



Clinical trial results:

A Phase 1/2 Study of VX-121 in Healthy Subjects and in Subjects with Cystic Fibrosis

Summary

EudraCT number	2018-000126-55
Trial protocol	NL
Global end of trial date	03 May 2019

Results information

Result version number	v2 (current)
This version publication date	03 July 2022
First version publication date	17 May 2020
Version creation reason	<ul style="list-style-type: none">New data added to full data setUpdating secondary outcomes

Trial information

Trial identification

Sponsor protocol code	VX17-121-001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03768089
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	28 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 May 2019
Global end of trial reached?	Yes
Global end of trial date	03 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of single or multiple ascending doses of VX-121 alone or in combination with Tezacaftor/Ivacaftor (TEZ/IVA).

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	20 March 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 109
Country: Number of subjects enrolled	United Kingdom: 6
Worldwide total number of subjects	115
EEA total number of subjects	115

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)	115
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study included 4 parts: Parts A, B, and C were conducted in healthy adult subjects; Part D was conducted in adult cystic fibrosis (CF) subjects.

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	Part A: Pooled Placebo (Except Cohorts A3 and A9)

Arm description:

Subjects received single dose of placebo matched to VX-121 in Cohorts A1 to A5 (Except Cohorts A3 and A9).

Arm type	Placebo
Investigational medicinal product name	Placebo (matched to VX-121)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received single dose of placebo matched to VX-121.

Arm title	Part A: VX-121 (Except Cohorts A3 and A9)
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Arm description:

Subjects received single dose of VX-121 in Cohorts A1 (10 milligrams [mg]), A2 (20 mg), A4 (40 mg), A5 (60 mg).

Arm type	Experimental
Investigational medicinal product name	VX-121
Investigational medicinal product code	VX-121
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received single ascending dose of VX-121 in Cohorts A1 to A5 (except Cohorts A3 and A9).

Arm title	Part A: VX-121 (Cohort A3)
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Arm description:

Subjects received single dose of VX-121 5 mg or matched placebo without milk, followed by open label VX-121 5 mg with milk in Cohort A3.

Arm type	Experimental
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Investigational medicinal product name	VX-121
Investigational medicinal product code	VX-121
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
Subjects received single dose VX-121 without milk, followed by VX-121 with milk in Cohort A3.	
Investigational medicinal product name	Placebo (matched to VX-121)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
Subjects received placebo matched to VX-121 without milk, followed by VX-121 with milk in Cohort A3.	
Arm title	Part A: VX-121 (Cohort A9)
Arm description:	
Subjects received single dose of VX-121 10 mg suspension on Day 1, VX-121 10 mg tablet without milk on Day 9, followed by VX-121 10 mg tablet with milk on Day 17 in Cohort A9.	
Arm type	Experimental
Investigational medicinal product name	VX-121
Investigational medicinal product code	VX-121
Other name	
Pharmaceutical forms	Tablet, Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
Subjects received single dose of VX-121 suspension on Day 1, VX-121 tablet on Day 9, and then VX-121 tablet with milk on Day 17 in Cohort A9.	
Arm title	Part B: Pooled Placebo (Cohorts B1 to B4)
Arm description:	
Subjects received placebo matched to VX-121 in Cohorts B1 to B4 for 10 days.	
Arm type	Placebo
Investigational medicinal product name	Placebo (matched to VX-121)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
Subjects received multiple doses of placebo matched to VX-121 once daily.	
Arm title	Part B: VX-121 (Cohorts B1 to B4)
Arm description:	
Subjects received VX-121 once daily (qd) in Cohorts B1 (10 mg), B2 (20 mg), B3 (40 mg) and B4 (60 mg) for 10 days.	
Arm type	Experimental
Investigational medicinal product name	VX-121
Investigational medicinal product code	VX-121
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
Subjects received multiple ascending doses of VX-121 once daily.	
Arm title	Part C: Pooled Placebo (Cohorts C1 to C3)

Arm description:

Subjects received placebo matched to VX-121/TEZ/IVA in Cohorts C1 to C3 for 14 days.

Arm type	Placebo
Investigational medicinal product name	Placebo (matched to VX-121)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to VX-121 suspension once daily.

Investigational medicinal product name	Placebo (matched to TEZ/IVA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to TEZ/IVA once daily in the morning.

Investigational medicinal product name	Placebo (matched to IVA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to IVA once daily in the evening.

Arm title	Part C: VX-121/TEZ/IVA (Cohorts C1 to C3)
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Arm description:

Subjects received VX-121 10 mg qd/TEZ 100 mg qd/IVA 150 mg every 12 hours (q12h) in Cohort C1; VX-121 20 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in Cohort C2; VX-121 5 mg/TEZ 100 mg qd/IVA 150 mg q12h in Cohort C3 for 14 days.

Arm type	Experimental
Investigational medicinal product name	VX-121
Investigational medicinal product code	VX-121
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-121 suspension once daily.

Investigational medicinal product name	TEZ/IVA
Investigational medicinal product code	VX-661/VX-770
Other name	Tezacaftor/Ivacaftor fixed dose combination
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received TEZ/IVA 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.

Arm title	Part D: Placebo
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Arm description:

Subjects received placebo matched to VX-121/TEZ/IVA for 4 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo (matched to VX-121)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects with CF received placebo matched to VX-121 once daily.

Investigational medicinal product name	Placebo (matched to TEZ/IVA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects with CF received placebo matched to TEZ/IVA once daily in the morning.

Investigational medicinal product name	Placebo (matched to IVA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects with CF received placebo matched to IVA once daily in the evening.

Arm title	Part D: VX-121/TEZ/IVA
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Arm description:

Subjects received VX-121 5 mg qd/TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	VX-121
Investigational medicinal product code	VX-121
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects with CF received VX-121 once daily.

Investigational medicinal product name	TEZ/IVA
Investigational medicinal product code	VX-661/VX-770
Other name	Tezacaftor/Ivacaftor fixed dose combination
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects with CF received TEZ/IVA 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 with CF received IVA once daily in the evening.

Number of subjects in period 1	Part A: Pooled Placebo (Except Cohorts A3 and A9)	Part A: VX-121 (Except Cohorts A3 and A9)	Part A: VX-121 (Cohort A3)
Started	8	23	6
Completed	8	22	6
Not completed	0	1	0
Lost to follow-up	-	1	-

Number of subjects in period 1	Part A: VX-121 (Cohort A9)	Part B: Pooled Placebo (Cohorts B1 to B4)	Part B: VX-121 (Cohorts B1 to B4)
Started	8	9	24
Completed	8	9	24
Not completed	0	0	0
Lost to follow-up	-	-	-

Number of subjects in period 1	Part C: Pooled Placebo (Cohorts C1 to C3)	Part C: VX-121/TEZ/IVA (Cohorts C1 to C3)	Part D: Placebo
Started	6	19	3
Completed	6	19	3
Not completed	0	0	0
Lost to follow-up	-	-	-

Number of subjects in period 1	Part D: VX-121/TEZ/IVA
Started	9
Completed	9
Not completed	0
Lost to follow-up	-

Baseline characteristics

Reporting groups^[1]

Reporting group title	Part A: Pooled Placebo (Except Cohorts A3 and A9)
Reporting group description: Subjects received single dose of placebo matched to VX-121 in Cohorts A1 to A5 (Except Cohorts A3 and A9).	
Reporting group title	Part A: VX-121 (Except Cohorts A3 and A9)
Reporting group description: Subjects received single dose of VX-121 in Cohorts A1 (10 milligrams [mg]), A2 (20 mg), A4 (40 mg), A5 (60 mg).	
Reporting group title	Part A: VX-121 (Cohort A3)
Reporting group description: Subjects received single dose of VX-121 5 mg or matched placebo without milk, followed by open label VX-121 5 mg with milk in Cohort A3.	
Reporting group title	Part A: VX-121 (Cohort A9)
Reporting group description: Subjects received single dose of VX-121 10 mg suspension on Day 1, VX-121 10 mg tablet without milk on Day 9, followed by VX-121 10 mg tablet with milk on Day 17 in Cohort A9.	
Reporting group title	Part B: Pooled Placebo (Cohorts B1 to B4)
Reporting group description: Subjects received placebo matched to VX-121 in Cohorts B1 to B4 for 10 days.	
Reporting group title	Part B: VX-121 (Cohorts B1 to B4)
Reporting group description: Subjects received VX-121 once daily (qd) in Cohorts B1 (10 mg), B2 (20 mg), B3 (40 mg) and B4 (60 mg) for 10 days.	
Reporting group title	Part C: Pooled Placebo (Cohorts C1 to C3)
Reporting group description: Subjects received placebo matched to VX-121/TEZ/IVA in Cohorts C1 to C3 for 14 days.	
Reporting group title	Part C: VX-121/TEZ/IVA (Cohorts C1 to C3)
Reporting group description: Subjects received VX-121 10 mg qd/TEZ 100 mg qd/IVA 150 mg every 12 hours (q12h) in Cohort C1; VX-121 20 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in Cohort C2; VX-121 5 mg/TEZ 100 mg qd/IVA 150 mg q12h in Cohort C3 for 14 days.	
Reporting group title	Part D: Placebo
Reporting group description: Subjects received placebo matched to VX-121/TEZ/IVA for 4 weeks.	
Reporting group title	Part D: VX-121/TEZ/IVA
Reporting group description: Subjects received VX-121 5 mg qd/TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks.	

Notes:

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

Justification: There were 115 unique enrolled subjects in the study. One subject was randomized, but not dosed. Therefore, baseline accounts for 114 unique dosed subjects (one subject participated in 2 parts and thus was counted twice in Baseline section).

Reporting group values	Part A: Pooled Placebo (Except Cohorts A3 and A9)	Part A: VX-121 (Except Cohorts A3 and A9)	Part A: VX-121 (Cohort A3)
Number of subjects	8	23	6
Age categorical			
Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	29.8 ± 10.6	30.3 ± 11.5	25.8 ± 4.16
Gender categorical Units: Subjects			
Female	0	2	0
Male	8	21	6
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	2	1
Not Hispanic or Latino	8	21	5
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	1	2	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	2
White	5	20	4
More than one race	1	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Part A: VX-121 (Cohort A9)	Part B: Pooled Placebo (Cohorts B1 to B4)	Part B: VX-121 (Cohorts B1 to B4)
Number of subjects	8	9	24
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	33.9 ± 11.5	31.7 ± 14.0	29.6 ± 10.5
Gender categorical Units: Subjects			
Female	0	1	0
Male	8	8	24
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	7	9	24
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	0	0
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	2	0
White	4	6	22
More than one race	1	1	1

Unknown or Not Reported	0	0	0
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Reporting group values	Part C: Pooled Placebo (Cohorts C1 to C3)	Part C: VX-121/TEZ/IVA (Cohorts C1 to C3)	Part D: Placebo
Number of subjects	6	19	3
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	30.3 ± 12.1	36.6 ± 13.2	22.8 ± 4.9
Gender categorical Units: Subjects			
Female	0	1	0
Male	6	18	3
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	0
Not Hispanic or Latino	6	18	3
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	0
White	4	15	3
More than one race	1	1	0
Unknown or Not Reported	0	1	0

Reporting group values	Part D: VX-121/TEZ/IVA	Total	
Number of subjects	9	114	
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	34.8 ± 12.8	-	
Gender categorical Units: Subjects			
Female	1	5	
Male	8	109	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	5	
Not Hispanic or Latino	9	109	

Unknown or Not Reported	0	0	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	2	
Asian	0	7	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	7	
White	8	90	
More than one race	1	7	
Unknown or Not Reported	0	1	

End points

End points reporting groups

Reporting group title	Part A: Pooled Placebo (Except Cohorts A3 and A9)
Reporting group description: Subjects received single dose of placebo matched to VX-121 in Cohorts A1 to A5 (Except Cohorts A3 and A9).	
Reporting group title	Part A: VX-121 (Except Cohorts A3 and A9)
Reporting group description: Subjects received single dose of VX-121 in Cohorts A1 (10 milligrams [mg]), A2 (20 mg), A4 (40 mg), A5 (60 mg).	
Reporting group title	Part A: VX-121 (Cohort A3)
Reporting group description: Subjects received single dose of VX-121 5 mg or matched placebo without milk, followed by open label VX-121 5 mg with milk in Cohort A3.	
Reporting group title	Part A: VX-121 (Cohort A9)
Reporting group description: Subjects received single dose of VX-121 10 mg suspension on Day 1, VX-121 10 mg tablet without milk on Day 9, followed by VX-121 10 mg tablet with milk on Day 17 in Cohort A9.	
Reporting group title	Part B: Pooled Placebo (Cohorts B1 to B4)
Reporting group description: Subjects received placebo matched to VX-121 in Cohorts B1 to B4 for 10 days.	
Reporting group title	Part B: VX-121 (Cohorts B1 to B4)
Reporting group description: Subjects received VX-121 once daily (qd) in Cohorts B1 (10 mg), B2 (20 mg), B3 (40 mg) and B4 (60 mg) for 10 days.	
Reporting group title	Part C: Pooled Placebo (Cohorts C1 to C3)
Reporting group description: Subjects received placebo matched to VX-121/TEZ/IVA in Cohorts C1 to C3 for 14 days.	
Reporting group title	Part C: VX-121/TEZ/IVA (Cohorts C1 to C3)
Reporting group description: Subjects received VX-121 10 mg qd/TEZ 100 mg qd/IVA 150 mg every 12 hours (q12h) in Cohort C1; VX-121 20 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in Cohort C2; VX-121 5 mg/TEZ 100 mg qd/IVA 150 mg q12h in Cohort C3 for 14 days.	
Reporting group title	Part D: Placebo
Reporting group description: Subjects received placebo matched to VX-121/TEZ/IVA for 4 weeks.	
Reporting group title	Part D: VX-121/TEZ/IVA
Reporting group description: Subjects received VX-121 5 mg qd/TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks.	
Subject analysis set title	Part A: VX-121 (Cohort A1)
Subject analysis set type	Full analysis
Subject analysis set description: Subjects received single dose of VX-121 10 mg in Cohort A1.	
Subject analysis set title	Part A: VX-121 (Cohort A2)
Subject analysis set type	Full analysis
Subject analysis set description: Subjects received single dose of VX-121 20 mg in Cohort A2.	
Subject analysis set title	Part A: VX-121 (Cohort A3: Without Milk)
Subject analysis set type	Full analysis
Subject analysis set description: Subjects received single dose of VX-121 5 mg without milk in Cohort A3.	
Subject analysis set title	Part A: VX-121 (Cohort A3: With Milk)

Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received single dose of VX-121 5 mg with milk in Cohort A3.	
Subject analysis set title	Part A: VX-121 (Cohort A4)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received single dose of VX-121 40 mg in Cohort A4.	
Subject analysis set title	Part A: VX-121 (Cohort A5)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received single dose of VX-121 60 mg in Cohort A5.	
Subject analysis set title	Part A: VX-121 (Cohort A9: Suspension)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received single dose of VX-121 10 mg suspension on Day 1 in Cohort A9.	
Subject analysis set title	Part A: VX-121 (Cohort A9: Tablet Without Milk)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received single dose of VX-121 10 mg tablet without milk on Day 9 in Cohort A9.	
Subject analysis set title	Part A: VX-121 (Cohort A9: Tablet With Milk)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received single dose of VX-121 10 mg tablet with milk on Day 17 in Cohort A9.	
Subject analysis set title	Part B: VX-121 (Cohort B1)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received VX-121 10 mg qd for 10 days.	
Subject analysis set title	Part B: VX-121 (Cohort B2)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received VX-121 20 mg qd for 10 days	
Subject analysis set title	Part B: VX-121 (Cohort B3)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received VX-121 40 mg qd for 10 days.	
Subject analysis set title	Part B: VX-121 (Cohort B4)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received VX-121 60 mg qd for 10 days.	
Subject analysis set title	Part C: VX-121 (Cohort C1)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received VX-121 10 mg qd/TEZ 100 mg qd/IVA 150 mg q12h for 14 days.	
Subject analysis set title	Part C: VX-121 (Cohort C2)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received VX-121 20 mg qd/TEZ 100 mg qd/IVA 150 mg q12h for 14 days.	
Subject analysis set title	Part C: VX-121 (Cohort C3)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received VX-121 5 mg qd/TEZ 100 mg qd/IVA 150 mg q12h for 14 days.	

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]
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End point description:

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

End point type	Primary
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End point timeframe:

Day 1 Through Safety Follow-up (up to Day 12 for Part A [except Cohorts A3 and A9], up to Day 20 for Cohort A3, up to Day 28 for Cohort A9, up to Day 21 for Part B, up to Day 25 for Part C and up to Week 9 for Part D)

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 primary safety endpoint.

End point values	Part A: Pooled Placebo (Except Cohorts A3 and A9)	Part A: VX-121 (Except Cohorts A3 and A9)	Part A: VX-121 (Cohort A3)	Part A: VX-121 (Cohort A9)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	23	6	8
Units: Subjects				
Subjects with AEs	1	9	4	7
Subjects with SAEs	0	0	0	0

End point values	Part B: Pooled Placebo (Cohorts B1 to B4)	Part B: VX-121 (Cohorts B1 to B4)	Part C: Pooled Placebo (Cohorts C1 to C3)	Part C: VX-121/TEZ/IVA (Cohorts C1 to C3)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	24	6	19
Units: Subjects				
Subjects with AEs	7	17	4	12
Subjects with SAEs	0	0	0	0

End point values	Part D: Placebo	Part D: VX-121/TEZ/IVA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	9		
Units: Subjects				
Subjects with AEs	2	7		
Subjects with SAEs	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Maximum Observed Concentration (C_{max}) of VX-121

End point title Part A: Maximum Observed Concentration (C_{max}) of VX-121

End point description:

End point type Secondary

End point timeframe:

Cohorts A1-5 (Except A3): Pre-dose up to 240 hours post-dose; Cohorts A3 and A9: Pre-dose up to 168 hours post-dose

End point values	Part A: VX-121 (Cohort A1)	Part A: VX-121 (Cohort A2)	Part A: VX-121 (Cohort A3: Without Milk)	Part A: VX-121 (Cohort A3: With Milk)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	6	5	5
Units: microgram per milliliter (mcg/mL)				
arithmetic mean (standard deviation)	0.134 (± 0.0295)	0.247 (± 0.0515)	0.0705 (± 0.0152)	0.061 (± 0.0143)

End point values	Part A: VX-121 (Cohort A4)	Part A: VX-121 (Cohort A5)	Part A: VX-121 (Cohort A9: Suspension)	Part A: VX-121 (Cohort A9: Tablet Without Milk)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	8	8
Units: microgram per milliliter (mcg/mL)				
arithmetic mean (standard deviation)	0.893 (± 0.216)	1.04 (± 0.263)	0.181 (± 0.0458)	0.178 (± 0.0447)

End point values	Part A: VX-121 (Cohort A9: Tablet With Milk)			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: microgram per milliliter (mcg/mL)				
arithmetic mean (standard deviation)	0.156 (± 0.0352)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Area Under the Concentration Versus Time Curve From the Time of Dosing to the Last Measurable Concentration (AUC[0-last]) of VX-121

End point title	Part A: Area Under the Concentration Versus Time Curve From the Time of Dosing to the Last Measurable Concentration (AUC[0-last]) of VX-121
End point description: PK set.	
End point type	Secondary
End point timeframe: Cohorts A1-5 (Except A3): Pre-dose up to 240 hours post-dose; Cohorts A3 and A9: Pre-dose up to 168 hours post-dose	

End point values	Part A: VX-121 (Cohort A1)	Part A: VX-121 (Cohort A2)	Part A: VX-121 (Cohort A3: Without Milk)	Part A: VX-121 (Cohort A3: With Milk)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	6	5	5
Units: microgram*hour per milliliter (mcg*h/mL)				
arithmetic mean (standard deviation)	7.72 (± 1.93)	20.7 (± 7.03)	6.32 (± 2.54)	5.36 (± 2.09)

End point values	Part A: VX-121 (Cohort A4)	Part A: VX-121 (Cohort A5)	Part A: VX-121 (Cohort A9: Suspension)	Part A: VX-121 (Cohort A9: Tablet Without Milk)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	8	8
Units: microgram*hour per milliliter (mcg*h/mL)				
arithmetic mean (standard deviation)	72.2 (± 28.9)	66.6 (± 9.18)	15.7 (± 3.88)	14.6 (± 3.85)

End point values	Part A: VX-121 (Cohort A9: Tablet With Milk)			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: microgram*hour per milliliter (mcg*h/mL)				
arithmetic mean (standard deviation)	13.1 (± 2.56)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Maximum Observed Concentration (Cmax) of VX-121

End point title	Part B: Maximum Observed Concentration (Cmax) of VX-121
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End point description:

PK set. Here, the "n" signifies those subjects who were evaluable for this endpoint at specified time points for each arm respectively.

End point type	Secondary
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End point timeframe:

Day 1, Day 5, and Day 10

End point values	Part B: VX-121 (Cohort B1)	Part B: VX-121 (Cohort B2)	Part B: VX-121 (Cohort B3)	Part B: VX-121 (Cohort B4)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	6	6
Units: mcg/mL				
arithmetic mean (standard deviation)				
Day 1 (n=6, 6, 6, 6)	0.153 (± 0.0260)	0.418 (± 0.0667)	0.803 (± 0.0529)	1.43 (± 0.217)
Day 5 (n=6, 6, 6, 6)	0.497 (± 0.0889)	1.41 (± 0.316)	2.67 (± 0.564)	4.36 (± 0.789)
Day 10 (n=6, 6, 5, 5)	0.574 (± 0.122)	1.94 (± 0.410)	3.07 (± 0.667)	5.07 (± 0.803)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Area Under the Concentration Versus Time Curve During the Dosing Interval (AUCtau) of VX-121

End point title	Part B: Area Under the Concentration Versus Time Curve During the Dosing Interval (AUCtau) of VX-121
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End point description:

PK set. Here, the "n" signifies those subjects who were evaluable for this endpoint at specified time points for each arm respectively.

End point type	Secondary
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End point timeframe:

Day 1, Day 5, and Day 10

End point values	Part B: VX-121 (Cohort B1)	Part B: VX-121 (Cohort B2)	Part B: VX-121 (Cohort B3)	Part B: VX-121 (Cohort B4)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	6	6
Units: mcg*h/mL				
arithmetic mean (standard deviation)				
Day 1 (n=6, 6, 6, 6)	2.62 (± 0.435)	7.11 (± 1.27)	14.4 (± 1.08)	27.5 (± 4.30)
Day 5 (n=6, 6, 6, 6)	10.3 (± 1.84)	30.1 (± 6.76)	53.8 (± 10.7)	86.6 (± 16.6)
Day 10 (n=6, 6, 5, 5)	11.5 (± 2.52)	38.2 (± 9.26)	58.7 (± 12.6)	97.5 (± 17.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Observed Pre-dose Plasma Concentration (C_{trough}) of VX-121

End point title	Part B: Observed Pre-dose Plasma Concentration (C _{trough}) of VX-121
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End point description:

PK set. Here, the "n" signifies those subjects who were evaluable for this endpoint at specified time points for each arm respectively.

End point type	Secondary
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End point timeframe:

Pre-dose at Day 5 and Day 10

End point values	Part B: VX-121 (Cohort B1)	Part B: VX-121 (Cohort B2)	Part B: VX-121 (Cohort B3)	Part B: VX-121 (Cohort B4)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	6	6
Units: mcg/mL				
arithmetic mean (standard deviation)				
Day 5 (n=6, 6, 6, 6)	0.391 (± 0.0694)	1.16 (± 0.266)	2.07 (± 0.537)	2.94 (± 0.759)
Day 10 (n=6, 6, 5, 5)	0.484 (± 0.109)	1.64 (± 0.414)	2.40 (± 0.637)	3.81 (± 0.792)

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Maximum Observed Concentration (C_{max}) of VX-121, TEZ and Its Metabolites (M1-TEZ and M2-TEZ) and, IVA and Its Metabolites (M1-IVA and M6-IVA)

End point title	Part C: Maximum Observed Concentration (C _{max}) of VX-121, TEZ and Its Metabolites (M1-TEZ and M2-TEZ) and, IVA and Its Metabolites (M1-IVA and M6-IVA)
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End point description:

End point type	Secondary
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End point timeframe:

Day 1, Day 7, and Day 14

End point values	Part C: VX-121 (Cohort C1)	Part C: VX-121 (Cohort C2)	Part C: VX-121 (Cohort C3)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	7	6	
Units: mcg/mL				
arithmetic mean (standard deviation)				
VX-121: Day 1 (n=6, 7, 6)	0.212 (± 0.0501)	0.408 (± 0.122)	0.0728 (± 0.0102)	
VX-121: Day 7 (n=5, 6, 6)	1.18 (± 0.735)	1.77 (± 0.416)	0.364 (± 0.122)	
VX-121: Day 14 (n=5, 6, 4)	1.39 (± 0.651)	2.14 (± 0.476)	0.385 (± 0.108)	
TEZ: Day 1 (n=6, 7, 6)	5.97 (± 1.33)	6.75 (± 0.936)	5.11 (± 1.35)	
TEZ: Day 7 (n=5, 6, 6)	9.48 (± 3.09)	8.72 (± 0.561)	7.50 (± 1.24)	
TEZ: Day 14 (n=5, 6, 4)	9.49 (± 3.76)	9.08 (± 0.547)	7.27 (± 1.40)	
M1-TEZ: Day 1 (n=6, 7, 6)	1.09 (± 0.327)	1.24 (± 0.399)	1.12 (± 0.259)	
M1-TEZ: Day 7 (n=5, 6, 6)	5.07 (± 1.10)	6.48 (± 1.48)	5.20 (± 0.606)	
M1-TEZ: Day 14 (n=5, 6, 4)	6.44 (± 1.36)	8.12 (± 1.41)	6.70 (± 1.19)	
M2-TEZ: Day 1 (n=6, 7, 6)	0.521 (± 0.191)	0.622 (± 0.390)	0.662 (± 0.320)	
M2-TEZ: Day 7 (n=5, 6, 6)	4.79 (± 2.03)	6.16 (± 2.17)	5.56 (± 3.67)	
M2-TEZ: Day 14 (n=5, 6, 4)	6.45 (± 2.88)	8.78 (± 3.54)	9.07 (± 6.13)	
IVA: Day 1 (n=6, 7, 6)	1.02 (± 0.158)	1.00 (± 0.235)	0.770 (± 0.169)	
IVA: Day 7 (n=5, 6, 6)	2.15 (± 1.27)	1.40 (± 0.288)	1.37 (± 0.309)	
IVA: Day 14 (n=5, 6, 4)	2.14 (± 1.20)	1.35 (± 0.231)	1.20 (± 0.402)	
M1-IVA: Day 1 (n=6, 7, 6)	1.91 (± 0.573)	2.34 (± 0.602)	1.51 (± 0.349)	
M1-IVA: Day 7 (n=5, 6, 6)	3.91 (± 1.80)	3.42 (± 0.534)	2.65 (± 0.434)	
M1-IVA: Day 14 (n=5, 6, 4)	4.11 (± 1.86)	2.97 (± 0.640)	3.14 (± 1.32)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Area Under the Concentration Versus Time Curve During a Dosing Interval (AUC_{tau}) of VX-121, TEZ and Its Metabolites (M1-TEZ and M2-TEZ) and IVA and Its Metabolites (M1-IVA and M6-IVA)

End point title	Part C: Area Under the Concentration Versus Time Curve During a Dosing Interval (AUC _{tau}) of VX-121, TEZ and Its Metabolites (M1-TEZ and M2-TEZ) and IVA and Its Metabolites (M1-IVA and M6-IVA)
End point description:	PK set. Here, the "n" signifies those subjects who were evaluable for this endpoint at specified time points for each arm respectively.
End point type	Secondary
End point timeframe:	Day 1, Day 7, and Day 14

End point values	Part C: VX-121 (Cohort C1)	Part C: VX-121 (Cohort C2)	Part C: VX-121 (Cohort C3)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	7	6	
Units: mcg*h/mL				
arithmetic mean (standard deviation)				
VX-121: Day 1 (n=6, 7, 6)	3.51 (± 0.813)	7.96 (± 0.789)	1.18 (± 0.130)	
VX-121: Day 7 (n=5, 6, 6)	21.7 (± 10.6)	35.4 (± 8.27)	6.52 (± 1.20)	
VX-121: Day 14 (n=5, 6, 4)	26.6 (± 14.5)	41.1 (± 8.29)	7.34 (± 1.63)	
TEZ: Day 1 (n=6, 7, 6)	56.1 (± 16.6)	50.9 (± 7.11)	44.6 (± 11.5)	
TEZ: Day 7 (n=5, 6, 6)	133 (± 60.8)	103 (± 13.9)	88.8 (± 21.0)	
TEZ: Day 14 (n=5, 6, 4)	20.7 (± 7.03)	112 (± 10.4)	87.6 (± 28.6)	
M1-TEZ: Day 1 (n=6, 7, 6)	107 (± 24.8)	24.9 (± 6.61)	20.7 (± 4.99)	
M1-TEZ: Day 7 (n=5, 6, 6)	139 (± 29.7)	130 (± 22.3)	109 (± 14.1)	
M1-TEZ: Day 14 (n=5, 6, 4)	6.68 (± 2.49)	167 (± 24.7)	142 (± 27.0)	
M2-TEZ: Day 1 (n=6, 7, 6)	103 (± 41.1)	9.61 (± 5.51)	7.57 (± 3.18)	
M2-TEZ: Day 7 (n=5, 6, 6)	143 (± 64.1)	130 (± 46.7)	117 (± 72.6)	
M2-TEZ: Day 14 (n=5, 6, 4)	6.16 (± 1.36)	194 (± 82.7)	200 (± 144)	
IVA: Day 1 (n=6, 7, 6)	18.8 (± 12.3)	5.85 (± 1.64)	4.30 (± 0.504)	
IVA: Day 7 (n=5, 6, 6)	18.4 (± 10.7)	11.6 (± 3.26)	11.0 (± 3.73)	
IVA: Day 14 (n=5, 6, 4)	11.5 (± 3.01)	11.2 (± 3.26)	9.02 (± 2.62)	
M1-IVA: Day 1 (n=6, 7, 6)	32.6 (± 17.3)	14.1 (± 1.68)	9.37 (± 1.97)	
M1-IVA: Day 7 (n=5, 6, 6)	32.2 (± 17.3)	27.3 (± 4.79)	22.3 (± 3.70)	
M1-IVA: Day 14 (n=5, 6, 4)	32.2 (± 17.3)	25.3 (± 4.35)	24.2 (± 3.70)	
M6-IVA: Day 1 (n=6, 7, 6)	4.08 (± 1.63)	9.42 (± 4.83)	4.99 (± 2.99)	
M6-IVA: Day 7 (n=5, 6, 6)	15.2 (± 9.34)	26.5 (± 12.7)	19.2 (± 12.8)	
M6-IVA: Day 14 (n=5, 6, 4)	17.6 (± 10.2)	22.6 (± 8.19)	26.4 (± 24.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Pre-dose Plasma Concentration (Ctough) of VX-121, TEZ and Its Metabolites (M1-TEZ and M2-TEZ) and IVA and Its Metabolites (M1-IVA and M6-IVA)

End point title	Part C: Pre-dose Plasma Concentration (Ctough) of VX-121, TEZ and Its Metabolites (M1-TEZ and M2-TEZ) and IVA and Its Metabolites (M1-IVA and M6-IVA)
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End point description:

PK set. Here, the "number of subjects analysed" signifies those subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for this endpoint at specified timepoints for each arm respectively.

End point type	Secondary
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End point timeframe:

Pre-dose at Day 7 and Day 14

End point values	Part C: VX-121 (Cohort C1)	Part C: VX-121 (Cohort C2)	Part C: VX-121 (Cohort C3)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	6	6	
Units: mcg/mL				
arithmetic mean (standard deviation)				
VX-121: Day 7 (n=5, 6, 6)	0.916 (± 0.369)	1.37 (± 0.321)	0.258 (± 0.0426)	
VX-121: Day 14 (n=5, 6, 4)	1.24 (± 0.665)	1.72 (± 0.452)	0.357 (± 0.0966)	
TEZ: Day 7 (n=5, 6, 6)	3.95 (± 1.84)	2.57 (± 0.776)	2.31 (± 0.735)	
TEZ: Day 14 (n=5, 6, 4)	4.55 (± 2.50)	3.27 (± 0.646)	2.27 (± 0.851)	
M1-TEZ: Day 7 (n=5, 6, 6)	4.09 (± 1.22)	4.53 (± 0.512)	3.96 (± 0.685)	
M1-TEZ: Day 14 (n=5, 6, 4)	5.45 (± 1.46)	6.40 (± 1.17)	5.03 (± 1.18)	
M2-TEZ: Day 7 (n=5, 6, 6)	4.30 (± 1.66)	5.08 (± 2.06)	4.75 (± 2.97)	
M2-TEZ: Day 14 (n=5, 6, 4)	6.20 (± 2.60)	5.51 (± 1.72)	8.63 (± 6.24)	
IVA: Day 7 (n=5, 6, 6)	1.33 (± 0.834)	0.768 (± 0.230)	0.780 (± 0.317)	
IVA: Day 14 (n=5, 6, 4)	1.34 (± 0.889)	0.750 (± 0.252)	0.601 (± 0.164)	
M1-IVA: Day 7 (n=5, 6, 6)	2.46 (± 1.53)	2.00 (± 0.589)	1.67 (± 0.334)	
M1-IVA: Day 14 (n=5, 6, 4)	2.45 (± 1.37)	1.87 (± 0.509)	1.73 (± 0.977)	
M6-IVA: Day 7 (n=5, 6, 6)	1.28 (± 0.763)	2.09 (± 1.11)	1.67 (± 1.31)	
M6-IVA: Day 14 (n=5, 6, 4)	1.60 (± 0.926)	1.85 (± 0.738)	2.27 (± 2.26)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Maximum Observed Concentration (C_{max}) of VX-121, TEZ and Its Metabolites (M1-TEZ and M2-TEZ) and IVA and Its Metabolites (M1-IVA and M6-IVA)

End point title	Part D: Maximum Observed Concentration (C _{max}) of VX-121, TEZ and Its Metabolites (M1-TEZ and M2-TEZ) and IVA and Its Metabolites (M1-IVA and M6-IVA) ^[2]
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End point description:

PK set.

End point type	Secondary
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End point timeframe:

Day 1 and Day 15

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The only Part D arm was applicable for this endpoint.

End point values	Part D: VX-121/TEZ/IVA			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: mcg/mL				
arithmetic mean (standard deviation)				
VX-121: Day 1	0.553 (± 0.0207)			
VX-121: Day 15	0.389 (± 0.116)			
TEZ: Day 1	5.38 (± 1.39)			
TEZ: Day 15	6.80 (± 2.13)			
M1-TEZ: Day 1	1.26 (± 0.162)			
M1-TEZ: Day 15	5.56 (± 1.19)			
M2-TEZ: Day 1	0.243 (± 0.0629)			
M2-TEZ: Day 15	3.99 (± 1.41)			
IVA: Day 1	0.745 (± 0.279)			
IVA: Day 15	1.47 (± 0.472)			
M1-IVA: Day 1	1.34 (± 0.478)			
M1-IVA: Day 15	2.69 (± 0.829)			
M6-IVA: Day 1	0.531 (± 0.229)			
M6-IVA: Day 15	1.17 (± 0.589)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Area Under the Concentration Versus Time Curve From the Time of Dosing to the Last Measurable Concentration (AUC[0-last]) of VX-121, TEZ and Its Metabolites (M1-TEZ and M2-TEZ) and IVA and Its Metabolites (M1-IVA and M6-IVA)

End point title	Part D: Area Under the Concentration Versus Time Curve From the Time of Dosing to the Last Measurable Concentration (AUC[0-last]) of VX-121, TEZ and Its Metabolites (M1-TEZ and M2-TEZ) and IVA and Its Metabolites (M1-IVA and M6-IVA) ^[3]
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End point description:

PK set.

End point type	Secondary
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End point timeframe:

Day 1 and Day 15

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The only Part D arm was applicable for this endpoint.

End point values	Part D: VX-121/TEZ/IVA			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: mcg*h/mL				
arithmetic mean (standard deviation)				
VX-121: Day 1	0.160 (\pm 0.0766)			
VX-121: Day 15	2.50 (\pm 1.07)			
TEZ: Day 1	21.9 (\pm 5.48)			
TEZ: Day 15	37.4 (\pm 16.0)			
M1-TEZ: Day 1	4.66 (\pm 1.42)			
M1-TEZ: Day 15	37.8 (\pm 14.3)			
M2-TEZ: Day 1	0.630 (\pm 0.213)			
M2-TEZ: Day 15	28.6 (\pm 13.7)			
IVA: Day 1	2.74 (\pm 1.24)			
IVA: Day 15	9.27 (\pm 4.06)			
M1-IVA: Day 1	4.51 (\pm 1.97)			
M1-IVA: Day 15	16.4 (\pm 6.70)			
M6-IVA: Day 1	1.25 (\pm 0.529)			
M6-IVA: Day 15	7.58 (\pm 4.49)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Pre-dose Plasma Concentration (Ctough) of VX-121, TEZ and Its Metabolites (M1-TEZ and M2-TEZ) and IVA and Its Metabolites (M1-IVA and M6-IVA)

End point title	Part D: Pre-dose Plasma Concentration (Ctough) of VX-121, TEZ and Its Metabolites (M1-TEZ and M2-TEZ) and IVA and Its Metabolites (M1-IVA and M6-IVA) ^[4]
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End point description:

PK set.

End point type	Secondary
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End point timeframe:

Pre-dose at Day 8, Day 15, and Day 29

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The only Part D arm was applicable for this endpoint.

End point values	Part D: VX-121/TEZ/IVA			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: mcg/mL				
arithmetic mean (standard deviation)				
VX-121: Day 8	0.258 (\pm 0.0834)			

VX-121: Day 15	0.348 (± 0.109)			
VX-121: Day 29	0.323 (± 0.110)			
TEZ: Day 8	1.78 (± 0.525)			
TEZ: Day 15	2.01 (± 0.543)			
TEZ: Day 29	2.02 (± 0.927)			
M1-TEZ: Day 8	4.15 (± 0.648)			
M1-TEZ: Day 15	4.52 (± 1.06)			
M1-TEZ: Day 29	5.11 (± 1.50)			
M2-TEZ: Day 8	3.29 (± 1.41)			
M2-TEZ: Day 15	3.76 (± 1.29)			
M2-TEZ: Day 29	4.57 (± 2.28)			
IVA: Day 8	0.873 (± 0.367)			
IVA: Day 15	0.998 (± 0.367)			
IVA: Day 29	0.916 (± 0.586)			
M1-IVA: Day 8	1.38 (± 0.427)			
M1-IVA: Day 15	1.76 (± 0.619)			
M1-IVA: Day 29	1.62 (± 0.620)			
M6-IVA: Day 8	0.823 (± 0.573)			
M6-IVA: Day 15	0.819 (± 0.412)			
M6-IVA: Day 29	0.990 (± 0.632)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Absolute Change in Sweat Chloride (SwCl) Concentrations

End point title	Part D: Absolute Change in Sweat Chloride (SwCl) Concentrations ^[5]
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End point description:

Sweat samples were collected using an approved collection device. Full analysis set (FAS) included all randomized subjects who carry the intended CF transmembrane conductance regulator protein (CFTR) allele mutation and have received at least 1 dose of study drug in the treatment period.

End point type	Secondary
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End point timeframe:

From Baseline Through Day 29

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The only Part D arm was applicable for this endpoint.

End point values	Part D: Placebo	Part D: VX-121/TEZ/IVA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	9		
Units: millimole per liter (mmol/L)				
least squares mean (confidence interval 95%)	2.6 (-19.7 to 24.9)	-47.7 (-58.2 to -37.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Absolute Change in Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1)

End point title	Part D: Absolute Change in Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1) ^[6]
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End point description:

FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. FAS.

End point type	Secondary
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End point timeframe:

From Baseline Through Day 29

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The only Part D arm was applicable for this endpoint.

End point values	Part D: Placebo	Part D: VX-121/TEZ/IVA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	9		
Units: percentage points				
least squares mean (confidence interval 95%)	-2.0 (-12.9 to 8.9)	8.3 (2.8 to 13.8)		

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 Day 12 for Part A [except Cohorts A3 and A9], up to Day 20 for Cohort A3, up to Day 28 for Cohort A9, up to Day 21 for Part B, up to Day 25 for Part C and up to Week 9 for Part D)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Part A: VX-121 (Except Cohorts A3 and A9)
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Reporting group description:

Subjects received single dose of VX-121 in Cohorts A1 (10 milligrams [mg]), A2 (20 mg), A4 (40 mg), A5 (60 mg).

Reporting group title	Part A: Pooled Placebo (Except Cohorts A3 and A9)
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Reporting group description:

Subjects received single dose of placebo matched to VX-121 in Cohorts A1 to A5 (Except Cohorts A3 and A9).

Reporting group title	Part A: VX-121 (Cohort A9)
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Reporting group description:

Subjects received single dose of VX-121 10 mg suspension on Day 1, VX-121 10 mg tablet without milk on Day 9, followed by VX-121 10 mg tablet with milk on Day 17 in Cohort A9.

Reporting group title	Part A: VX-121 (Cohort A3)
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Reporting group description:

Subjects received single dose of VX-121 5 mg or matched placebo without milk, followed by open label VX-121 5 mg with milk in Cohort A3.

Reporting group title	Part B: Pooled Placebo (Cohorts B1 to B4)
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Reporting group description:

Subjects received placebo matched to VX-121 in Cohorts B1 to B4 for 10 days.

Reporting group title	Part B: VX-121 (Cohorts B1 to B4)
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Reporting group description:

Subjects received VX-121 qd in Cohorts B1 (10 mg), B2 (20 mg), B3 (40 mg) and B4 (60 mg) for 10 days.

Reporting group title	Part C: Pooled Placebo (Cohorts C1 to C3)
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Reporting group description:

Subjects received placebo matched to VX-121/TEZ/IVA in Cohorts C1 to C3 for 14 days.

Reporting group title	Part C: VX-121/TEZ/IVA (Cohorts C1 to C3)
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Reporting group description:

Subjects received VX-121 10 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in Cohort C1; VX-121 20 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in Cohort C2; VX-121 5 mg/TEZ 100 mg qd/IVA 150 mg q12h in Cohort C3 for 14 days.

Reporting group title	Part D: Placebo
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Reporting group description:

Subjects received placebo matched to VX-121/TEZ/IVA for 4 weeks.

Reporting group title	Part D: VX-121/TEZ/IVA
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Reporting group description:

Subjects received VX-121 5 mg qd/TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks.

Serious adverse events	Part A: VX-121 (Except Cohorts A3 and A9)	Part A: Pooled Placebo (Except Cohorts A3 and A9)	Part A: VX-121 (Cohort A9)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part A: VX-121 (Cohort A3)	Part B: Pooled Placebo (Cohorts B1 to B4)	Part B: VX-121 (Cohorts B1 to B4)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part C: Pooled Placebo (Cohorts C1 to C3)	Part C: VX- 121/TEZ/IVA (Cohorts C1 to C3)	Part D: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 3 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part D: VX- 121/TEZ/IVA		
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Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part A: VX-121 (Except Cohorts A3 and A9)	Part A: Pooled Placebo (Except Cohorts A3 and A9)	Part A: VX-121 (Cohort A9)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 23 (39.13%)	1 / 8 (12.50%)	7 / 8 (87.50%)
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Catheter site bruise			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Catheter site erythema			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Catheter site irritation			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	1 / 23 (4.35%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

Catheter site pruritus			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Fatigue			
subjects affected / exposed	1 / 23 (4.35%)	0 / 8 (0.00%)	2 / 8 (25.00%)
occurrences (all)	1	0	5
Feeling cold			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Puncture site pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Vessel puncture site bruise			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			

subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	1 / 8 (12.50%) 1
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Painful respiration subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Productive cough subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Sputum increased subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	1 / 8 (12.50%) 1
Tension subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	1 / 8 (12.50%) 1
Faecal volume decreased subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Influenza A virus test positive			

subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 23 (4.35%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Procedural complication			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Dizziness postural			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 23 (8.70%)	1 / 8 (12.50%)	4 / 8 (50.00%)
occurrences (all)	2	1	4
Nerve compression			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	1 / 23 (4.35%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Defaecation urgency			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	2 / 23 (8.70%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Flatulence			
subjects affected / exposed	1 / 23 (4.35%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oral pain			

subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dermal cyst			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Papule			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 23 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1

Rash macular subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Seborrhoeic dermatitis subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Skin hypertrophy subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Skin hypopigmentation subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Skin irritation subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	1 / 8 (12.50%) 1
Swelling face subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Flank pain subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Muscle twitching subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Musculoskeletal chest pain			

subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Myalgia subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	1 / 8 (12.50%) 1
Infections and infestations Infective pulmonary exacerbation of cystic fibrosis subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	1 / 8 (12.50%) 1
Periodontitis subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0

Non-serious adverse events	Part A: VX-121 (Cohort A3)	Part B: Pooled Placebo (Cohorts B1 to B4)	Part B: VX-121 (Cohorts B1 to B4)
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 6 (66.67%)	7 / 9 (77.78%)	16 / 24 (66.67%)
Vascular disorders Phlebitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 24 (4.17%) 1
Catheter site bruise subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Catheter site erythema subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Catheter site irritation			

subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	2 / 24 (8.33%)
occurrences (all)	1	0	2
Catheter site pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	2 / 24 (8.33%)
occurrences (all)	1	2	2
Catheter site pruritus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Feeling cold			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Feeling hot			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Puncture site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	3 / 24 (12.50%)
occurrences (all)	1	0	4
Vessel puncture site pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Dyspnoea			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Painful respiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Sputum increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Tension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood creatine phosphokinase increased			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Faecal volume decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Influenza A virus test positive subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Injury, poisoning and procedural complications			
Arthropod bite subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 2	2 / 24 (8.33%) 2
Contusion subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	2 / 24 (8.33%) 2
Procedural complication subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 24 (4.17%) 1
Dizziness postural subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	2 / 9 (22.22%) 2	3 / 24 (12.50%) 3
Nerve compression subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Somnolence subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 9 (11.11%) 1	0 / 24 (0.00%) 0
Blood and lymphatic system disorders			

Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Eye disorders Eye irritation subjects affected / exposed occurrences (all) Ocular hyperaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1 0 / 6 (0.00%) 0	0 / 9 (0.00%) 0 1 / 9 (11.11%) 1	0 / 24 (0.00%) 0 0 / 24 (0.00%) 0
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Defaecation urgency subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Flatulence	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0	1 / 9 (11.11%) 1 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0	0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0

subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Oral pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	3 / 24 (12.50%)
occurrences (all)	0	1	3
Dermal cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Papule			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1

Pruritus generalised subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 24 (4.17%) 2
Rash subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 24 (4.17%) 1
Rash macular subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	2 / 24 (8.33%) 3
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	2 / 24 (8.33%) 2
Seborrhoeic dermatitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Skin hypertrophy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Skin hypopigmentation subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Skin irritation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 24 (4.17%) 1
Swelling face subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 24 (4.17%) 1
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	4 / 9 (44.44%) 4	2 / 24 (8.33%) 2
Flank pain			

subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Muscle twitching			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part C: Pooled Placebo (Cohorts C1 to C3)	Part C: VX-121/TEZ/IVA (Cohorts C1 to C3)	Part D: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	12 / 19 (63.16%)	2 / 3 (66.67%)
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site bruise			

subjects affected / exposed	1 / 6 (16.67%)	3 / 19 (15.79%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Catheter site erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Catheter site pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Feeling cold			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Puncture site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal			

disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Painful respiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Sputum increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 19 (15.79%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Tension			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	0 / 3 (0.00%) 0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Faecal volume decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Influenza A virus test positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Procedural complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 6 (33.33%)	4 / 19 (21.05%)	0 / 3 (0.00%)
occurrences (all)	3	4	0
Dizziness postural			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	1 / 6 (16.67%)	6 / 19 (31.58%)	0 / 3 (0.00%)
occurrences (all)	2	7	0
Nerve compression			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Somnolence			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	0 / 3 (0.00%) 0
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	0 / 3 (0.00%) 0
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	0 / 3 (0.00%) 0
Eye disorders Eye irritation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	0 / 3 (0.00%) 0
Ocular hyperaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	0 / 3 (0.00%) 0
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 2	0 / 3 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	0 / 3 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	0 / 3 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	0 / 3 (0.00%) 0
Defaecation urgency subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	0 / 3 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 19 (10.53%) 4	0 / 3 (0.00%) 0
Dyspepsia			

subjects affected / exposed	1 / 6 (16.67%)	2 / 19 (10.53%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Oral pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Salivary hypersecretion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermal cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Papule			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pruritus generalised			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Rash macular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin hypertrophy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin hypopigmentation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle twitching			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	3 / 19 (15.79%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Periodontitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Part D: VX-121/TEZ/IVA		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 9 (77.78%)		
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Catheter site bruise			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Catheter site erythema			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Catheter site irritation			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Catheter site pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Catheter site pruritus			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Chest discomfort			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Feeling cold			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Feeling hot			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Puncture site pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Vessel puncture site bruise			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Vessel puncture site pain			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Dyspnoea			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Nasal congestion			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Painful respiration			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Rhinorrhoea			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Sputum increased			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	4		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Insomnia			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Tension</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 9 (0.00%)</p> <p>0</p> <p>0 / 9 (0.00%)</p> <p>0</p>		
<p>Investigations</p> <p>Blood creatine phosphokinase increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Faecal volume decreased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Influenza A virus test positive</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 9 (0.00%)</p> <p>0</p> <p>0 / 9 (0.00%)</p> <p>0</p> <p>1 / 9 (11.11%)</p> <p>1</p>		
<p>Injury, poisoning and procedural complications</p> <p>Arthropod bite</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Contusion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Procedural complication</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 9 (0.00%)</p> <p>0</p> <p>0 / 9 (0.00%)</p> <p>0</p> <p>0 / 9 (0.00%)</p> <p>0</p>		
<p>Nervous system disorders</p> <p>Dizziness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dizziness postural</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Headache</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nerve compression</p>	<p>0 / 9 (0.00%)</p> <p>0</p> <p>0 / 9 (0.00%)</p> <p>0</p> <p>1 / 9 (11.11%)</p> <p>1</p>		

subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0 0 / 9 (0.00%) 0		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Eye disorders Eye irritation subjects affected / exposed occurrences (all) Ocular hyperaemia subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0 0 / 9 (0.00%) 0		
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Defaecation urgency subjects affected / exposed occurrences (all) Diarrhoea	0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 1 / 9 (11.11%) 1 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0		

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Oral pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Salivary hypersecretion			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Dermal cyst			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		

Papule			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pruritus generalised			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Rash macular			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Skin hypertrophy			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Skin hypopigmentation			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Skin irritation			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Swelling face			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Pollakiuria			

subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Muscle twitching			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Periodontitis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 May 2018	Refined study design and revised exclusion criteria
27 July 2018	Updated dosing guidance and prohibited medications

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported