



Clinical trial results:

A Phase 3b Open-label Extension Study Evaluating the Safety of Elexacaftor/Tezacaftor/Ivacaftor Combination Therapy in Cystic Fibrosis Subjects

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2019-003455-11 |
| Trial protocol | GB DE BE |
| Global end of trial date | 21 December 2022 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 06 July 2023 |
| First version publication date | 06 July 2023 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | VX19-445-115 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04362761 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Vertex Pharmaceuticals Incorporated |
| Sponsor organisation address | 50 Northern Avenue , Boston, Massachusetts, United States, |
| Public contact | Medical Information, Vertex Pharmaceuticals Incorporated, +1 617-341-6777, medicalinfo@vrtx.com |
| Scientific contact | Medical Information, Vertex Pharmaceuticals Incorporated, +1 617-341-6777, medicalinfo@vrtx.com |

Notes:

Paediatric regulatory details

| | |
|--|-----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| 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 | 18 January 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 21 December 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 21 December 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of elexacaftor (VX-445; ELX)/tezacaftor (TEZ)/ivacaftor (IVA)

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 04 May 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United Kingdom: 86 |
| Country: Number of subjects enrolled | Belgium: 20 |
| Country: Number of subjects enrolled | Germany: 36 |
| Country: Number of subjects enrolled | Australia: 30 |
| Worldwide total number of subjects | 172 |
| EEA total number of subjects | 56 |

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) | 51 |
| Adults (18-64 years) | 121 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total 172 subjects were enrolled from the parent study VX18-445-109 (NCT04105972). The study was conducted in 2 parts, Part A and Part B.

Period 1

| | |
|------------------------------|----------------|
| Period 1 title | Part A |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|---------------------|
| Arm title | Part A: ELX/TEZ/IVA |
|-----------|---------------------|

Arm description:

Subjects received ELX (elexacaftor) 200 milligram (mg) once daily (qd)/TEZ 100 mg qd/IVA 150 mg every 12 hours (q12h) in the treatment period for 48 weeks.

| | |
|--|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Elexacaftor/Tezacaftor/Ivacaftor |
| Investigational medicinal product code | VX-445/VX-661/VX-770 |
| Other name | ELX/TEZ/IVA |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received ELX/TEZ/IVA fixed dose combination once daily in the morning.

| | |
|--|-----------|
| Investigational medicinal product name | Ivacaftor |
| Investigational medicinal product code | VX-770 |
| Other name | IVA |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received IVA once daily in the evening.

| | |
|--|---------------------|
| Number of subjects in period 1 | Part A: ELX/TEZ/IVA |
| Started | 172 |
| Completed | 159 |
| Not completed | 13 |
| Adverse Event | 2 |
| Other | 5 |
| Withdrawal of consent (not due to AE) | 4 |
| Commercial drug is available for subject | 2 |

Period 2

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

Arms

| | |
|------------------|---------------------|
| Arm title | Part B: ELX/TEZ/IVA |
|------------------|---------------------|

Arm description:

Subjects received ELX 200 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in the treatment period up to 86 weeks.

| | |
|--|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Elexacaftor/Tezacaftor/Ivacaftor |
| Investigational medicinal product code | VX-445/VX-661/VX-770 |
| Other name | ELX/TEZ/IVA |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received ELX/TEZ/IVA fixed dose combination once daily in the morning.

| | |
|--|-----------|
| Investigational medicinal product name | Ivacaftor |
| Investigational medicinal product code | VX-770 |
| Other name | IVA |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received IVA once daily in the evening.

| | |
|---|---------------------|
| Number of subjects in period 2^[1] | Part B: ELX/TEZ/IVA |
| Started | 50 |
| Completed | 0 |
| Not completed | 50 |
| Other | 4 |
| Commercial drug is available for subject | 46 |

Notes:

[1] - 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: A total of 172 subjects were enrolled in the parent study on Part A. However, only 50 subjects rolled over to Part B from Part A of the study.

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | Part A |
|-----------------------|--------|

Reporting group description:

Subjects received ELX 200 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in the treatment period for 48 weeks.

| Reporting group values | Part A | Total | |
|------------------------|--------|-------|--|
| Number of subjects | 172 | 172 | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|--------|-----|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 27.9 | | |
| standard deviation | ± 11.4 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 87 | 87 | |
| Male | 85 | 85 | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 3 | 3 | |
| Not Hispanic or Latino | 167 | 167 | |
| Not collected per local regulations | 2 | 2 | |
| Race | | | |
| Units: Subjects | | | |
| White | 169 | 169 | |
| Black or African American | 0 | 0 | |
| Asian | 2 | 2 | |
| American Indian or Alaska Native | 0 | 0 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Not collected per local regulations | 0 | 0 | |
| White, Asian | 1 | 1 | |

End points

End points reporting groups

| | |
|---|---------------------|
| Reporting group title | Part A: ELX/TEZ/IVA |
| Reporting group description: Subjects received ELX (elexacaftor) 200 milligram (mg) once daily (qd)/TEZ 100 mg qd/IVA 150 mg every 12 hours (q12h) in the treatment period for 48 weeks. | |
| Reporting group title | Part B: ELX/TEZ/IVA |
| Reporting group description: Subjects received ELX 200 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in the treatment period up to 86 weeks. | |

Primary: Part A: Safety and Tolerability as Assessed by Number of Subjects With Treatment- Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

| | |
|--|--|
| End point title | Part A: Safety and Tolerability as Assessed by Number of Subjects With Treatment- Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) ^[1] |
| End point description: Safety set included all subjects who received at least 1 dose of study drug. | |
| End point type | Primary |
| End point timeframe: From Day 1 up to Week 52 | |

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: Only descriptive statistics were planned. No statistical comparisons were planned for this endpoint.

| | | | | |
|-----------------------------|------------------------|--|--|--|
| End point values | Part A: ELX/TEZ/IVA | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 172 | | | |
| Units: Subjects | | | | |
| Subjects with TEAEs | 160 | | | |
| Subjects with SAEs | 26 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Safety and Tolerability as Assessed by Number of Subjects With Treatment- Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

| | |
|--|--|
| End point title | Part B: Safety and Tolerability as Assessed by Number of Subjects With Treatment- Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) ^[2] |
| End point description: Safety set included all subjects who received at least 1 dose of study drug. | |
| End point type | Primary |

End point timeframe:

From Day 1 up to Week 86

Notes:

[2] - 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: Only descriptive statistics were planned. No statistical comparisons were planned for this endpoint.

| | | | | |
|-----------------------------|------------------------|--|--|--|
| End point values | Part B: ELX/TEZ/IVA | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: Subjects | | | | |
| Subjects with TEAEs | 50 | | | |
| Subjects with SAEs | 8 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Week 52 for Part A, Day 1 up to Week 86 for Part B

Adverse event reporting additional description:

MedDRA 24.0 applied for Part A and MedDRA 25.1 applied for Part B.

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

Dictionary used

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

| | |
|--------------------|-----------|
| Dictionary version | 24.0,25.1 |
|--------------------|-----------|

Reporting groups

| | |
|-----------------------|---------------------|
| Reporting group title | Part A: ELX/TEZ/IVA |
|-----------------------|---------------------|

Reporting group description:

Subjects received ELX 200 mg qd/TEZ 100 mg qd/IVA 150 mg qd in the treatment period for 48 weeks.

| | |
|-----------------------|---------------------|
| Reporting group title | Part B: ELX/TEZ/IVA |
|-----------------------|---------------------|

Reporting group description:

Subjects received ELX 200 mg qd/TEZ 100 mg qd/IVA 150 mg qd in the treatment period up to 86 weeks.

| Serious adverse events | Part A: ELX/TEZ/IVA | Part B: ELX/TEZ/IVA | |
|--|---------------------|---------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 26 / 172 (15.12%) | 8 / 50 (16.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| General disorders and administration site conditions | | | |
| Vascular device occlusion | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Heavy menstrual bleeding | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine polyp | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|----------------|--|
| Respiratory, thoracic and mediastinal disorders | | | |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasal polyps | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Productive cough | | | |
| subjects affected / exposed | 0 / 172 (0.00%) | 1 / 50 (2.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Aggression | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dissociative disorder | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 2 / 172 (1.16%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alanine aminotransferase increased | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 2 / 172 (1.16%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Forced expiratory volume decreased | | | |
| subjects affected / exposed | 0 / 172 (0.00%) | 1 / 50 (2.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Limb traumatic amputation | | | |
| subjects affected / exposed | 0 / 172 (0.00%) | 1 / 50 (2.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus arrest | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|----------------|--|
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Loss of consciousness | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Ileus | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 172 (0.00%) | 1 / 50 (2.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema nodosum | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Dupuytren's contracture | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Chronic sinusitis | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infective pulmonary exacerbation of cystic fibrosis | | | |
| subjects affected / exposed | 8 / 172 (4.65%) | 5 / 50 (10.00%) | |
| occurrences causally related to treatment / all | 1 / 9 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia pseudomonal | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|----------------|--|
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 1 / 172 (0.58%) | 0 / 50 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Part A: ELX/TEZ/IVA | Part B: ELX/TEZ/IVA | |
|---|---------------------|---------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 127 / 172 (73.84%) | 47 / 50 (94.00%) | |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 11 / 172 (6.40%) | 1 / 50 (2.00%) | |
| occurrences (all) | 12 | 1 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 11 / 172 (6.40%) | 0 / 50 (0.00%) | |
| occurrences (all) | 13 | 0 | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 9 / 172 (5.23%) | 1 / 50 (2.00%) | |
| occurrences (all) | 18 | 1 | |
| Injury, poisoning and procedural complications | | | |
| Vaccination complication | | | |
| subjects affected / exposed | 24 / 172 (13.95%) | 0 / 50 (0.00%) | |
| occurrences (all) | 36 | 0 | |
| Procedural pain | | | |
| subjects affected / exposed | 2 / 172 (1.16%) | 3 / 50 (6.00%) | |
| occurrences (all) | 2 | 3 | |
| Nervous system disorders | | | |
| Dizziness | | | |

| | | | |
|--|-------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 11 / 172 (6.40%) 17 | 0 / 50 (0.00%) 0 | |
| Headache subjects affected / exposed occurrences (all) | 42 / 172 (24.42%) 73 | 10 / 50 (20.00%) 18 | |
| General disorders and administration site conditions | | | |
| Pyrexia subjects affected / exposed occurrences (all) | 7 / 172 (4.07%) 9 | 8 / 50 (16.00%) 8 | |
| Fatigue subjects affected / exposed occurrences (all) | 13 / 172 (7.56%) 14 | 1 / 50 (2.00%) 1 | |
| Malaise subjects affected / exposed occurrences (all) | 3 / 172 (1.74%) 4 | 3 / 50 (6.00%) 3 | |
| Immune system disorders | | | |
| Immunisation reaction subjects affected / exposed occurrences (all) | 0 / 172 (0.00%) 0 | 7 / 50 (14.00%) 10 | |
| Gastrointestinal disorders | | | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 12 / 172 (6.98%) 15 | 2 / 50 (4.00%) 3 | |
| Constipation subjects affected / exposed occurrences (all) | 10 / 172 (5.81%) 11 | 4 / 50 (8.00%) 5 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 13 / 172 (7.56%) 27 | 2 / 50 (4.00%) 2 | |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 8 / 172 (4.65%) 20 | 3 / 50 (6.00%) 3 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 16 / 172 (9.30%) 32 | 3 / 50 (6.00%) 4 | |
| Nausea | | | |

| | | | |
|--|-------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 9 / 172 (5.23%) 13 | 1 / 50 (2.00%) 1 | |
| Vomiting subjects affected / exposed occurrences (all) | 8 / 172 (4.65%) 8 | 3 / 50 (6.00%) 3 | |
| Respiratory, thoracic and mediastinal disorders Sputum increased subjects affected / exposed occurrences (all) | 19 / 172 (11.05%) 20 | 5 / 50 (10.00%) 6 | |
| Productive cough subjects affected / exposed occurrences (all) | 4 / 172 (2.33%) 7 | 6 / 50 (12.00%) 10 | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 16 / 172 (9.30%) 19 | 5 / 50 (10.00%) 7 | |
| Cough subjects affected / exposed occurrences (all) | 23 / 172 (13.37%) 29 | 5 / 50 (10.00%) 7 | |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 12 / 172 (6.98%) 17 | 2 / 50 (4.00%) 2 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 12 / 172 (6.98%) 15 | 4 / 50 (8.00%) 4 | |
| Infections and infestations Infective pulmonary exacerbation of cystic fibrosis subjects affected / exposed occurrences (all) | 17 / 172 (9.88%) 22 | 21 / 50 (42.00%) 29 | |
| COVID-19 subjects affected / exposed occurrences (all) | 2 / 172 (1.16%) 2 | 17 / 50 (34.00%) 17 | |
| Influenza | | | |

| | | | |
|-----------------------------------|-------------------|------------------|--|
| subjects affected / exposed | 2 / 172 (1.16%) | 3 / 50 (6.00%) | |
| occurrences (all) | 2 | 3 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 28 / 172 (16.28%) | 16 / 50 (32.00%) | |
| occurrences (all) | 39 | 23 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 10 / 172 (5.81%) | 11 / 50 (22.00%) | |
| occurrences (all) | 13 | 15 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 04 January 2021 | Amended to extend treatment period. |
| 19 March 2021 | Amended to allow subjects who depart this study to enroll in another qualified Vertex study to return to this study if they did not receive study drug in the Treatment Period of the other qualified Vertex study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported