Clinical trial results:
A Phase 2a, Open-label, Single-arm, 2-Part Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of VX-147 in Adults With APOL1-mediated Focal Segmental Glomerulosclerosis.

Summary

EudraCT number	2020-000185-42
Trial protocol	GB FR
Global end of trial date	09 December 2021

Results information

Result version number	v2 (current)
This version publication date	27 July 2023
First version publication date	25 December 2022
Version creation reason	• New data added to full data set Update to match CT.gov

Trial information

Trial identification

Sponsor protocol code	VX19-147-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04340362
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 February 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 November 2021
Global end of trial reached?	Yes
Global end of trial date	09 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy, safety and pharmacokinetics (PK) of VX-147 in subjects with apolipoprotein L1 (APOL1)-mediated focal segmental glomerulosclerosis (FSGS).

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	08 June 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	France: 2
Country: Number of subjects enrolled	United States: 11
Country: Number of subjects enrolled	United Kingdom: 3
Worldwide total number of subjects	16
EEA total number of subjects	2

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)	0
Adults (18-64 years)	15
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was planned in 2 parts: Part A (Treatment Period), which consisted of 2 cohorts (i.e., cohort 1 and 2) and Part B (Optional Exploratory Off-treatment Follow-up Period). The primary and secondary efficacy analyses and safety analyses were planned for only Part A.

Pre-assignment

Screening details:

This study was conducted on adult subjects who had APOL1-mediated focal segmental glomerulosclerosis (FSGS).

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	VX-147

Arm description:

All subjects received VX-147 at a dosage of 15 mg once daily (qd) for 2 weeks and VX-147 at a dosage of 45 mg qd for 11 weeks. Part A was enrolled in 2 cohorts: Cohort 1 and Cohort 2. Cohort 1 included subjects with urine protein to creatinine ratio (UPCR) approximately greater than or equal to (≥) 3 g/g (± 10%) and less than (<) 10 g/g and estimated glomerular filtration rate (eGFR) approximately ≥30 mL/min/1.73 m2 (± 10%). Cohort 2 included subjects with UPCR approximately ≥0.8 g/g (± 10%) and <2.7 g/g and eGFR approximately ≥30 mL/min/1.73 m2.

Arm type	Experimental
Investigational medicinal product name	Inaxaplin
Investigational medicinal product code	VX-147
Other name	IXP
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subject received VX-147 once daily.

Number of subjects in period 1	VX-147
Started	16
Cohort 1	3 [1]
Cohort 2	13 [2]
Completed	15
Not completed	1
Withdrawal of consent (not due to adverse event)	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The milestone represents the number of subjects in Cohort 1.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The milestone represents the number of subjects in Cohort 2.

Baseline characteristics

Reporting groups	
Reporting group title	VX-147

Reporting group description:

All subjects received VX-147 at a dosage of 15 mg once daily (qd) for 2 weeks and VX-147 at a dosage of 45 mg qd for 11 weeks. Part A was enrolled in 2 cohorts: Cohort 1 and Cohort 2. Cohort 1 included subjects with urine protein to creatinine ratio (UPCR) approximately greater than or equal to (≥) 3 g/g (± 10%) and less than (<) 10 g/g and estimated glomerular filtration rate (eGFR) approximately ≥30 mL/min/1.73 m2 (± 10%). Cohort 2 included subjects with UPCR approximately ≥0.8 g/g (± 10%) and <2.7 g/g and eGFR approximately ≥30 mL/min/1.73 m2.

Reporting group values	VX-147	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	38.8		
standard deviation	± 14.5	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	7	7	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	16	16	
Unknown or Not Reported	0	0	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	16	16	
White	0	0	
More than one Race	0	0	
Unknown or Not Reported	0	0	
Urine Protein to Creatinine Ratio (UPCR) Units: g/g			
arithmetic mean	2.08		
standard deviation	± 0.90	-	

End points

End points reporting groups

Reporting group title	VX-147

Reporting group description:

All subjects received VX-147 at a dosage of 15 mg once daily (qd) for 2 weeks and VX-147 at a dosage of 45 mg qd for 11 weeks. Part A was enrolled in 2 cohorts: Cohort 1 and Cohort 2. Cohort 1 included subjects with urine protein to creatinine ratio (UPCR) approximately greater than or equal to (≥) 3 g/g (± 10%) and less than (<) 10 g/g and estimated glomerular filtration rate (eGFR) approximately ≥30 mL/min/1.73 m2 (± 10%). Cohort 2 included subjects with UPCR approximately ≥0.8 g/g (± 10%) and <2.7 g/g and eGFR approximately ≥30 mL/min/1.73 m2.

Primary: Percent Change From Baseline in UPCR

End point title	Percent Change From Baseline in UPCR[1]

End point description:

End point type	Primary

End point timeframe:

From Baseline up to Week 13

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: This is a single arm study. Only descriptive statistics for geometric mean percent change from baseline were planned . No statistical comparisons were planned for this endpoint.

End point values	VX-147			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Percent Change				
geometric mean (confidence interval 95%)				
Cohort 1 (n=3)	-47.7 (-70.1 to -8.5)			
Cohort 2 (n=10)	-47.5 (-63.4 to -24.6)			
Total (n=13)	-47.6 (-60.0 to -31.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: 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)

End point description:

Safety set included all subjects who received at least 1 dose of study drug in the treatment period. Here, the "n" signifies subjects who were evaluable for the specified cohorts.

End point type	Secondary

End point timeframe:

From Baseline up to Week 17

End point values	VX-147			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Subjects				
Cohort 1 : Subjects with TEAEs (n=3)	3			
Cohort 1 : Subjects with SAEs (n=3)	0			
Cohort 2 : Subjects with TEAEs (n=13)	12			
Cohort 2 : Subjects with SAEs (n=13)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Concentration (Cmax) of VX-147

End point title	Maximum Observed Concentration (Cmax) of VX-147

End point description:

Pharmacokinetic (PK) set included all subjects who have received at least 1 dose of study drug in the treatment period. Here, the "n" signifies subjects who were evaluable for the specified time point.

End point type	Secondary

End point timeframe:

Pre-dose and at 0.25, 0.5, 1, 2, 4 and 12 hours post-dose on Day 1 and Week 5

End point values	VX-147			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: micrograms per milliliter (mcg/ml)				
arithmetic mean (standard deviation)				
15 mg qd: Day 1 (n=15)	0.168 (± 0.0630)			
45 mg qd: Week 5 (n=14)	0.846 (± 0.303)			

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Pre-dose Concentration (Ctrough) of VX-147

End point title	Observed Pre-dose Concentration (Ctrough) of VX-147

End point description:

PK set included all subjects who have received at least 1 dose of study drug in the treatment period. Here, the "n" signifies subjects who were evaluable for the specified time point.

End point type	Secondary

End point timeframe:

Pre-dose and on Day 8, 15, Week 3, 5, 9 and 13

End point values	VX-147			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: mcg/ml				
arithmetic mean (standard deviation)				
15 mg qd: Day 8 (n=16)	0.153 (± 0.0984)			
15 mg qd: Day 15 (n=15)	0.123 (± 0.0796)			
45 mg qd: Week 3 (n=15)	0.379 (± 0.249)			
45 mg qd: Week 5 (n=15)	0.492 (± 0.265)			
45 mg qd: Week 9 (n=14)	0.446 (± 0.342)			
45 mg qd: Week 13 (n=13)	0.529 (± 0.302)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Time-curve From 0 to 24 hours (AUC0-24hr) of VX-147

End point title	Area Under the Concentration Time-curve From 0 to 24 hours (AUC0-24hr) of VX-147

End point description:

PK set included all subjects who have received at least 1 dose of study drug in the treatment period. Here, the "n" signifies subjects who were evaluable for the specified time point.

End point type	Secondary

End point timeframe:

Pre-dose and at 0.25, 0.5, 1, 2, 4, 12 and 24 hours Post-dose on Week 5

End point values	VX-147			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: micrograms per hour milliliter(mcg-h/ml)				
arithmetic mean (standard deviation)	15.3 (± 6.37)			

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	24.1

Reporting groups	
Reporting group title	VX-147: Cohort 1
Reporting group description: Cohort 1 included subjects with urine protein to creatinine ratio (UPCR) approximately ≥3 g/g (± 10%) and <10 g/g and estimated glomerular filtration rate (eGFR) approximately ≥30 mL/min/1.73 m2 (± 10%).	
Reporting group title	VX-147: Cohort 2
Reporting group description: Cohort 2 included subjects with UPCR approximately ≥0.8 g/g (± 10%) and <2.7 g/g and eGFR approximately ≥30 mL/min/1.73 m2.	
Reporting group title	VX-147: Total
Reporting group description: All subjects received VX-147 at a dosage of 15 mg qd for 2 weeks and VX-147 at a dosage of 45 mg qd for 11 weeks. Part A was enrolled in 2 cohorts: Cohort 1 and Cohort 2. Cohort 1 included subjects with urine protein to creatinine ratio (UPCR) approximately ≥3 g/g (± 10%) and <10 g/g and estimated glomerular filtration rate (eGFR) approximately ≥30 mL/min/1.73 m2 (± 10%). Cohort 2 included subjects with UPCR approximately ≥0.8 g/g (± 10%) and <2.7 g/g and eGFR approximately ≥30 mL/min/1.73 m2.	

Serious adverse events	VX-147: Cohort 1	VX-147: Cohort 2	VX-147: Total
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	VX-147: Cohort 1	VX-147: Cohort 2	VX-147: Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	12 / 13 (92.31%)	15 / 16 (93.75%)
Investigations			
Blood bicarbonate decreased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 13 (15.38%)	2 / 16 (12.50%)
occurrences (all)	0	3	3
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Electrocardiogram ST segment depression			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Transaminases increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 3 (33.33%)	3 / 13 (23.08%)	4 / 16 (25.00%)
occurrences (all)	1	4	5
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	2 / 13 (15.38%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	2 / 13 (15.38%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	2	2
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 13 (15.38%)	2 / 16 (12.50%)
occurrences (all)	0	3	3
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 13 (7.69%)	2 / 16 (12.50%)
occurrences (all)	1	1	2
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Nausea			

subjects affected / exposed	1 / 3 (33.33%)	2 / 13 (15.38%)	3 / 16 (18.75%)
occurrences (all)	1	2	3
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Eczema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Psychiatric disorders			
Thinking abnormal			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 13 (23.08%)	3 / 16 (18.75%)
occurrences (all)	0	3	3
Musculoskeletal chest pain			

subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Synovitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Tinea pedis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Tooth abscess			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 16 (6.25%)
occurrences (all)	0	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2020	Amended to specify the doses to be used, added optional Cohort 2 and modified the schedule of assessments and eligibility criteria.
23 September 2020	Amended the eligibility criteria.
11 December 2020	Amended the eligibility criteria and also specified that both cohorts will be analyzed for the primary endpoint.
09 April 2021	Amended the eligibility criteria, updated the study restrictions, and contraceptive requirements.
26 July 2021	Amended to specify that Cohort 1 will enroll "up to 10 subjects" to clarify that enrollment could be stopped before 10 subjects were enrolled.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported