planned doses of study drug per schedule, complied with immunogenicity testing schedule, and had no major protocol deviations that impacted key or critical data.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 57 Study P203/Day 57 Study P301

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| End point values | Part 1A: mRNA-1273 100 µg | Study mRNA- 1273-P301 (NCT04470427) mRNA-1273 100 µg | | |
|-----------------------------------|---------------------------------|---|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 340 | 295 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 98.8 (97.0 to 99.7) | 99.0 (97.1 to 99.8) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: SRR difference of P203 vs P301 | |
| Comparison groups | Part 1A: mRNA-1273 100 µg v Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 µg |
| Number of subjects included in analysis | 635 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | percentage difference |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.1 |
| upper limit | 1.9 |

Primary: Part 1A Geometric Mean Value of Serum Pseudovirus Neutralizing Antibody (nAb) ID50 Titers From Study P203 Vaccine Recipients at Day 57 Compared With Those From Young Adult (18 to 25 Years of Age) Vaccine Recipients (Day 57) in Study P301

| | |
|-----------------|--|
| End point title | Part 1A Geometric Mean Value of Serum Pseudovirus Neutralizing Antibody (nAb) ID50 Titers From Study P203 Vaccine Recipients at Day 57 Compared With Those From Young Adult (18 to 25 Years of Age) Vaccine Recipients (Day 57) in Study P301 ^[6] |
|-----------------|--|

End point description:

Pseudovirus nAb ID50 titers were measured using pseudovirus neutralization assay (PsVNA) assay. Antibody values reported as below the lower limit of quantification (LLOQ) were replaced by 0.5*LLOQ. Values greater than the upper limit of quantification (ULOQ) were replaced by the ULOQ if actual values were not available (LLOQ: 18.5, ULOQ: 45118). Antibody levels were analyzed using an analysis of covariance (ANCOVA) model with the group variable (adolescents in P203 and young adults in P301) as fixed effect. The geometric least squares means are presented. PP Immunogenicity Set (PPIS): all randomized participants who received planned doses of study drug per schedule, complied with immunogenicity testing schedule, and had no major protocol deviations that impacted key or critical data.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 57 Study P203/Day 57 Study P301

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| | | | | |
|--|---------------------------------------|--|--|--|
| End point values | Part 1A: mRNA-1273 100 µg | Study mRNA- 1273-P301 (NCT04470427) mRNA-1273 100 µg | | |
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 340 | 295 | | |
| Units: titer | | | | |
| geometric mean (confidence interval 95%) | 1401.670 (1276.218 to 1539.453) | 1299.855 (1175.380 to 1437.511) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: Geometric mean ratio (GMR) of P203 vs P301 | |
| Comparison groups | Part 1A: mRNA-1273 100 µg v Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 µg |
| Number of subjects included in analysis | 635 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | GMR |
| Point estimate | 1.078 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.94 |
| upper limit | 1.237 |

Primary: Part 1C-1 Geometric Mean Concentration (GMC) of Serum Pseudovirus nAb Against the Original Strain After the BD in Study P203 at BD Day 29 Compared With Those From Young Adult (18 to 25 Years of Age) Vaccine Recipients (Day 57) in Study P301

| | |
|-----------------|--|
| End point title | Part 1C-1 Geometric Mean Concentration (GMC) of Serum Pseudovirus nAb Against the Original Strain After the BD in Study P203 at BD Day 29 Compared With Those From Young Adult (18 to 25 Years of Age) Vaccine Recipients (Day 57) in Study P301 |
|-----------------|--|

End point description:

Pseudovirus nAb were measured using PsVNA assay. Antibody values reported as below the LLOQ were replaced by 0.5*LLOQ. Values greater than the ULOQ were replaced by the ULOQ if actual values were not available (LLOQ: 10, ULOQ: 281600). PPIS-Neg: All participants who received mRNA-1273 in the Blinded Phase per schedule, received BD, had a negative SARS-CoV-2 status at baseline (pre-Dose 1 of the Blinded Phase), had BD-Day 1 and BD-Day 29 Ab assessment for the analysis endpoint, had no major protocol deviations that impacted key or critical data, and were pre-booster SARS-CoV-2 negative, defined as no virologic or serologic evidence of SARSCoV-2 infection on or before BD-Day 1 (pre-booster). P301 mRNA-1273 group included young adults (≥ 18 and ≤ 25 years) who received 2 doses of mRNA-1273 in P301 Part A and who were baseline SARS-CoV-2 negative in P301 Part A. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

| | |
|--|---------|
| End point type | Primary |
| End point timeframe: | |
| BD Day 29 Study P203/Day 57 Study P301 | |

| | | | | |
|--|-------------------------------------|--|--|--|
| End point values | Part 1C-1: mRNA-1273 50 µg BD | Study mRNA- 1273-P301 (NCT04470427) mRNA-1273 100 µg | | |
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 264 | 294 | | |
| Units: arbitrary units (AU)/mL | | | | |
| geometric mean (confidence interval 95%) | 7102.0 (6553.2 to 7696.8) | 1400.4 (1272.7 to 1541.0) | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: GMC Comparison of BD-Day 29 P203 vs Day 57 P301 | |
| Comparison groups | Part 1C-1: mRNA-1273 50 µg BD v Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 µg |
| Number of subjects included in analysis | 558 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | GMR |
| Point estimate | 5.071 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.477 |
| upper limit | 5.745 |

Primary: Part 3 GMC of nAb post Dose 1 mRNA 1273.222 Against Omicron BA.4/BA.5 Compared With Those From Young Adult (18 to 25 Years of Age) Vaccine Recipients (Day 57) in Study P301

| | |
|-----------------|---|
| End point title | Part 3 GMC of nAb post Dose 1 mRNA 1273.222 Against Omicron BA.4/BA.5 Compared With Those From Young Adult (18 to 25 Years of Age) Vaccine Recipients (Day 57) in Study P301 ^[7] |
|-----------------|---|

End point description:

Antibody values reported as below the LLOQ were replaced by 0.5*LLOQ. Values greater than the ULOQ were replaced by the ULOQ if actual values were not available (LLOQ: 103 AU/mL, ULOQ: 28571 AU/mL). ANCOVA model with the group variable (adolescents in P203 and young adults in P301) as fixed effect. The geometric least squares means are presented. P301 mRNA-1273 group included young adults (≥ 18 and ≤ 25 years) who received 2 doses of mRNA 1273 and were baseline SARS-CoV-2 negative. PPIS-Baseline SARS-CoV-2 Positive (PPIS-POS): all participants who received Dose 1 of mRNA-1273.222, had both Baseline (pre Dose 1) and Day 29 antibody assessment, had no major protocol deviations that impacted key or critical data, had not received off-study COVID-19 vaccination prior to Day 29, and were SARS-CoV-2 positive (serologic and/or virologic evidence of prior SARS-CoV-2 infection) at baseline. "Overall number of participants analyzed" = participants evaluable for this endpoint.

| | |
|---|---------|
| End point type | Primary |
| End point timeframe: | |
| Day 29 Study P203/Day 57 Study P301 | |
| Notes: | |
| [7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. | |
| Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint. | |

| | | | | |
|--|-----------------------------|---|--|--|
| End point values | Part 3: mRNA-1273.222 50 µg | Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 µg | | |
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 372 | 294 | | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | 2727.8 (2558.7 to 2908.1) | 56.6 (52.7 to 60.8) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| GMR of P203 vs P301 | |
| Comparison groups | Part 3: mRNA-1273.222 50 µg v Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 µg |
| Number of subjects included in analysis | 666 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | GMR |
| Point estimate | 48.191 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 43.765 |
| upper limit | 53.065 |

Primary: Part 2 GMC of the Pseudovirus nAb Against Ancestral Strain at Day 57

| | |
|--|--|
| End point title | Part 2 GMC of the Pseudovirus nAb Against Ancestral Strain at Day 57 ^[8] ^[9] |
| End point description: | |
| Antibody values reported as below the LLOQ were replaced by 0.5 * LLOQ. Values greater than the ULOQ were replaced by the ULOQ if actual values were not available (LLOQ: 10 AU/mL, ULOQ: 111433 AU/mL). PPIS: all randomized participants who received at least 1 dose of the planned study drug, had Ab assessment for the analysis endpoint, and had no major protocol deviations that could impact key or critical data. | |
| End point type | Primary |
| End point timeframe: | |
| Day 57 | |

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Part 2, due to the smaller number of participants enrolled, hypothesis testing was not conducted. Descriptive analysis included.

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Part 2, due to the smaller number of participants enrolled, hypothesis testing was not conducted. Descriptive analysis included.

| | | | | |
|--|---------------------------|--|--|--|
| End point values | Part 2: mRNA-1273 50 µg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 46 | | | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | 7351.5 (5621.7 to 9613.7) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Part 1C-1 SRR of Serum Pseudovirus nAb Against the Original Strain After the BD in Study P203 at BD Day 29 Compared With Those From Young Adult (18 to 25 Years of Age) Vaccine Recipients (Day 57) in Study P301

| | |
|-----------------|---|
| End point title | Part 1C-1 SRR of Serum Pseudovirus nAb Against the Original Strain After the BD in Study P203 at BD Day 29 Compared With Those From Young Adult (18 to 25 Years of Age) Vaccine Recipients (Day 57) in Study P301 |
|-----------------|---|

End point description:

Percentage of participants with seroresponse for pseudovirus nAb measured using PsVNA assay are reported. Seroresponse relative to pre-Dose 1 (baseline) at a participant level was defined as a change from below the LLOQ to equal or above 4 * LLOQ, or at least a 4-fold-rise if baseline was equal to or above LLOQ. PPIS-Neg: all participants who received mRNA-1273 in the Blinded Phase per schedule, received BD, had a negative SARS-CoV-2 status at baseline (pre-Dose 1 of the Blinded Phase), had BD-Day 1 and BD-Day 29 Ab assessment, had no major protocol deviations that impacted key or critical data, and were pre-booster SARS-CoV-2 negative, defined as no virologic or serologic evidence of SARSCoV-2 infection on or before BD-Day 1. P301 mRNA-1273 group included young adults (≥18 and ≤25 years) who received 2 doses of mRNA-1273 in P301 Part A and who were baseline SARS-CoV-2 negative in P301 Part A.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

BD Day 29 Study P203/Day 57 Study P301

| | | | | |
|-----------------------------------|-------------------------------|---|--|--|
| End point values | Part 1C-1: mRNA-1273 50 µg BD | Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 µg | | |
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 264 | 294 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 100.0 (98.6 to | 99.3 (97.6 to | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: SRR difference of P203 BD-Day 29 vs P301 Day 57 | |
| Comparison groups | Part 1C-1: mRNA-1273 50 µg BD v Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 µg |
| Number of subjects included in analysis | 558 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | SRR Difference |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.8 |
| upper limit | 2.4 |

Primary: Part 1C-2 GMC of Post-booster Pseudovirus nAb Against Ancestral Strain at BD Day 29

| | |
|--|---|
| End point title | Part 1C-2 GMC of Post-booster Pseudovirus nAb Against Ancestral Strain at BD Day 29 ^[10] ^[11] |
| End point description: Antibody values reported as below the LLOQ were replaced by 0.5 * LLOQ. Values greater than the ULOQ were replaced by the ULOQ if actual values were not available (LLOQ: 10 AU/mL, ULOQ: 111433 AU/mL). PPIS: all randomized participants who received BD in Part 1C-2, had BD-Day 29 Ab assessment for the analysis endpoint, and had no major protocol deviations that impacted key or critical data. 'Overall number of participants analyzed' = participants evaluable for this endpoint. | |
| End point type | Primary |
| End point timeframe: BD Day 29 | |

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Part 1C-2 enrollment discontinued before planned number of participants were met for prespecified statistical analysis to be conducted.

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Part 1C-2 enrollment discontinued before planned number of participants were met for prespecified statistical analysis to be conducted.

| | | | | |
|--|-------------------------------------|--|--|--|
| End point values | Part 1C-2: mRNA-1273 50 µg BD | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 134 | | | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | 9433.4 (8496.8 to 10473.3) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Part 3 GMC of nAb post Dose 1 mRNA 1273.222 Against SARS-CoV-2 Ancestral Strain Compared With Those From Young Adult (18 to 25 Years of Age) Vaccine Recipients (Day 57) in Study P301

| | |
|-----------------|--|
| End point title | Part 3 GMC of nAb post Dose 1 mRNA 1273.222 Against SARS-CoV-2 Ancestral Strain Compared With Those From Young Adult (18 to 25 Years of Age) Vaccine Recipients (Day 57) in Study P301 ^[12] |
|-----------------|--|

End point description:

Antibody values reported as below the LLOQ were replaced by 0.5*LLOQ. Values greater than the ULOQ were replaced by the ULOQ if actual values were not available (LLOQ: 10 AU/mL, ULOQ: 111433 AU/mL). ANCOVA model with the group variable (adolescents in P203 and young adults in P301) as fixed effect. The geometric least squares means are presented. P301 mRNA-1273 group included young adults (≥18 and ≤25 years) who received 2 doses of mRNA-1273 and were baseline SARS-CoV-2 negative. PPIS-POS: all participants who received Dose 1 of mRNA-1273.222, had both Baseline (pre Dose 1) and Day 29 antibody assessment, had no major protocol deviations that impacted key or critical data, had not received off-study COVID-19 vaccination prior to Day 29, and were SARS-CoV-2 positive (serologic and/or virologic evidence of prior SARS-CoV-2 infection) at baseline. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 29 Study P203/Day 57 Study P301

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| | | | | |
|--|------------------------------|---|--|--|
| End point values | Part 3: mRNA-1273.222 50 µg | Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 µg | | |
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 371 | 295 | | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | 7603.9 (7004.6 to 8254.6) | 1692.3 (1543.4 to 1855.5) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|--|---|
| Statistical analysis description: GMR of P203 vs P301 | |
| Comparison groups | Part 3: mRNA-1273.222 50 µg v Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 µg |
| Number of subjects included in analysis | 666 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | GMR |
| Point estimate | 4.493 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.972 |
| upper limit | 5.083 |

Primary: Part 2 SRR of Pseudovirus nAb Against Ancestral Strain

| | |
|---|--|
| End point title | Part 2 SRR of Pseudovirus nAb Against Ancestral Strain ^{[13][14]} |
| End point description: Percentage of participants with seroresponse for pseudovirus nAb measured using PsVNA assay are reported. Seroresponse relative to pre-Dose 1 (baseline) at a participant level was defined as a change from below the LLOQ to equal or above 4 * LLOQ, or at least a 4-fold-rise if baseline was equal to or above the LLOQ. PPIS: all randomized participants who received at least 1 dose of the planned study drug, had Ab assessment for the analysis endpoint, and had no major protocol deviations that could impact key or critical data. | |
| End point type | Primary |
| End point timeframe: Day 57 | |

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Part 2, due to the smaller number of participants enrolled, hypothesis testing was not conducted. Descriptive analysis included.

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Part 2, due to the smaller number of participants enrolled, hypothesis testing was not conducted. Descriptive analysis included.

| | | | | |
|-----------------------------------|-------------------------|--|--|--|
| End point values | Part 2: mRNA-1273 50 µg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 46 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 91.3 (79.2 to 97.6) | | | |

Statistical analyses

Primary: Number of Participants With SAEs, AEs of Special Interest (AESIs), Medically Attended AEs (MAAEs), and AEs leading to Study Discontinuation

| | |
|-----------------|---|
| End point title | Number of Participants With SAEs, AEs of Special Interest (AESIs), Medically Attended AEs (MAAEs), and AEs leading to Study Discontinuation ^{[15][16]} |
|-----------------|---|

End point description:

SAE was defined as any AE that resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in disability/permanent damage, was a congenital anomaly/birth defect, or was an important medical event. AESIs included thrombocytopenia, new onset of or worsening of the protocol specified neurologic diseases, anaphylaxis, and myocarditis/pericarditis. MAAE was an AE that led to an unscheduled visit to a healthcare practitioner, included visits to a study site for unscheduled assessments (for example, abnormal laboratory follow-up, and visits to healthcare practitioners external to the study site [for example, urgent care, primary care physician]). Number of participants with SAEs, AESIs, MAAEs, and AEs leading to study discontinuation up to end of study (EOS) are reported in this endpoint. Participants who received at least 1 dose of mRNA-1273 were included in the analysis.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 1 up to Day 751 (end of study [EOS])

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| End point values | Part 1A: mRNA-1273 100 µg | Part 1C-1: mRNA-1273 50 µg BD | Part 1C-2: mRNA-1273 50 µg BD | Part 2: mRNA- 1273 50 µg |
|--------------------------------------|---------------------------------|-------------------------------------|-------------------------------------|-----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2486 | 1408 | 155 | 52 |
| Units: participants | | | | |
| SAEs | 21 | 9 | 3 | 0 |
| AESIs | 17 | 9 | 1 | 0 |
| MAAEs | 1040 | 541 | 45 | 12 |
| AEs Leading to Study Discontinuation | 0 | 0 | 0 | 0 |

| End point values | Part 3: mRNA- 1273.222 50 µg | Part 2: mRNA- 1273 50 µg BD | Part 1B: mRNA-1273 100 µg | |
|--------------------------------------|------------------------------------|--------------------------------|---------------------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 388 | 19 | 96 | |
| Units: participants | | | | |
| SAEs | 16 | 0 | 2 | |
| AESIs | 3 | 0 | 0 | |
| MAAEs | 183 | 7 | 31 | |
| AEs Leading to Study Discontinuation | 1 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1A Number of Participants with a SARS-CoV-2 Infection (Symptomatic or Asymptomatic)

| | |
|-----------------|--|
| End point title | Part 1A Number of Participants with a SARS-CoV-2 Infection (Symptomatic or Asymptomatic) ^[17] |
|-----------------|--|

End point description:

SARS-CoV-2 infection was defined in participants with negative SARS-CoV-2 status at baseline: bAb level against SARS-CoV-2 nucleocapsid protein negative at Day 1, that became positive postbaseline; or positive postbaseline. PP Set for Efficacy: all randomized participants who received planned doses of study drug, had no immunologic or virologic evidence of prior COVID-19, and had no major protocol deviations that impact key or critical efficacy data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 43 (14 days after second injection) up to a median follow up of 2.5 months after second injection

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| End point values | Part 1A: mRNA-1273 100 µg | Part 1A: Placebo | | |
|-----------------------------|---------------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2142 | 1044 | | |
| Units: participants | 22 | 25 | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Vaccine efficacy (VE, percent), was defined as 1 - ratio of incidence rate (mRNA-1273 vs. placebo).

| | |
|---|--|
| Comparison groups | Part 1A: mRNA-1273 100 µg v Part 1A: Placebo |
| Number of subjects included in analysis | 3186 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[18] |
| Method | VE |
| Parameter estimate | VE |
| Point estimate | 60.3 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 26.6 |
| upper limit | 78.6 |

Notes:

[18] - The 95% confidence interval (CI) of the ratio was calculated using the exact method conditional upon the total number of cases, adjusting for person-years.

Secondary: Part 1A Number of Participants with a First Occurrence of Symptomatic COVID-19

| | |
|-----------------|--|
| End point title | Part 1A Number of Participants with a First Occurrence of Symptomatic COVID-19 ^[19] |
|-----------------|--|

End point description:

COVID-19 was defined as symptomatic disease based on the following criteria: participants experienced at least 2 of the following systemic symptoms: fever ($\geq 38^{\circ}\text{C}/\geq 100.4^{\circ}\text{F}$), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s); or experienced at least 1 of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, or clinical or radiographical evidence of pneumonia; and had at least 1 NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2. PP Set for Efficacy: all randomized participants who received planned doses of study drug, had no immunologic or virologic evidence of prior COVID-19, and had no major protocol deviations that impact key or critical efficacy data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 43 (14 days after second injection) up to 2.5 months after second injection

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| End point values | Part 1A: mRNA-1273 100 µg | Part 1A: Placebo | | |
|-----------------------------|---------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2142 | 1044 | | |
| Units: participants | 0 | 6 | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

VE (percent), was defined as 1 - ratio of incidence rate (mRNA-1273 vs. placebo).

| | |
|---|--|
| Comparison groups | Part 1A: mRNA-1273 100 µg v Part 1A: Placebo |
| Number of subjects included in analysis | 3186 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[20] |
| Method | VE |
| Parameter estimate | VE |
| Point estimate | 100 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 61.2 |
| upper limit | 9999 |

Notes:

[20] - The 95% CI of the ratio was calculated using the exact method conditional upon the total number of cases, adjusting for person-years. 9999= not estimable (NE, not reached).

Secondary: Part 1A Number of Participants With Asymptomatic SARS-CoV-2 Infection

| | |
|-----------------|---|
| End point title | Part 1A Number of Participants With Asymptomatic SARS-CoV-2 Infection ^[21] |
|-----------------|---|

End point description:

Asymptomatic SARS-CoV-2 infection was defined as absence of symptoms and a positive RT-PCR or serology test (bAb levels against SARS-CoV-2 nucleocapsid protein) post dosing in participants who did not have an infection at baseline or pre-Dose 1. PP Set for Efficacy: all randomized participants who received planned doses of study drug, had no immunologic or virologic evidence of prior COVID-19, and had no major protocol deviations that impact key or critical efficacy data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 43 (14 days after second injection) up to a median follow up of 2.5 months after second injection

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| End point values | Part 1A: mRNA-1273 100 µg | Part 1A: Placebo | | |
|-----------------------------|---------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2142 | 1044 | | |
| Units: participants | 20 | 16 | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

VE (percent), was defined as 1 - ratio of incidence rate (mRNA-1273 vs. placebo).

| | |
|---|--|
| Comparison groups | Part 1A: mRNA-1273 100 µg v Part 1A: Placebo |
| Number of subjects included in analysis | 3186 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[22] |
| Method | VE |
| Parameter estimate | VE |
| Point estimate | 43.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.5 |
| upper limit | 72.2 |

Notes:

[22] - The 95% CI of the ratio was calculated using the exact method conditional upon the total number of cases, adjusting for person-years.

Secondary: Part 1C-1 SRR of the Post-booster Serum bAb Against Variants of Interest (B.1.1.7, B.1.351, B.1.617.2, and P.1) as Measured by MSD

| | |
|-----------------|--|
| End point title | Part 1C-1 SRR of the Post-booster Serum bAb Against Variants of Interest (B.1.1.7, B.1.351, B.1.617.2, and P.1) as Measured by MSD |
|-----------------|--|

End point description:

Seroresponse from baseline (pre-Dose 1) at a participant level was defined as a change from below the LLOQ to equal or above 4 * LLOQ, or at least a 4-fold-rise if baseline (pre-Dose 1 is equal to or above the LLOQ. PPIS: all randomized participants who received planned doses of study drug per schedule, complied with immunogenicity testing schedule, and had no major protocol deviations that impacted key or critical data. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

BD Day 29

| | | | | |
|-----------------------------------|-------------------------------------|--|--|--|
| End point values | Part 1C-1: mRNA-1273 50 µg BD | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 324 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| B.1.1.7 | 100.0 (98.9 to 100.0) | | | |
| B.1.351 | 100.0 (98.9 to 100.0) | | | |
| B.1.617.2 | 100.0 (98.9 to 100.0) | | | |
| P.1 | 100.0 (98.9 to 100.0) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1A Number of Participants with Secondary Case Definition of COVID-19 (Center for Disease Control and Prevention [CDC] Case Definition)

| | |
|-----------------|---|
| End point title | Part 1A Number of Participants with Secondary Case Definition of COVID-19 (Center for Disease Control and Prevention [CDC] Case Definition) ^[23] |
|-----------------|---|

End point description:

Secondary case definition of COVID-19 was defined by the following criteria: 1 systemic or respiratory symptoms: fever (temperature > 38°C/≥ 100.4°F), or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches, or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea, or vomiting or diarrhea, and at least one positive test for SARS-CoV-2. PP Set for Efficacy: all randomized participants who received planned doses of study drug, had no immunologic or virologic evidence of prior COVID-19, and had no major protocol deviations that impact key or critical efficacy data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 43 (14 days after second injection) up to a median follow up of 2.5 months after second injection

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| End point values | Part 1A: mRNA-1273 100 µg | Part 1A: Placebo | | |
|-----------------------------|---------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2142 | 1044 | | |
| Units: participants | 2 | 9 | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|--|
| Statistical analysis description: | |
| VE (percent), was defined as 1 - ratio of incidence rate (mRNA-1273 vs. placebo). | |
| Comparison groups | Part 1A: mRNA-1273 100 µg v Part 1A: Placebo |
| Number of subjects included in analysis | 3186 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[24] |
| Method | VE |
| Parameter estimate | VE |
| Point estimate | 89.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 51 |
| upper limit | 98.9 |

Notes:

[24] - The 95% CI of the ratio was calculated using the exact method conditional upon the total number of cases, adjusting for person-years.

Secondary: Part 3 Pseudovirus nAb SRR of post Dose 1 of mRNA-1273.222 Against Ancestral Strain Compared to Study P301

| | |
|-----------------|--|
| End point title | Part 3 Pseudovirus nAb SRR of post Dose 1 of mRNA-1273.222 Against Ancestral Strain Compared to Study P301 ^[25] |
|-----------------|--|

End point description:

Seroresponse from pre Dose 1 Baseline at a participant level was defined as a change from below the LLOQ to equal or above 4 * LLOQ, or at least a 4-fold rise if Baseline was equal to or above the LLOQ. P301 mRNA-1273 group included young adults (≥ 18 and ≤ 25 years) who received 2 doses of mRNA-1273 in P301 Part A and who were baseline SARS-CoV-2 negative in P301 Part A. PPIS-POS: all participants who received Dose 1 of mRNA-1273.222, had both Baseline (pre Dose 1) and Day 29 antibody assessment, had no major protocol deviations that impacted key or critical data, had not received off-study COVID-19 vaccination prior to Day 29 Visit, and who were SARS-CoV-2 positive (serologic and/or virologic evidence of prior SARS-CoV-2 infection) at baseline. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 29 P203/Day 57 P301

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| | | | | |
|-----------------------------------|-----------------------------|---|--|--|
| End point values | Part 3: mRNA-1273.222 50 µg | Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 µg | | |
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 370 | 295 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 94.9 (92.1 to 96.9) | 99.3 (97.6 to 99.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1C-1 GMC of Post-booster Pseudovirus nAb Against Variant Strain (B.1.1.529)

| | |
|-----------------|--|
| End point title | Part 1C-1 GMC of Post-booster Pseudovirus nAb Against Variant Strain (B.1.1.529) |
|-----------------|--|

End point description:

Post-booster Pseudovirus nAb against B.1.1.529 (LLOQ: 8 AU/mL, ULOQ: 24503 AU/mL). Antibody values reported as below the LLOQ were replaced by 0.5 * LLOQ. Values greater than the ULOQ were replaced by the ULOQ if actual values were not available. PP IS: all randomized participants who received planned doses of study drug per schedule, complied with immunogenicity testing schedule, and had no major protocol deviations that impacted key or critical data. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

BD Day 29

| | | | | |
|--|-------------------------------|--|--|--|
| End point values | Part 1C-1: mRNA-1273 50 µg BD | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 331 | | | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | 943.4 (853.5 to 1042.8) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 3 SRR of Serum Pseudovirus nAb Post Dose 1 of mRNA-1273.222 Against Omicron BA.4/BA.5 Compared with Young Adults (Study P301)

| | |
|-----------------|--|
| End point title | Part 3 SRR of Serum Pseudovirus nAb Post Dose 1 of mRNA-1273.222 Against Omicron BA.4/BA.5 Compared with Young Adults (Study P301) ^[26] |
|-----------------|--|

End point description:

Seroresponse from pre Dose 1 Baseline at a participant level was defined as a change from below the LLOQ to equal or above 4 * LLOQ, or at least a 4-fold rise if Baseline was equal to or above the LLOQ. P301 mRNA-1273 group included young adults (≥ 18 and ≤ 25 years) who received 2 doses of mRNA-1273 in P301 Part A and who were baseline SARS-CoV-2 negative in P301 Part A. PPIS-POS: all participants who received Dose 1 of mRNA-1273.222, had both Baseline (pre Dose 1) and Day 29 antibody assessment, had no major protocol deviations that impacted key or critical data, had not received off-study COVID-19 vaccination prior to Day 29 Visit, and who were SARS-CoV-2 positive (serologic and/or virologic evidence of prior SARS-CoV-2 infection) at baseline. 'Overall number of participants analyzed = participants evaluable for this endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 29 Study P203/Day 57 Study P301

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| | | | | |
|-----------------------------------|----------------------------------|--|--|--|
| End point values | Part 3: mRNA-1273.222 50 μ g | Study mRNA-1273-P301 (NCT04470427) mRNA-1273 100 μ g | | |
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 372 | 294 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 95.4 (92.8 to 97.3) | 0.0 (0.0 to 1.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 3 GM Value of Post Dose 1 (Day 29) of mRNA-1273.222 bAb Against Other Variants of Interest

| | |
|-----------------|---|
| End point title | Part 3 GM Value of Post Dose 1 (Day 29) of mRNA-1273.222 bAb Against Other Variants of Interest ^[27] |
|-----------------|---|

End point description:

mRNA-1273.222 bAb was measured using a S-binding IgG immunoassay. Antibody values reported as below the LLOQ were replaced by 0.5 * LLOQ. Values greater than the ULOQ are replaced by the ULOQ if actual values are not available (LLOQ: 397 AU/ml, ULOQ: 2200000 AU/mL). PPIS: all participants who received Dose 1 of mRNA-1273.222 and had both Baseline (pre Dose 1) and Day 29 antibody assessment, had no major protocol deviations that impacted key or critical data; and had not received off-study COVID-19 vaccination prior to Day 29 visit.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 29

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| | | | | |
|--|------------------------------------|--|--|--|
| End point values | Part 3: mRNA-1273.222 50 µg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 372 | | | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| BA.5 (n=372) | 282734.2 (266581.0 to 299866.1) | | | |
| AY.4 (n=372) | 557963.4 (529270.6 to 588211.6) | | | |
| B.1.1.7 (n=372) | 434879.0 (412699.2 to 458250.8) | | | |
| B.1.351 (n=372) | 431476.5 (409656.1 to 454459.1) | | | |
| B.1.1.529 (n=372) | 189826.0 (178578.0 to 201782.5) | | | |
| P.1 (n=372) | 471868.9 (446431.3 to 498756.0) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1C-2 GM Value of mRNA-1273 booster Against Variants of Interest at Day 29

| | |
|-----------------|--|
| End point title | Part 1C-2 GM Value of mRNA-1273 booster Against Variants of Interest at Day 29 ^[28] |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 29

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| | | | | |
|--|-------------------------------------|--|--|--|
| End point values | Part 1C-2: mRNA-1273 50 µg BD | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[29] | | | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | (to) | | | |

Notes:

[29] - Data not collected due to discontinuation of enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 A GM Level of SARS-CoV-2 Spike Protein-specific bAb at Days 1, 57, 209, 394

| | |
|-----------------|--|
| End point title | Part 1 A GM Level of SARS-CoV-2 Spike Protein-specific bAb at Days 1, 57, 209, 394 ^[30] |
|-----------------|--|

End point description:

SARS-CoV-2 Spike Protein-specific binding antibody (bAb) were measured using MesoScale Discovery (MSD) electrochemiluminescence multiplex assay. Antibody values reported as below the LLOQ were replaced by 0.5*LLOQ. Values greater than the ULOQ are replaced by the ULOQ if actual values are not available (LLOQ: 69, ULOQ: 14400000). PPIS for long term analysis included all randomized participants who received planned doses of study drug per schedule, complied with immunogenicity testing schedule, and had no major protocol deviations that impacted key or critical data. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Days 1, 57, 209, 394

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| | | | | |
|--|---------------------------------------|--|--|--|
| End point values | Part 1A: mRNA-1273 100 µg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 369 | | | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 1 (n=369) | 65.848 (60.348 to 71.850) | | | |
| Day 57 (n=366) | 346830.736 (330758.387 to 363684.079) | | | |
| Day 209 (n=366) | 79624.290 (73959.321 to 85723.172) | | | |
| Day 394 (n=356) | 58647.246 (52309.921 to 65752.336) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1A GM Value of SARS-CoV-2-Specific nAb at Days 1, 57, 209, 394

| | |
|-----------------|---|
| End point title | Part 1A GM Value of SARS-CoV-2-Specific nAb at Days 1, 57, 209, 394 ^[31] |
|-----------------|---|

End point description:

SARS-CoV-2-Specific nAb were measured using PsVNA assay. Antibody values reported as below the LLOQ were replaced by 0.5*LLOQ. Values greater than the ULOQ are replaced by the ULOQ if actual values are not available (LLOQ: 10, ULOQ: 281600). PPIS for long term analysis included all randomized participants who received planned doses of study drug per schedule, complied with immunogenicity testing schedule, and had no major protocol deviations that impacted key or critical data. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Days 1, 57, 209, 394

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As prespecified in the protocol, no statistical analysis was conducted for this endpoint.

| End point values | Part 1A: mRNA-1273 100 µg | | | |
|--|---------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 369 | | | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 1 (n=369) | 11.249 (10.712 to 11.812) | | | |
| Day 57 (n=366) | 1868.363 (1758.809 to 1984.742) | | | |
| Day 209 (n=366) | 625.363 (583.319 to 670.437) | | | |
| Day 394 (n=363) | 550.262 (489.875 to 618.093) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1C-1 GM Value of Post-booster Dose Serum bAb Against Variants of Interest (B.1.1.7, B.1.351, B.1.617.2, and P.1) as Measured by MSD

| | |
|-----------------|--|
| End point title | Part 1C-1 GM Value of Post-booster Dose Serum bAb Against Variants of Interest (B.1.1.7, B.1.351, B.1.617.2, and P.1) as Measured by MSD |
|-----------------|--|

End point description:

Antibody values reported as below the LLOQ were replaced by 0.5*LLOQ. Values greater than the ULOQ were replaced by the ULOQ if actual values were not available. B.1.1.7 (LLOQ: 52, ULOQ: 8800000), B.1.351 (LLOQ: 111, ULOQ: 5000000), B.1.617.2 (LLOQ: 49, ULOQ: 7400000), P.1 (LLOQ: 143, ULOQ: 5800000). PPIS: all randomized participants who received planned doses of study drug per schedule, complied with immunogenicity testing schedule, and had no major protocol deviations that impacted key or critical data. 'Overall number of participants analyzed' = participants evaluable for this endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

BD Day 29

| | | | | |
|--|---------------------------------------|--|--|--|
| End point values | Part 1C-1: mRNA-1273 50 µg BD | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 324 | | | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| B.1.1.7 | 581097.8 (543987.7 to 620739.5) | | | |
| B.1.351 | 431569.2 (404983.2 to 459900.6) | | | |
| B.1.617.2 | 456423.3 (429083.9 to 485504.8) | | | |
| P.1 | 417277.2 (391682.5 to 444544.5) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to EOS (Day 751)

Adverse event reporting additional description:

All-cause mortality: enrolled; AEs: participants received 1 dose of study drug.

Non-serious SARs persisting beyond 7 days, leading to discontinuation, or medically attended were defined as AEs in Part 1/2 but not in Part 3. COVID-19/SARS-CoV-2 infections were AEs in Part 1/2 but were considered clinical events for efficacy in Part 3 and not AEs.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Part 1A: Placebo |
|-----------------------|------------------|

Reporting group description:

Participants received 2 doses of placebo by IM injection (Day 1 and Day 29).

| | |
|-----------------------|---------------------------|
| Reporting group title | Part 1A: mRNA-1273 100 µg |
|-----------------------|---------------------------|

Reporting group description:

Participants received 2 doses of 100 µg mRNA-1273 by IM injection (Day 1 and Day 29).

| | |
|-----------------------|----------------------------|
| Reporting group title | Part 1 B: mRNA-1273 100 µg |
|-----------------------|----------------------------|

Reporting group description:

Participants previously received 2 doses of placebo in the blinded phase and then received crossover vaccination with 100 µg of mRNA-1273.

| | |
|-----------------------|----------------------------|
| Reporting group title | Part 2: mRNA-1273 50 ug BD |
|-----------------------|----------------------------|

Reporting group description:

Participants received open-label mRNA-1273 50 µg in Part 2 and then a single BD of 50 µg mRNA-1273 IM injection on BD Day 1 in Part 2.

| | |
|-----------------------|---|
| Reporting group title | Part 3: mRNA-1273.222 50 ug Second Dose |
|-----------------------|---|

Reporting group description:

Participants received 1 dose of mRNA-1273.222 50 µg by IM injection (Day 1). and a second dose approximately 6 months after the first dose (Day 181).

| | |
|-----------------------|-------------------------|
| Reporting group title | Part 2: mRNA-1273 50 µg |
|-----------------------|-------------------------|

Reporting group description:

Participants received 2 doses of 50 µg mRNA-1273 by IM injection (Day 1 and Day 29).

| | |
|-----------------------|-------------------------------|
| Reporting group title | Part 1C-2: mRNA-1273 50 µg BD |
|-----------------------|-------------------------------|

Reporting group description:

Participants who completed primary COVID-19 vaccination series with a non-Moderna vaccine under EUA, received a single booster of 50 µg mRNA-1273 IM injection on BD Day 1.

| | |
|-----------------------|-------------------------------|
| Reporting group title | Part 1C-1: mRNA-1273 50 µg BD |
|-----------------------|-------------------------------|

Reporting group description:

Participants received mRNA-1273 100 µg in blinded or cross-over phase and then a single booster of 50 µg mRNA-1273 IM injection on Booster Dose Day 1.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Part 3: mRNA1273.222 50 µg 1 Dose |
|-----------------------|-----------------------------------|

Reporting group description:

Participants received 1 dose of mRNA-1273.222 50 µg by IM injection (Day 1).

| Serious adverse events | Part 1A: Placebo | Part 1A: mRNA-1273 100 µg | Part 1 B: mRNA- 1273 100 µg |
|---|------------------|------------------------------|--------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 1240 (0.32%) | 21 / 2486 (0.84%) | 2 / 96 (2.08%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Vaginal haematoma | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression suicidal | | | |

| | | | |
|---|------------------|------------------|----------------|
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Emotional distress | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Major depression | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 2 / 2486 (0.08%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 5 / 2486 (0.20%) | 1 / 96 (1.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | | | |
| subjects affected / exposed | 1 / 1240 (0.08%) | 3 / 2486 (0.12%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Clavicle fracture | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Concussion | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|------------------|----------------|
| Cervical vertebral fracture | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gun shot wound | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural fever | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 1 / 96 (1.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial bones fracture | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sunburn | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Splenic injury | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vulvovaginal injury | | | |

| | | | |
|---|---|------------------|----------------|
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Pectus excavatum | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syringomyelia | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arnold-Chiari malformation | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiogenic shock | Additional description: Sponsor assessment was Not related based on medical history, results of the heart biopsy, including findings of long-standing pre-existing heart failure and long time to onset (256 days). | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Status migrainosus | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Idiopathic generalised epilepsy | | | |

| | | | |
|---|---|------------------|----------------|
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epilepsy | | | |
| subjects affected / exposed | 1 / 1240 (0.08%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Normochromic normocytic anaemia | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercoagulation | Additional description: Sponsor assessment was Not related based on medical history, results of the heart biopsy, including findings of long-standing pre-existing heart failure and long time to onset (256 days). | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia neonatal | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug-induced liver injury | | | |

| | | | |
|---|------------------|------------------|----------------|
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrotic syndrome | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic kidney disease | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive nephropathy | | | |
| subjects affected / exposed | 1 / 1240 (0.08%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Amoebic dysentery | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Murine typhus | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 1 / 2486 (0.04%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |

| | | | |
|---|------------------|------------------|----------------|
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 1240 (0.08%) | 2 / 2486 (0.08%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypocalcaemia | | | |

| | | | |
|---|------------------|------------------|----------------|
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Part 2: mRNA-1273 50 ug BD | Part 3: mRNA-1273.222 50 ug Second Dose | Part 2: mRNA-1273 50 µg |
|---|-------------------------------|--|----------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 4 / 335 (1.19%) | 0 / 52 (0.00%) |
| number of deaths (all causes) | 0 | 1 | 0 |
| number of deaths resulting from adverse events | | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 335 (0.30%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 2 / 335 (0.60%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Vaginal haematoma | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |

| | | | |
|---|----------------|-----------------|----------------|
| Depression | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression suicidal | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Emotional distress | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Major depression | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Clavicle fracture | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|----------------|
| Concussion | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical vertebral fracture | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gun shot wound | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 335 (0.30%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Post procedural fever | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial bones fracture | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sunburn | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Splenic injury | | | |

| | | | |
|---|---|-----------------|----------------|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vulvovaginal injury | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Pectus excavatum | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syringomyelia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arnold-Chiari malformation | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiogenic shock | Additional description: Sponsor assessment was Not related based on medical history, results of the heart biopsy, including findings of long-standing pre-existing heart failure and long time to onset (256 days). | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Status migrainosus | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |

| | | | |
|---|---|-----------------|----------------|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Idiopathic generalised epilepsy | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Normochromic normocytic anaemia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 335 (0.30%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercoagulation | Additional description: Sponsor assessment was Not related based on medical history, results of the heart biopsy, including findings of long-standing pre-existing heart failure and long time to onset (256 days). | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia neonatal | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrotic syndrome | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 335 (0.30%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic kidney disease | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 335 (0.30%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive nephropathy | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Amoebic dysentery | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Murine typhus | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dengue fever | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 335 (0.30%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 335 (0.30%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperkalaemia | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 335 (0.30%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 335 (0.30%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Part 1C-2: mRNA-1273 50 µg BD | Part 1C-1: mRNA-1273 50 µg BD | Part 3: mRNA1273.222 50 |
|---|-------------------------------|-------------------------------|-------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 155 (1.94%) | 9 / 1408 (0.64%) | 12 / 388 (3.09%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 1 / 388 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 1 / 388 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 1 / 155 (0.65%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Vaginal haematoma | | | |

| | | | |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed | 0 / 155 (0.00%) | 1 / 1408 (0.07%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 1 / 1408 (0.07%) | 1 / 388 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression suicidal | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Emotional distress | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 1 / 1408 (0.07%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Major depression | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 2 / 1408 (0.14%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 1 / 1408 (0.07%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 1 / 1408 (0.07%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural | | | |

| | | | |
|---|-----------------|------------------|-----------------|
| complications | | | |
| Clavicle fracture | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Concussion | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical vertebral fracture | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 1 / 1408 (0.07%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gun shot wound | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural fever | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial bones fracture | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sunburn | | | |

| | | | |
|---|---|------------------|-----------------|
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Splenic injury | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vulvovaginal injury | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 1 / 1408 (0.07%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Pectus excavatum | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syringomyelia | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arnold-Chiari malformation | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiogenic shock | Additional description: Sponsor assessment was Not related based on medical history, results of the heart biopsy, including findings of long-standing pre-existing heart failure and long time to onset (256 days). | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 1 / 388 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Status migrainosus | | | |

| | | | |
|---|---|------------------|-----------------|
| subjects affected / exposed | 0 / 155 (0.00%) | 1 / 1408 (0.07%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 1 / 155 (0.65%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Idiopathic generalised epilepsy | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Normochromic normocytic anaemia | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercoagulation | Additional description: Sponsor assessment was Not related based on medical history, results of the heart biopsy, including findings of long-standing pre-existing heart failure and long time to onset (256 days). | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 1 / 388 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|------------------|-----------------|
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia neonatal | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 1 / 388 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 155 (0.65%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrotic syndrome | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic kidney disease | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive nephropathy | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Amoebic dysentery | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 1 / 388 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Murine typhus | | | |

| | | | |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 5 / 388 (1.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 1 / 388 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 1 / 388 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 1 / 1408 (0.07%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 1 / 1408 (0.07%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 1 / 1408 (0.07%) | 1 / 388 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic acidosis | | | |

| | | | |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 0 / 1408 (0.00%) | 0 / 388 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Part 1A: Placebo | Part 1A: mRNA-1273 100 µg | Part 1 B: mRNA- 1273 100 µg |
|---|------------------------|------------------------------|--------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 155 / 1240 (12.50%) | 943 / 2486 (37.93%) | 22 / 96 (22.92%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 51 / 1240 (4.11%) | 117 / 2486 (4.71%) | 1 / 96 (1.04%) |
| occurrences (all) | 57 | 129 | 1 |
| General disorders and administration site conditions | | | |
| Injection site lymphadenopathy | | | |
| subjects affected / exposed | 6 / 1240 (0.48%) | 137 / 2486 (5.51%) | 0 / 96 (0.00%) |
| occurrences (all) | 6 | 146 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 1240 (0.24%) | 8 / 2486 (0.32%) | 0 / 96 (0.00%) |
| occurrences (all) | 3 | 9 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Mechanical urticaria | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 0 / 2486 (0.00%) | 0 / 96 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Parapsoriasis | | | |

| | | | |
|--|-----------------------|-----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 1240 (0.00%) 0 | 0 / 2486 (0.00%) 0 | 0 / 96 (0.00%) 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 3 / 1240 (0.24%) | 58 / 2486 (2.33%) | 1 / 96 (1.04%) |
| occurrences (all) | 3 | 60 | 1 |
| Attention deficit hyperactivity disorder | | | |
| subjects affected / exposed | 6 / 1240 (0.48%) | 41 / 2486 (1.65%) | 0 / 96 (0.00%) |
| occurrences (all) | 6 | 41 | 0 |
| Infections and infestations | | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 4 / 1240 (0.32%) | 11 / 2486 (0.44%) | 0 / 96 (0.00%) |
| occurrences (all) | 4 | 12 | 0 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 3 / 2486 (0.12%) | 1 / 96 (1.04%) |
| occurrences (all) | 0 | 3 | 1 |
| COVID-19 | | | |
| subjects affected / exposed | 34 / 1240 (2.74%) | 382 / 2486 (15.37%) | 11 / 96 (11.46%) |
| occurrences (all) | 35 | 383 | 11 |
| Influenza | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 19 / 2486 (0.76%) | 1 / 96 (1.04%) |
| occurrences (all) | 0 | 20 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 6 / 1240 (0.48%) | 60 / 2486 (2.41%) | 4 / 96 (4.17%) |
| occurrences (all) | 6 | 64 | 4 |
| Asymptomatic COVID-19 | | | |
| subjects affected / exposed | 25 / 1240 (2.02%) | 81 / 2486 (3.26%) | 6 / 96 (6.25%) |
| occurrences (all) | 25 | 82 | 6 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 1240 (0.00%) | 2 / 2486 (0.08%) | 0 / 96 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 28 / 1240 (2.26%) | 257 / 2486 (10.34%) | 3 / 96 (3.13%) |
| occurrences (all) | 32 | 293 | 3 |

| Non-serious adverse events | Part 2: mRNA-1273 50 ug BD | Part 3: mRNA-1273.222 50 ug Second Dose | Part 2: mRNA-1273 50 µg |
|--|--|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 7 / 19 (36.84%) | 51 / 335 (15.22%) | 12 / 52 (23.08%) |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 5 / 335 (1.49%) 5 | 1 / 52 (1.92%) 1 |
| General disorders and administration site conditions Injection site lymphadenopathy subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 0 / 335 (0.00%) 0 | 1 / 52 (1.92%) 1 |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 1 / 335 (0.30%) 1 | 0 / 52 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Mechanical urticaria subjects affected / exposed occurrences (all) Parapsoriasis subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1 | 0 / 335 (0.00%) 0 0 / 335 (0.00%) 0 | 0 / 52 (0.00%) 0 0 / 52 (0.00%) 0 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Attention deficit hyperactivity disorder subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 0 / 19 (0.00%) 0 | 1 / 335 (0.30%) 1 0 / 335 (0.00%) 0 | 0 / 52 (0.00%) 0 3 / 52 (5.77%) 3 |
| Infections and infestations Respiratory tract infection subjects affected / exposed occurrences (all) Parainfluenzae virus infection subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 1 / 19 (5.26%) 1 | 22 / 335 (6.57%) 30 0 / 335 (0.00%) 0 | 0 / 52 (0.00%) 0 0 / 52 (0.00%) 0 |

| | | | |
|-----------------------------------|-----------------|------------------|----------------|
| COVID-19 | | | |
| subjects affected / exposed | 3 / 19 (15.79%) | 0 / 335 (0.00%) | 3 / 52 (5.77%) |
| occurrences (all) | 3 | 0 | 3 |
| Influenza | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | 0 / 335 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 2 | 0 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 23 / 335 (6.87%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 26 | 0 |
| Asymptomatic COVID-19 | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 335 (0.00%) | 2 / 52 (3.85%) |
| occurrences (all) | 0 | 0 | 2 |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 1 / 335 (0.30%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 335 (0.00%) | 2 / 52 (3.85%) |
| occurrences (all) | 1 | 0 | 2 |

| Non-serious adverse events | Part 1C-2: mRNA-1273 50 µg BD | Part 1C-1: mRNA-1273 50 µg BD | Part 3: mRNA1273.222 50 |
|---|-------------------------------|-------------------------------|-------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 28 / 155 (18.06%) | 429 / 1408 (30.47%) | 77 / 388 (19.85%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 155 (0.65%) | 28 / 1408 (1.99%) | 20 / 388 (5.15%) |
| occurrences (all) | 1 | 29 | 27 |
| General disorders and administration site conditions | | | |
| Injection site lymphadenopathy | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 5 / 1408 (0.36%) | 0 / 388 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 155 (0.00%) | 6 / 1408 (0.43%) | 1 / 388 (0.26%) |
| occurrences (all) | 0 | 6 | 1 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|--|------------------------|----------------------------|------------------------|
| Mechanical urticaria subjects affected / exposed occurrences (all) | 0 / 155 (0.00%) 0 | 0 / 1408 (0.00%) 0 | 0 / 388 (0.00%) 0 |
| Parapsoriasis subjects affected / exposed occurrences (all) | 0 / 155 (0.00%) 0 | 0 / 1408 (0.00%) 0 | 0 / 388 (0.00%) 0 |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 1 / 155 (0.65%) 1 | 26 / 1408 (1.85%) 27 | 0 / 388 (0.00%) 0 |
| Attention deficit hyperactivity disorder subjects affected / exposed occurrences (all) | 2 / 155 (1.29%) 2 | 14 / 1408 (0.99%) 14 | 0 / 388 (0.00%) 0 |
| Infections and infestations | | | |
| Respiratory tract infection subjects affected / exposed occurrences (all) | 1 / 155 (0.65%) 1 | 2 / 1408 (0.14%) 2 | 26 / 388 (6.70%) 34 |
| Parainfluenzae virus infection subjects affected / exposed occurrences (all) | 1 / 155 (0.65%) 1 | 2 / 1408 (0.14%) 2 | 1 / 388 (0.26%) 1 |
| COVID-19 subjects affected / exposed occurrences (all) | 10 / 155 (6.45%) 10 | 257 / 1408 (18.25%) 267 | 0 / 388 (0.00%) 0 |
| Influenza subjects affected / exposed occurrences (all) | 7 / 155 (4.52%) 8 | 30 / 1408 (2.13%) 30 | 5 / 388 (1.29%) 6 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 155 (0.00%) 0 | 16 / 1408 (1.14%) 17 | 30 / 388 (7.73%) 34 |
| Asymptomatic COVID-19 subjects affected / exposed occurrences (all) | 2 / 155 (1.29%) 2 | 39 / 1408 (2.77%) 39 | 0 / 388 (0.00%) 0 |
| Tooth abscess subjects affected / exposed occurrences (all) | 0 / 155 (0.00%) 0 | 1 / 1408 (0.07%) 1 | 0 / 388 (0.00%) 0 |
| Upper respiratory tract infection | | | |

| | | | |
|-----------------------------|-----------------|-------------------|-----------------|
| subjects affected / exposed | 6 / 155 (3.87%) | 81 / 1408 (5.75%) | 4 / 388 (1.03%) |
| occurrences (all) | 8 | 101 | 4 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 23 March 2021 | - Addition of the crossover design - Study design was updated to describe the updated crossover design of the study, including Part A (the Blinded Phase) and Part B (the Open-label Observational Phase). |
| 27 July 2021 | - Added CDC case definitions for myocarditis and pericarditis. - Added assessment of risk of myocarditis and pericarditis. |
| 04 November 2021 | - Added Part C to the study. - Updated long-term analysis and Booster Phase analysis. - Addition of booster interim analyses. - Added nasal swab for samples for SARS-CoV-2. - Clarified that only Part A and Part C will have primary immunogenicity analyses. |
| 25 January 2022 | - Added Part 1C-2 and Part 2. |
| 11 October 2022 | - Modifications to primary objectives and endpoints, secondary endpoints, statistical hypothesis, power and sample size, analysis, and procedures in Part 2 of the study. - Clarified that immunogenicity hypothesis testing will not be performed for Part 2. - Discontinuation of enrollment in Part 1C-2 and Part 2 of the study. - Clarified that Convalescent Visits are applicable to Part 1A and 1B only. - Removed BD from Part 2 and convalescent visits from Part 1C-1, Part 1C-2, and Part 2 of the study. - Added an open-label Part 3 of the study. - Updated exclusion criteria. - Updated study assessments and procedures. |
| 22 June 2023 | -Modifications to primary and (key) secondary immunogenicity objectives and endpoints, statistical hypothesis, power and sample size, and analysis in Part 3 of the study. - Updated inclusion/exclusion criteria - Clarifying the definition of the SARS-CoV-2 status at baseline. |
| 19 October 2023 | - Updated Part 3 study design and objective to single dosing. - Updated to single dosing in Part 3. - Reduced safety follow-up duration for Part 3 participants who receive Dose 2. - Updated timepoints for collection of blood samples and nasopharyngeal or nasal swab samples. -Clarification of the end-of-study definition. - Clarification added on the time period for recording all concomitant medications and nonstudy vaccinations in the electronic case report form. - Updated safety assessments related to single dosing in Part 3. -Updated PP Immunogenicity Subset for Part 3. - Addition of schedule of assessments for Part 3 participants who receive only 1 dose. - Addition of schedule of assessments for Part 2 participants who receive the booster dose. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Part 1C-2 enrollment discontinued before planned number of participants. Part 2 discontinued early due to availability of updated variant vaccine (mRNA-1273.222); no hypothesis testing done for primary endpoint/other endpoints not assessed.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/34379915>

<http://www.ncbi.nlm.nih.gov/pubmed/39091673>

<http://www.ncbi.nlm.nih.gov/pubmed/39332418>