Clinical trial results:
A Phase 3b Open-label Study Evaluating the Safety of Elexacaftor/Tezacaftor/Ivacaftor Combination Therapy in Subjects With Cystic Fibrosis

Summary

EudraCT number	2020-004885-21
Trial protocol	CZ BE NL ES
Global end of trial date	20 December 2022

Results information

Result version number	v1 (current)
This version publication date	05 July 2023
First version publication date	05 July 2023

Trial information

Trial identification

Sponsor protocol code	VX20-445-121

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05111145
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vertex Pharmaceuticals Incorporated
Sponsor organisation address	50 Northern Avenue, Boston, 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	06 February 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 December 2022
Global end of trial reached?	Yes
Global end of trial date	20 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 (ELX)/Tezacaftor (TEZ)/Ivacaftor (IVA) in subjects with Cystic Fibrosis (CF).

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	14 January 2022
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	Australia: 24
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Belgium: 38
Country: Number of subjects enrolled	Czechia: 3
Worldwide total number of subjects	86
EEA total number of subjects	61

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)	27
Adults (18-64 years)	59

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects from Parent Studies VX19-445-117(NCT04599465) and VX20-445-126(NCT04969224) were enrolled in this study. A total of 86 subjects were enrolled in this study.

Period 1

Period 1 title	Overall Trial (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 Elexacaftor (ELX) 200 mg once daily (qd)/Tezacaftor (TEZ) 100 mg qd/Ivacaftor (IVA) 150 mg every 12 hours (q12h) in the treatment period for up to 36 weeks.

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 fixed-dose 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 once daily in the evening.

Number of subjects in period 1	ELX/TEZ/IVA
Started	86
Completed	0
Not completed	86
Commercial drug available to the subject	76
Subject enrolled in another qualified Vertex study	10

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial (overall period)

Reporting group description:

Baseline data is based on the parent study baseline, which is defined as the most recent non-missing measurement collected before the first dose of study drug in the treatment period of parent studies. Baseline data is presented for subjects who received at least 1 dose of study drug in this study.

Reporting group values	Overall Trial (overall period)	Total	
Number of subjects	86	86	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	25.3		
standard deviation	± 9.9	-	
Gender categorical Units: Subjects			
Female	37	37	
Male	49	49	
Ethnicity Units: Subjects			
Hispanic or Latino	11	11	
Not Hispanic or Latino	68	68	
Not collected per local regulations	7	7	
Race Units: Subjects			
White	79	79	
Black or African American	0	0	
Asian	0	0	
American Indian or Alaska Native	0	0	
Native Hawaiian or other Pacific Islander	0	0	
Other	0	0	
Not collected per local regulations	7	7	

End points

End points reporting groups

Reporting group title	ELX/TEZ/IVA

Reporting group description:

Subjects received Elexacaftor (ELX) 200 mg once daily (qd)/Tezacaftor (TEZ) 100 mg qd/Ivacaftor (IVA) 150 mg every 12 hours (q12h) in the treatment period for up to 36 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 included all subjects who received at least 1 dose of study drug in the treatment period.

End point type	Primary

End point timeframe:

Day 1 up to Week 36

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	86			
Units: Subjects				
Subjects with TEAEs	61			
Subjects with SAEs	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Week 36

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	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 up to 36 weeks.

Serious adverse events	ELX/TEZ/IVA		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 86 (4.65%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis viral			

subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Malnutrition			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 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	33 / 86 (38.37%)		
Infections and infestations			
COVID-19			
subjects affected / exposed	16 / 86 (18.60%)		
occurrences (all)	16		
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	11 / 86 (12.79%)		
occurrences (all)	14		
Nasopharyngitis			
subjects affected / exposed	9 / 86 (10.47%)		
occurrences (all)	9		
Upper respiratory tract infection			
subjects affected / exposed	6 / 86 (6.98%)		
occurrences (all)	6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 February 2022	Updated that study drug does not need to be discontinued for a male subject whose female partner becomes pregnant during study participation; Removed parent study VX19-445-114 and updated the number of planned subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported