# Clinical trial results:
# A Phase 3, Open-label Study Evaluating the Long-term Safety and Efficacy of VX-445 Combination Therapy in Subjects With Cystic Fibrosis Who Are Heterozygous for the F508del Mutation and a Gating or Residual Function Mutation (F/G and F/RF Genotypes)

## Summary

| | |
|---|---|
| EudraCT number | 2019-000833-37 |
| Trial protocol | DE GB IE DK FR BE ES NL IT |
| Global end of trial date | 16 December 2022 |

### Results information

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 01 July 2023 |
| First version publication date | 01 July 2023 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | VX18-445-110 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04058366 |
| 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 Monitor, Vertex Pharmaceuticals Incorporated, +1 617-341-6777, medicalinfo@vrtx.com |
| Scientific contact | Medical Monitor, 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 | 09 February 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 16 December 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 December 2022 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of VX-445/tezacaftor (TEZ)/ivacaftor (IVA) in subjects with cystic fibrosis who are heterozygous for the F508del mutation and a gating (F/G) or residual function (F/RF) mutation.

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 | 05 December 2019 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 34 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Netherlands: 14 |
| Country: Number of subjects enrolled | Spain: 12 |
| Country: Number of subjects enrolled | United Kingdom: 20 |
| Country: Number of subjects enrolled | Belgium: 13 |
| Country: Number of subjects enrolled | Denmark: 2 |
| Country: Number of subjects enrolled | France: 27 |
| Country: Number of subjects enrolled | Germany: 14 |
| Country: Number of subjects enrolled | Ireland: 10 |
| Country: Number of subjects enrolled | Italy: 20 |
| Country: Number of subjects enrolled | United States: 81 |
| Country: Number of subjects enrolled | Australia: 26 |
| Country: Number of subjects enrolled | Canada: 12 |
| Worldwide total number of subjects | 251 |
| EEA total number of subjects | 112 |

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) | 22 |
| Adults (18-64 years) | 224 |
| From 65 to 84 years | 5 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects from parent study VX18-445-104 (NCT04058353) were enrolled in this study. A total of 251 subjects were enrolled in this study.

### 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 96 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 (FDC) 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 | 251 |
| Completed | 215 |
| Not completed | 36 |
| Commercial drug is available for subjects | 6 |
| Death | 1 |
| Other | 6 |
| Adverse event | 14 |
| Other non-compliance | 2 |

| | |
|---|---|
| Withdrawal of Consent (not due to AE) | 7 |

## 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 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 (FDC) 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 | 84 |
| Completed | 1 |
| Not completed | 83 |
| Commercial drug is available for subjects | 81 |
| Physician decision | 1 |
| Withdrawal of Consent (not due to AE) | 1 |

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 251 subjects were enrolled from the parent study on Part A. However, only 84 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 every 12 hours (q12h) in the treatment period for 96 weeks. | |

| Reporting group values | Part A | Total | |
|---|---|---|---|
| Number of subjects | 251 | 251 | |
| Age categorical<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age continuous<br>Units: years | | | |
| arithmetic mean | 37.9 | | |
| standard deviation | ± 14.4 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 124 | 124 | |
| Male | 127 | 127 | |

## 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 96 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 for 48 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 in the treatment period. | |
| End point type | Primary |
| End point timeframe: | |
| From Baseline up to Week 100 | |

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 | 251 | | | |
| Units: Subjects | | | | |
| Subjects with TEAEs | 241 | | | |
| Subjects with SAEs | 38 | | | |

### 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 in the treatment period. | |
| End point type | Primary |

End point timeframe:

From Baseline up to Week 52

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 | 84 | | | |
| Units: Subjects | | | | |
| Subjects with TEAEs | 62 | | | |
| Subjects with SAEs | 3 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Day 1 through Safety follow-up (up to Week 100 for Part A and up to Week 52 for Part B) | |
| Adverse event reporting additional description: | |
| MedDRA 24.1 for Part A and MedDRA 25.1 for Part B | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24.1, 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 q12h in the treatment period for 96 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 for 48 weeks. | |

| Serious adverse events | Part A: ELX/TEZ/IVA | Part B: ELX/TEZ/IVA | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 38 / 251 (15.14%) | 3 / 84 (3.57%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 1 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon cancer | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Intraductal proliferative breast lesion | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 84 (1.19%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Epididymal cyst | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (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 | 3 / 251 (1.20%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax spontaneous | | | |
| subjects affected / exposed | 2 / 251 (0.80%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 84 (1.19%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |

| | | | |
|---|---|---|---|
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Tendon rupture | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Palpitations | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (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 | | | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematochezia | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 84 (1.19%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Vomiting | | | |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 84 (1.19%) | |
| 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 | | | |
| Rash erythematous | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 2 / 251 (0.80%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Aspergilloma | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infective exacerbation of bronchiectasis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 251 (0.80%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infective pulmonary exacerbation of cystic fibrosis | | | |
| subjects affected / exposed | 16 / 251 (6.37%) | 1 / 84 (1.19%) | |
| occurrences causally related to treatment / all | 0 / 25 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 84 (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 | 223 / 251 (88.84%) | 48 / 84 (57.14%) | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 16 / 251 (6.37%) | 0 / 84 (0.00%) | |
| occurrences (all) | 25 | 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 16 / 251 (6.37%) | 0 / 84 (0.00%) | |
| occurrences (all) | 23 | 0 | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 26 / 251 (10.36%) | 1 / 84 (1.19%) | |
| occurrences (all) | 26 | 1 | |
| Injury, poisoning and procedural complications | | | |
| Vaccination complication | | | |
| subjects affected / exposed | 28 / 251 (11.16%) | 0 / 84 (0.00%) | |
| occurrences (all) | 46 | 0 | |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Headache | | | |
| subjects affected / exposed | 71 / 251 (28.29%) | 4 / 84 (4.76%) | |
| occurrences (all) | 188 | 6 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 40 / 251 (15.94%) | 0 / 84 (0.00%) | |
| occurrences (all) | 52 | 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 36 / 251 (14.34%) | 2 / 84 (2.38%) | |
| occurrences (all) | 43 | 2 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 13 / 251 (5.18%) | 2 / 84 (2.38%) | |
| occurrences (all) | 15 | 4 | |
| Constipation | | | |
| subjects affected / exposed | 17 / 251 (6.77%) | 1 / 84 (1.19%) | |
| occurrences (all) | 26 | 1 | |
| Diarrhoea | | | |
| subjects affected / exposed | 48 / 251 (19.12%) | 4 / 84 (4.76%) | |
| occurrences (all) | 74 | 6 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 13 / 251 (5.18%) | 1 / 84 (1.19%) | |
| occurrences (all) | 15 | 1 | |
| Nausea | | | |
| subjects affected / exposed | 28 / 251 (11.16%) | 2 / 84 (2.38%) | |
| occurrences (all) | 83 | 8 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 65 / 251 (25.90%) | 5 / 84 (5.95%) | |
| occurrences (all) | 96 | 5 | |
| Dyspnoea | | | |
| subjects affected / exposed | 29 / 251 (11.55%) | 2 / 84 (2.38%) | |
| occurrences (all) | 38 | 2 | |
| Haemoptysis | | | |
| subjects affected / exposed | 20 / 251 (7.97%) | 5 / 84 (5.95%) | |
| occurrences (all) | 44 | 9 | |

| | | | |
|---|---|---|---|
| Nasal congestion | | | |
| subjects affected / exposed | 18 / 251 (7.17%) | 1 / 84 (1.19%) | |
| occurrences (all) | 22 | 1 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 42 / 251 (16.73%) | 5 / 84 (5.95%) | |
| occurrences (all) | 56 | 6 | |
| Productive cough | | | |
| subjects affected / exposed | 17 / 251 (6.77%) | 1 / 84 (1.19%) | |
| occurrences (all) | 21 | 1 | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 19 / 251 (7.57%) | 0 / 84 (0.00%) | |
| occurrences (all) | 20 | 0 | |
| Sinus congestion | | | |
| subjects affected / exposed | 15 / 251 (5.98%) | 0 / 84 (0.00%) | |
| occurrences (all) | 23 | 0 | |
| Sputum increased | | | |
| subjects affected / exposed | 34 / 251 (13.55%) | 3 / 84 (3.57%) | |
| occurrences (all) | 58 | 4 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 19 / 251 (7.57%) | 0 / 84 (0.00%) | |
| occurrences (all) | 22 | 0 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 16 / 251 (6.37%) | 0 / 84 (0.00%) | |
| occurrences (all) | 17 | 0 | |
| Anxiety | | | |
| subjects affected / exposed | 28 / 251 (11.16%) | 1 / 84 (1.19%) | |
| occurrences (all) | 31 | 1 | |
| Insomnia | | | |
| subjects affected / exposed | 15 / 251 (5.98%) | 2 / 84 (2.38%) | |
| occurrences (all) | 29 | 4 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 27 / 251 (10.76%) | 2 / 84 (2.38%) | |
| occurrences (all) | 33 | 2 | |

| | | | |
|---|---|---|---|
| Back pain | | | |
| subjects affected / exposed | 20 / 251 (7.97%) | 2 / 84 (2.38%) | |
| occurrences (all) | 20 | 2 | |
| Myalgia | | | |
| subjects affected / exposed | 16 / 251 (6.37%) | 1 / 84 (1.19%) | |
| occurrences (all) | 23 | 1 | |
| Pain in extremity | | | |
| subjects affected / exposed | 13 / 251 (5.18%) | 0 / 84 (0.00%) | |
| occurrences (all) | 18 | 0 | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 52 / 251 (20.72%) | 17 / 84 (20.24%) | |
| occurrences (all) | 53 | 17 | |
| Infective pulmonary exacerbation of cystic fibrosis | | | |
| subjects affected / exposed | 61 / 251 (24.30%) | 17 / 84 (20.24%) | |
| occurrences (all) | 102 | 26 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 40 / 251 (15.94%) | 7 / 84 (8.33%) | |
| occurrences (all) | 60 | 9 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 15 / 251 (5.98%) | 6 / 84 (7.14%) | |
| occurrences (all) | 17 | 7 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 14 May 2021 | Amended to extend the treatment Period by an additional 48 weeks (Part B)to evaluate the safety of ELX/TEZ/IVA beyond 96 weeks of treatment; Revised the statistical analysis section to reflect the updated study design; Clarified language regarding height measurement and ophthalmological examination timings for Parts A and B. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported