



Clinical trial results:

A Phase 3b Open-label Study Evaluating the Effects of Elexacaftor/Tezacaftor/Ivacaftor on Cough and Physical Activity in Cystic Fibrosis Subjects 12 Years of Age and Older Who Are Heterozygous for the F508del Mutation and a Minimal Function Mutation (F/MF)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2021-001628-16 |
| Trial protocol | ES BE |
| Global end of trial date | 26 July 2022 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 |
| This version publication date | 08 February 2023 |
| First version publication date | 08 February 2023 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | VX20-445-126 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04969224 |
| 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 | 14 September 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 26 July 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 26 July 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effects of elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) on cough and physical activity using wearable technology in Cystic Fibrosis(CF) subjects.

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 | 12 October 2021 |
| 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 | Spain: 7 |
| Country: Number of subjects enrolled | Belgium: 31 |
| Country: Number of subjects enrolled | Canada: 7 |
| Country: Number of subjects enrolled | Australia: 37 |
| Worldwide total number of subjects | 82 |
| EEA total number of subjects | 38 |

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) | 24 |
| Adults (18-64 years) | 58 |
| From 65 to 84 years | 0 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was conducted in subjects with cystic fibrosis, aged 12 years and older, who are heterozygous for the F508del mutation and the minimal function mutation (F/MF).

Period 1

| | |
|------------------------------|---------------------------------|
| Period 1 title | Overall Period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|-------------|
| Arm title | ELX/TEZ/IVA |
|-----------|-------------|

Arm description:

Subjects received ELX/TEZ/IVA fixed-dose combination (FDC) in the morning and IVA in the evening.

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

Dosage and administration details:

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

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

Dosage and administration details:

Subjects received IVA dose once daily in the evening.

| Number of subjects in period 1 ^[1] | ELX/TEZ/IVA |
|---|-------------|
| Started | 81 |
| Completed | 80 |
| Not completed | 1 |
| Adverse event | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 82 subjects were enrolled in the study. One subject was enrolled but not dosed in this study. Therefore, data for 81 subjects are reported in the subject disposition and baseline characteristics sections.

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------|
| Reporting group title | Overall Period |
|-----------------------|----------------|

Reporting group description:

Subjects received ELX/TEZ/IVA fixed-dose combination (FDC) in the morning and IVA in the evening.

| Reporting group values | Overall Period | Total | |
|-----------------------------------|----------------|-------|--|
| Number of subjects | 81 | 81 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Less than (<)18 years | 24 | 24 | |
| More than or equal to (≥)18 years | 57 | 57 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 25.7 | | |
| standard deviation | ± 9.6 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 37 | 37 | |
| Male | 44 | 44 | |

End points

End points reporting groups

| | |
|---|-------------|
| Reporting group title | ELX/TEZ/IVA |
| Reporting group description: | |
| Subjects received ELX/TEZ/IVA fixed-dose combination (FDC) in the morning and IVA in the evening. | |

Primary: Percent Reduction From Baseline in Cough Frequency (cough events per day) to the Average of Week 8 Through Week 12

| | |
|-----------------|---|
| End point title | Percent Reduction From Baseline in Cough Frequency (cough events per day) to the Average of Week 8 Through Week 12 ^[1] |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline, Week 8 through Week 12

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: Participants' post-baseline values were compared to their baseline values with a mixed model for repeated measures with change from baseline at each post-baseline visit on the natural log scale as the dependent variable. The primary result obtained from the model was the estimated percent reduction in cough frequency from baseline to the average of Week 8 through Week 12, i.e. $100\% \times (1 - \exp(\text{LS mean}))$.

| End point values | ELX/TEZ/IVA | | | |
|----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 80 | | | |
| Units: Percent | | | | |
| number (confidence interval 95%) | 91.7 (89.2 to 93.6) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Week 17

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 25.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | ELX/TEZ/IVA |
|-----------------------|-------------|

Reporting group description:

Subjects received ELX/TEZ/IVA FDC in the morning and IVA in the evening.

| Serious adverse events | ELX/TEZ/IVA | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 81 (2.47%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Gastrointestinal disorders | | | |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 81 (1.23%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 81 (1.23%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | ELX/TEZ/IVA | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 56 / 81 (69.14%) | | |
| Nervous system disorders | | | |
| Headache | | | |

| | | | |
|---|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 14 / 81 (17.28%) 19 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 8 / 81 (9.88%) 10 | | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 7 / 81 (8.64%) 7 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 11 / 81 (13.58%) 13 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 6 / 81 (7.41%) 6 | | |
| Nasal congestion subjects affected / exposed occurrences (all) | 5 / 81 (6.17%) 5 | | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 8 / 81 (9.88%) 8 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash subjects affected / exposed occurrences (all) | 5 / 81 (6.17%) 6 | | |
| Infections and infestations | | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 13 / 81 (16.05%) 15 | | |
| COVID-19 subjects affected / exposed occurrences (all) | 13 / 81 (16.05%) 15 | | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 7 / 81 (8.64%) 7 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported