Clinical trial results:
A Phase 3, Open-label Study Evaluating the Long-term Safety and Efficacy of VX-445/TEZ/IVA Combination Therapy in Subjects With Cystic Fibrosis Who Are 6 Years of Age and Older

Summary

EudraCT number	2019-001827-11
Trial protocol	GB IE
Global end of trial date	24 February 2024

Results information

Result version number	v1 (current)
This version publication date	07 September 2024
First version publication date	07 September 2024

Trial information

Trial identification

Sponsor protocol code	VX19-445-107

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04183790
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-002324-PIP01-17
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	20 March 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 February 2024
Global end of trial reached?	Yes
Global end of trial date	24 February 2024
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 elexacaftor (ELX)/tezacaftor (TEZ)/ivacaftor (IVA) in subjects with cystic fibrosis (CF) who are 6 years of age and older

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	17 February 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	45 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Ireland: 5
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	United States: 39
Worldwide total number of subjects	64
EEA total number of subjects	5

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)	64
Adolescents (12-17 years)	0

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

Subject disposition

Recruitment

Recruitment details:

The study was conducted in two parts, Part A and Part B. Subjects of both Parts A and B received the same treatment (ELX,TEZ,IVA). Therefore, results were planned to be collected and analyzed for the overall population of the study.

Pre-assignment

Screening details:

Subjects from parent study VX18-445-106 Part B (NCT03691779) were enrolled in this study. A total of 64 subjects were enrolled in this study.

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 greater than or equal to (≥) 6 years and less than (<) 12 years of age and weighing <30 kilograms (kg) received ELX (elexacaftor) 100 milligram (mg) once daily (qd) /TEZ (tezacaftor) 50 mg qd/IVA (ivacaftor) 75 mg every 12 hours (q12h) and those weighing (≥) 30 kg received ELX 200 mg qd/TEZ 100 mg qd/IVA 150 mg in the treatment period for 192 week. Subjects ≥ 12 years of age received ELX 200 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in the treatment period for 192 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	ELX/TEZ/IVA
Started	64
Part A completed	60
Rollover to Part B	48
Part B completed	39

Completed	39
Not completed	25
Subjects did not rollover to Part B	12
Adverse event	1
Withdrawal of Consent (not due to AE)	6
Commercial drug is available for subject	6

Baseline characteristics

Reporting groups	
Reporting group title	Overall Period
Reporting group description:	
Baseline data was analyzed on Full analysis set (FAS) which is defined as all subjects who received at least 1 dose of study drug.	

Reporting group values	Overall Period	Total	
Number of subjects	64	64	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	9.3		
standard deviation	± 1.8	-	
Gender categorical			
Units: Subjects			
Female	39	39	
Male	25	25	

End points

End points reporting groups

Reporting group title	ELX/TEZ/IVA

Reporting group description:

Subjects greater than or equal to (≥) 6 years and less than (<) 12 years of age and weighing <30 kilograms (kg) received ELX (elexacaftor) 100 milligram (mg) once daily (qd) /TEZ (tezacaftor) 50 mg qd/IVA (ivacaftor) 75 mg every 12 hours (q12h) and those weighing (≥) 30 kg received ELX 200 mg qd/TEZ 100 mg qd/IVA 150 mg in the treatment period for 192 week. Subjects ≥ 12 years of age received ELX 200 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in the treatment period for 192 weeks.

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

End point title	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 is defined as all subjects who received at least 1 dose of study drug in the study.

End point type	Primary

End point timeframe:

Day 1 up to Week 196

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	ELX/TEZ/IVA			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: Subjects				
Subjects with TEAEs	64			
Subjects with SAEs	7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Week 196

Adverse event reporting additional description:

Safety set included all subjects who received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	ELX/TEZ/IVA

Reporting group description:

Subjects ≥6 years and <12 years of age and weighing <30kg received ELX 100 mg qd /TEZ 50 mg qd/IVA 75 mg q12h and those weighing ≥30 kg received ELX 200 mg qd/TEZ 100 mg qd/IVA 150 mg in the treatment period for 192 weeks. Subjects ≥ 12 years of age received ELX 200 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in the treatment period for 192 weeks

Serious adverse events	ELX/TEZ/IVA		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 64 (10.94%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Haematuria traumatic			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Idiopathic intracranial hypertension			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences causally related to treatment / all	0 / 3		
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	62 / 64 (96.88%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	9		
Bacterial test positive			
subjects affected / exposed	7 / 64 (10.94%)		
occurrences (all)	12		
SARS-CoV-2 test positive			
subjects affected / exposed	8 / 64 (12.50%)		
occurrences (all)	8		
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	7		
Injury, poisoning and procedural complications			

Immunisation reaction subjects affected / exposed occurrences (all)	4 / 64 (6.25%) 4		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	26 / 64 (40.63%) 39		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all)	28 / 64 (43.75%) 52 10 / 64 (15.63%) 11		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	5 / 64 (7.81%) 6		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting	4 / 64 (6.25%) 5 14 / 64 (21.88%) 16 10 / 64 (15.63%) 15 10 / 64 (15.63%) 16 6 / 64 (9.38%) 10		

subjects affected / exposed	17 / 64 (26.56%)		
occurrences (all)	33		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	40 / 64 (62.50%)		
occurrences (all)	103		
Epistaxis			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	4		
Nasal congestion			
subjects affected / exposed	23 / 64 (35.94%)		
occurrences (all)	43		
Oropharyngeal pain			
subjects affected / exposed	24 / 64 (37.50%)		
occurrences (all)	43		
Productive cough			
subjects affected / exposed	11 / 64 (17.19%)		
occurrences (all)	23		
Rhinorrhoea			
subjects affected / exposed	21 / 64 (32.81%)		
occurrences (all)	36		
Sinus congestion			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	9		
Infections and infestations			
COVID-19			
subjects affected / exposed	18 / 64 (28.13%)		
occurrences (all)	21		
Ear infection			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	4		
Hordeolum			
subjects affected / exposed	9 / 64 (14.06%)		
occurrences (all)	16		
Infective pulmonary exacerbation of cystic fibrosis			

subjects affected / exposed	8 / 64 (12.50%)		
occurrences (all)	8		
Influenza			
subjects affected / exposed	7 / 64 (10.94%)		
occurrences (all)	7		
Nasopharyngitis			
subjects affected / exposed	10 / 64 (15.63%)		
occurrences (all)	22		
Pharyngitis streptococcal			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	6		
Sinusitis			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	9		
Upper respiratory tract infection			
subjects affected / exposed	19 / 64 (29.69%)		
occurrences (all)	61		
Viral upper respiratory tract infection			
subjects affected / exposed	7 / 64 (10.94%)		
occurrences (all)	12		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 June 2021	Amended to extend treatment period by adding Part B (additional 96 weeks of treatment duration) and updated monitoring text to include flexibility for remote monitoring.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported