Clinical trial results:
A Phase 2, Randomized, Double-blind, Controlled Study to Evaluate the Safety and Efficacy of VX-121 Combination Therapy in Subjects Aged 18 Years and Older With Cystic Fibrosis

Summary

EudraCT number	2018-002496-18
Trial protocol	DE GB PT NL
Global end of trial date	10 December 2019

Results information

Result version number	v1 (current)
This version publication date	14 April 2023
First version publication date	14 April 2023

Trial information

Trial identification

Sponsor protocol code	VX18-121-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03912233
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 January 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 December 2019
Global end of trial reached?	Yes
Global end of trial date	10 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety, tolerability and efficacy of VX-121 combination therapy in subjects with cystic fibrosis (CF).

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Council on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 2019
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	United States: 34
Country: Number of subjects enrolled	Netherlands: 15
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	Germany: 19
Worldwide total number of subjects	87
EEA total number of subjects	53

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)	87

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Three parts were planned for this study, only Parts 1 (subjects heterozygous for F508del and a minimal function mutation [F/MF genotypes]) and 2 (subjects homozygous for F508del [F/F genotypes]) were conducted. Part 3 was optional and not conducted at sponsor's discretion.

Period 1

Period 1 title	Overall Study (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?	Yes
Arm title	Part 1: Placebo (matched to VX-121/TEZ/VX-561)

Arm description:

Subjects received placebo matched to VX-121/TEZ/VX-561 triple combination (TC) for 4 weeks in the treatment period and placebo matched to TEZ/VX-561 for 18 days in the washout period.

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 received placebo matched to VX-121 once daily.

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

Dosage and administration details:

Subjects received placebo matched to TEZ once daily.

Investigational medicinal product name	Placebo (matched to VX-561)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to VX-561 once daily.

Arm title	Part 1: VX-121/TEZ/VX-561 TC - Low Dose

Arm description:

Subjects received VX-121 5 milligram (mg) once daily (qd)/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/VX-561 150 mg qd for 18 days in the washout period.

Arm type	Experimental

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

Dosage and administration details:

Subjects received VX-121 once daily.

Investigational medicinal product name	TEZ
Investigational medicinal product code	VX-661
Other name	Tezacaftor
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received TEZ once daily.

Investigational medicinal product name	VX-561
Investigational medicinal product code	CTP-656
Other name	Deuterated IVA (D-IVA)
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-561 once daily.

Arm title	Part 1: VX-121/TEZ/VX-561 TC - Medium Dose

Arm description:

Subjects received VX-121 10 mg qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/VX-561 150 mg qd for 18 days in the washout period.

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

Dosage and administration details:

Subjects received VX-121 once daily.

Investigational medicinal product name	TEZ
Investigational medicinal product code	VX-661
Other name	Tezacaftor
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received TEZ once daily.

Investigational medicinal product name	VX-561
Investigational medicinal product code	CTP-656
Other name	D-IVA
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-561 once daily.

Arm title	Part 1: VX-121/TEZ/VX-561 TC - High Dose

Arm description:

Subjects received VX-121 20 mg qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/VX-561 150 mg qd for 18 days in the washout period.

Arm type	Experimental

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

Dosage and administration details:

Subjects received VX-121 once daily.

Investigational medicinal product name	TEZ
Investigational medicinal product code	VX-661
Other name	Tezacaftor
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received TEZ once daily.

Investigational medicinal product name	VX-561
Investigational medicinal product code	CTP-656
Other name	D-IVA
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-561 once daily.

Arm title	Part 2: TEZ/IVA

Arm description:

Following run-in period with TEZ 100 mg qd/IVA 150 mg every 12 hours (q12h) for 4 weeks, subjects received TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks in the treatment period and TEZ 100 mg qd/IVA 150 mg
q12h for 4 weeks in the washout period.

Arm type	Active comparator
Investigational medicinal product name	TEZ/IVA
Investigational medicinal product code	VX-661/VX-770
Other name	Tezacaftor/Ivacaftor
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received TEZ/IVA fixed dose combination once daily in the morning.

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

Dosage and administration details:

Subjects received IVA once daily in the evening.

Arm title	Part 2: VX-121/TEZ/VX-561 TC - High Dose

Arm description:

Following run-in period with TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks, subjects received VX-121 20 mg
qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/IVA 150 mg
q12h for 4 weeks in the washout period.

Arm type	Experimental

Investigational medicinal product name	VX-121
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received VX-121 once daily.	
Investigational medicinal product name	TEZ
Investigational medicinal product code	VX-661
Other name	Tezacaftor
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received TEZ once daily.	
Investigational medicinal product name	VX-561
Investigational medicinal product code	CTP-656
Other name	D-IVA
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received VX-561 once daily.	
Investigational medicinal product name	TEZ/IVA
Investigational medicinal product code	VX-661/VX-770
Other name	Tezacaftor/Ivacaftor
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received TEZ/IVA fixed dose combination once daily in the morning.	
Investigational medicinal product name	IVA
Investigational medicinal product code	VX-770
Other name	Ivacaftor
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received IVA once daily in the evening.	

Number of subjects in period 1[1]	Part 1: Placebo (matched to VX-121/TEZ/VX-561)	Part 1: VX-121/TEZ/VX-561 TC - Low Dose	Part 1: VX-121/TEZ/VX-561 TC - Medium Dose
Started	10	9	19
Completed	8	9	19
Not completed	2	0	0
Physician decision	1	-	-
Adverse Event	1	-	-
Other	-	-	-

Number of subjects in period 1[1]	Part 1: VX-121/TEZ/VX-561 TC - High Dose	Part 2: TEZ/IVA	Part 2: VX-121/TEZ/VX-561 TC - High Dose

Started	20	10	18
Completed	20	3	6
Not completed	0	7	12
Physician decision	-	-	-
Adverse Event	-	-	-
Other	-	7	12

Notes:

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

Justification: Out of 87 subjects enrolled in the study (58 subjects in Part 1 and 29 subjects in Part 2 run-in Period), 1 subject in Part 2 run-in period discontinued from study and was not randomized in the treatment period. Therefore, only 86 subjects are included in the above subject disposition table and baseline characteristics section for the treatment period.

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: Placebo (matched to VX-121/TEZ/VX-561)
Reporting group description:	
Subjects received placebo matched to VX-121/TEZ/VX-561 triple combination (TC) for 4 weeks in the treatment period and placebo matched to TEZ/VX-561 for 18 days in the washout period.	
Reporting group title	Part 1: VX-121/TEZ/VX-561 TC - Low Dose
Reporting group description:	
Subjects received VX-121 5 milligram (mg) once daily (qd)/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/VX-561 150 mg qd for 18 days in the washout period.	
Reporting group title	Part 1: VX-121/TEZ/VX-561 TC - Medium Dose
Reporting group description:	
Subjects received VX-121 10 mg qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/VX-561 150 mg qd for 18 days in the washout period.	
Reporting group title	Part 1: VX-121/TEZ/VX-561 TC - High Dose
Reporting group description:	
Subjects received VX-121 20 mg qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/VX-561 150 mg qd for 18 days in the washout period.	
Reporting group title	Part 2: TEZ/IVA
Reporting group description:	
Following run-in period with TEZ 100 mg qd/IVA 150 mg every 12 hours (q12h) for 4 weeks, subjects received TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks in the treatment period and TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks in the washout period.	
Reporting group title	Part 2: VX-121/TEZ/VX-561 TC - High Dose
Reporting group description:	
Following run-in period with TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks, subjects received VX-121 20 mg qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks in the washout period.	

Reporting group values	Part 1: Placebo (matched to VX-121/TEZ/VX-561)	Part 1: VX-121/TEZ/VX-561 TC - Low Dose	Part 1: VX-121/TEZ/VX-561 TC - Medium Dose
Number of subjects	10	9	19
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	10	9	19
>=65 years	0	0	0
Gender categorical Units: Subjects			
Female	2	4	3
Male	8	5	16
Ethnicity (NIH/ OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	10	8	19
Unknown or Not Reported	0	1	0
Race (NIH/OMB)			

Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	1
White	9	8	18
More than one race	1	0	0
Unknown or Not Reported	0	1	0
Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1)			
FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration.			
Units: Subjects			
<40 percent	1	1	1
>=40 to <70 percent	9	6	14
>=70 to <=90 percent	0	2	4

Reporting group values	Part 1: VX-121/TEZ/VX-561 TC - High Dose	Part 2: TEZ/IVA	Part 2: VX-121/TEZ/VX-561 TC - High Dose
Number of subjects	20	10	18
Age categorical			
Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	20	10	18
>=65 years	0	0	0
Gender categorical			
Units: Subjects			
Female	9	2	7
Male	11	8	11
Ethnicity (NIH/ OMB)			
Units: Subjects			
Hispanic or Latino	2	1	0
Not Hispanic or Latino	17	8	18
Unknown or Not Reported	1	1	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	17	9	18
More than one race	0	0	0
Unknown or Not Reported	3	1	0
Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1)			
FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration.			
Units: Subjects			
<40 percent	0	1	2
>=40 to <70 percent	17	6	11
>=70 to <=90 percent	3	3	5

Reporting group values	Total		
Number of subjects	86		
Age categorical Units: Subjects			
<=18 years	0		
Between 18 and 65 years	86		
>=65 years	0		
Gender categorical Units: Subjects			
Female	27		
Male	59		
Ethnicity (NIH/ OMB) Units: Subjects			
Hispanic or Latino	3		
Not Hispanic or Latino	80		
Unknown or Not Reported	3		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	1		
White	79		
More than one race	1		
Unknown or Not Reported	5		
Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1)			
FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration.			
Units: Subjects			
<40 percent	6		
>=40 to <70 percent	63		
>=70 to <=90 percent	17		

End points

End points reporting groups

Reporting group title	Part 1: Placebo (matched to VX-121/TEZ/VX-561)
Reporting group description: Subjects received placebo matched to VX-121/TEZ/VX-561 triple combination (TC) for 4 weeks in the treatment period and placebo matched to TEZ/VX-561 for 18 days in the washout period.	
Reporting group title	Part 1: VX-121/TEZ/VX-561 TC - Low Dose
Reporting group description: Subjects received VX-121 5 milligram (mg) once daily (qd)/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/VX-561 150 mg qd for 18 days in the washout period.	
Reporting group title	Part 1: VX-121/TEZ/VX-561 TC - Medium Dose
Reporting group description: Subjects received VX-121 10 mg qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/VX-561 150 mg qd for 18 days in the washout period.	
Reporting group title	Part 1: VX-121/TEZ/VX-561 TC - High Dose
Reporting group description: Subjects received VX-121 20 mg qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/VX-561 150 mg qd for 18 days in the washout period.	
Reporting group title	Part 2: TEZ/IVA
Reporting group description: Following run-in period with TEZ 100 mg qd/IVA 150 mg every 12 hours (q12h) for 4 weeks, subjects received TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks in the treatment period and TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks in the washout period.	
Reporting group title	Part 2: VX-121/TEZ/VX-561 TC - High Dose
Reporting group description: Following run-in period with TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks, subjects received VX-121 20 mg qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks in the washout period.	
Subject analysis set title	Part 1: VX-121/TEZ/VX-561 TC - Combined
Subject analysis set type	Full analysis
Subject analysis set description: Subjects who either received VX-121 5 mg, 10 mg or 20 mg qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/VX-561 150 mg qd for 18 days in the washout period.	
Subject analysis set title	Part 2: VX-121/TEZ/VX-561 TC - High Dose
Subject analysis set type	Full analysis
Subject analysis set description: Following run-in period with TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks, participants received VX-121 20 mg qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks in the washout period.	

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

End point title	Safety and Tolerability as Assessed by Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)[1]
End point description: Safety set included all subjects who received at least 1 dose of study drug in the treatment period.	
End point type	Primary

End point timeframe:

From Day 1 Through Safety Follow-up (up to Day 75 for Part 1 and up to Day 85 for Part 2)

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 analyses were planned for the primary safety end point. No statistical comparisons were planned.

End point values	Part 1: Placebo (matched to VX-121/TEZ/VX-561)	Part 1: VX-121/TEZ/VX-561 TC - Low Dose	Part 1: VX-121/TEZ/VX-561 TC - Medium Dose	Part 1: VX-121/TEZ/VX-561 TC - High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	19	20
Units: Subjects				
Subjects with TEAEs	9	8	16	20
Subjects with SAEs	2	1	1	0

End point values	Part 2: TEZ/IVA	Part 2: VX-121/TEZ/VX-561 TC - High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	18		
Units: Subjects				
Subjects with TEAEs	8	16		
Subjects with SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Absolute Change in Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1)

End point title	Absolute Change in Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1)[2]

End point description:

FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. Full analysis set (FAS) included all randomized subjects who carry the intended cystic fibrosis transmembrane conductance regulator gene (CFTR) allele mutation(s) and received at least 1 dose of study drug in the treatment period.

End point type	Primary

End point timeframe:

From Baseline Through Day 29

Notes:

[2] - 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 within treatment group comparisons were planned for this endpoint. Therefore, no between groups comparisons are reported.

End point values	Part 1: Placebo (matched to VX-121/TEZ/VX-561)	Part 1: VX-121/TEZ/VX-561 TC - Low Dose	Part 1: VX-121/TEZ/VX-561 TC - Medium Dose	Part 1: VX-121/TEZ/VX-561 TC - High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	19	20
Units: percentage points				
least squares mean (confidence interval 95%)	1.9 (-4.1 to 8.0)	4.6 (-1.3 to 10.6)	14.2 (10.0 to 18.4)	9.8 (5.7 to 13.8)

End point values	Part 2: TEZ/IVA	Part 2: VX-121/TEZ/VX-561 TC - High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	18		
Units: percentage points				
least squares mean (confidence interval 95%)	-0.1 (-6.4 to 6.1)	15.9 (11.3 to 20.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change in Sweat Chloride (SwCl) Concentrations

End point title	Absolute Change in Sweat Chloride (SwCl) Concentrations
End point description:	
Sweat samples were collected using an approved collection device. FAS.	
End point type	Secondary
End point timeframe:	
From Baseline Through Day 29	

End point values	Part 1: Placebo (matched to VX-121/TEZ/VX-561)	Part 1: VX-121/TEZ/VX-561 TC - Low Dose	Part 1: VX-121/TEZ/VX-561 TC - Medium Dose	Part 1: VX-121/TEZ/VX-561 TC - High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	19	20
Units: millimole per liter (mmol/L)				
least squares mean (confidence interval 95%)	2.3 (-7.0 to 11.6)	-42.8 (-51.7 to -34.0)	-45.8 (-51.9 to -39.7)	-49.5 (-55.9 to -43.1)

End point values	Part 2:	Part 2: VX-		

	TEZ/IVA	121/TEZ/VX-561 TC - High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	18		
Units: millimole per liter (mmol/L)				
least squares mean (confidence interval 95%)	-2.6 (-8.2 to 3.1)	-45.5 (-49.7 to -41.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Respiratory Domain Score

End point title	Absolute Change in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Respiratory Domain Score

End point description:

The CFQ-R is a validated subject-reported outcome measuring health-related quality of life for subjects with
cystic fibrosis. Respiratory domain assessed respiratory symptoms, score range: 0-100; higher scores indicating fewer
symptoms and better health-related quality of life. FAS.

End point type	Secondary

End point timeframe:

From Baseline at Day 29

End point values	Part 1: Placebo (matched to VX-121/TEZ/VX-561)	Part 1: VX-121/TEZ/VX-561 TC - Low Dose	Part 1: VX-121/TEZ/VX-561 TC - Medium Dose	Part 1: VX-121/TEZ/VX-561 TC - High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	19	20
Units: units on a scale				
least squares mean (confidence interval 95%)	3.3 (-10.1 to 16.6)	17.6 (3.5 to 31.6)	21.2 (11.9 to 30.6)	29.8 (21.0 to 38.7)

End point values	Part 2: TEZ/IVA	Part 2: VX-121/TEZ/VX-561 TC - High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	18		
Units: units on a scale				
least squares mean (confidence interval 95%)	-5.0 (-16.9 to 7.0)	19.4 (10.5 to 28.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Pre-dose Plasma Concentration (Ctrough) of VX-121, TEZ and Its Metabolite (M1-TEZ) and, VX-561 and Its Metabolites (M1-VX-561 and M6-VX-561)

End point title	Observed Pre-dose Plasma Concentration (Ctrough) of VX-121, TEZ and Its Metabolite (M1-TEZ) and, VX-561 and Its Metabolites (M1-VX-561 and M6-VX-561)

End point description:

Pharmacokinetic (PK) set included all subjects who received at least 1 dose study drug in the treatment period and for whom the PK data are considered
sufficient and interpretable. Subjects who received VX-121/TEZ/VX-561 TC in Parts 1 or 2 were to be analyzed for Ctrough. Overall subjects in Part 1
were assessed for Ctrough, therefore data are reported in single Part 1: TC combined arm. The "n" signifies subjects who were evaluable
at specified time point for respective reporting arm. Here, "99999" represents "not applicable" category for respective Ctrough assessment.

End point type	Secondary

End point timeframe:

Pre-dose at Day 15 and Day 29

End point values	Part 1: VX-121/TEZ/VX-561 TC - Combined	Part 2: VX-121/TEZ/VX-561 TC - High Dose		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	18		
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 15: VX-121 5 mg (n=8, 0)	317 (± 119)	99999 (± 99999)		
Day 29: VX-121 5 mg (n=7, 0)	366 (± 130)	99999 (± 99999)		
Day 15: VX-121 10 mg (n=18, 0)	520 (± 214)	99999 (± 99999)		
Day 29: VX-121 10 mg (n=14, 0)	582 (± 342)	99999 (± 99999)		
Day 15: VX-121 20 mg (n=20, 17)	974 (± 500)	1050 (± 414)		
Day 29: VX-121 20 mg (n=18, 16)	1160 (± 592)	1030 (± 371)		
Day 15: TEZ (n=46, 17)	1890 (± 925)	1870 (± 675)		
Day 29: TEZ (n=46, 16)	1920 (± 994)	2070 (± 1340)		
Day 15: M1-TEZ (n=46, 17)	4500 (± 1290)	4550 (± 1200)		
Day 29: M1-TEZ (n=46, 16)	4640 (± 1730)	4440 (± 1680)		
Day 15: VX-561 (n=46, 17)	475 (± 247)	457 (± 264)		
Day 29: VX-561 (n=46, 16)	510 (± 285)	434 (± 257)		

Day 15: M1-VX-561 (n=46, 17)	311 (± 141)	326 (± 175)		
Day 29: M1-VX-561 (n=46, 16)	336 (± 173)	316 (± 188)		
Day 15: M6-VX-561 (n=46, 17)	148 (± 98.0)	174 (± 128)		
Day 29: M6-VX-561 (n=46, 16)	163 (± 128)	159 (± 94.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 Through Safety Follow-up (up to Day 75 for Part 1 and up to Day 85 for Part 2)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Part 1: Placebo (matched to VX-121/TEZ/VX-561)

Reporting group description:

Subjects received placebo matched to VX-121/TEZ/VX-561 TC for 4 weeks in the treatment period and placebo matched to TEZ/VX-561 for 18 days in the washout period.

Reporting group title	Part 1: VX-121/TEZ/VX-561 TC - Low Dose

Reporting group description:

Subjects received VX-121 5 qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/VX-561 150 mg qd for 18 days in the washout period.

Reporting group title	Part 1: VX-121/TEZ/VX-561 TC - Medium Dose

Reporting group description:

Subjects received VX-121 10 mg qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/VX-561 150 mg qd for 18 days in the washout period.

Reporting group title	Part 1: VX-121/TEZ/VX-561 TC - High Dose

Reporting group description:

Subjects received VX-121 20 mg qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/VX-561 150 mg qd for 18 days in the washout period.

Reporting group title	Part 2: TEZ/IVA

Reporting group description:

Following run-in period with TEZ 100 mg/IVA 150 mg q12h for 4 weeks, participants received TEZ 100 mg/IVA 150 mg q12h for 4 weeks in the treatment period and TEZ 100 mg/IVA 150 mg q12h for 4 weeks in the washout period.

Reporting group title	Part 2: VX-121/TEZ/VX-561 TC - High Dose

Reporting group description:

Following run-in period with TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks, participants received VX-121 20 mg qd/TEZ 100 mg qd/VX-561 150 mg qd TC for 4 weeks in the treatment period and TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks in the washout period.

Serious adverse events	Part 1: Placebo (matched to VX-121/TEZ/VX-561)	Part 1: VX-121/TEZ/VX-561 TC - Low Dose	Part 1: VX-121/TEZ/VX-561 TC - Medium Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	1 / 19 (5.26%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			

subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 1: VX-121/TEZ/VX-561 TC - High Dose	Part 2: TEZ/IVA	Part 2: VX-121/TEZ/VX-561 TC - High Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (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
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (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
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (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

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

Non-serious adverse events	Part 1: Placebo (matched to VX-121/TEZ/VX-561)	Part 1: VX-121/TEZ/VX-561 TC - Low Dose	Part 1: VX-121/TEZ/VX-561 TC - Medium Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)	8 / 9 (88.89%)	16 / 19 (84.21%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	5 / 19 (26.32%)
occurrences (all)	0	2	5
Feeling abnormal			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Pain			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 10 (50.00%)	4 / 9 (44.44%)	5 / 19 (26.32%)
occurrences (all)	7	4	5
Dysphonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	2 / 19 (10.53%)
occurrences (all)	1	1	2
Epistaxis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Haemoptysis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
Lower respiratory tract congestion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Nasal obstruction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			

subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	3 / 19 (15.79%)
occurrences (all)	0	2	3
Painful respiration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pleuritic pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	3 / 10 (30.00%)	0 / 9 (0.00%)	2 / 19 (10.53%)
occurrences (all)	3	0	4
Rales			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Respiration abnormal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Rhinorrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Sinus congestion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Sneezing			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Sputum increased			
subjects affected / exposed	3 / 10 (30.00%)	6 / 9 (66.67%)	3 / 19 (15.79%)
occurrences (all)	5	8	3
Throat clearing			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Wheezing			

subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Mood swings			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Somnambulism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Blood bilirubin increased			

subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin unconjugated increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	3 / 19 (15.79%)
occurrences (all)	0	1	4
Blood glucose increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood potassium increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood pressure diastolic increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Crystal urine present			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Eosinophil count increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Forced expiratory volume decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Glucose urine present			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
International normalised ratio increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Weight increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
White blood cell count increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Contusion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Limb injury			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	1 / 10 (10.00%)	2 / 9 (22.22%)	4 / 19 (21.05%)
occurrences (all)	1	3	5
Paraesthesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Lymphadenopathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Eye disorders			
Swelling of eyelid			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	4 / 19 (21.05%)
occurrences (all)	0	0	6
Dyspepsia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Post-tussive vomiting			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Exfoliative rash			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Rash pruritic			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Back pain			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Intervertebral disc protrusion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Tendon pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Infections and infestations			
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Infective pulmonary exacerbation of cystic fibrosis			

subjects affected / exposed	4 / 10 (40.00%)	3 / 9 (33.33%)	0 / 19 (0.00%)
occurrences (all)	5	3	0
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	2 / 9 (22.22%)	2 / 19 (10.53%)
occurrences (all)	1	2	2
Oral candidiasis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Viral rash			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	3 / 19 (15.79%)
occurrences (all)	0	0	3
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Hyperglycaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0

Hypoglycaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Polydipsia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

Non-serious adverse events	Part 1: VX-121/TEZ/VX-561 TC - High Dose	Part 2: TEZ/IVA	Part 2: VX-121/TEZ/VX-561 TC - High Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)	8 / 10 (80.00%)	16 / 18 (88.89%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 20 (0.00%)	3 / 10 (30.00%)	0 / 18 (0.00%)
occurrences (all)	0	4	0
Fatigue			
subjects affected / exposed	2 / 20 (10.00%)	2 / 10 (20.00%)	0 / 18 (0.00%)
occurrences (all)	2	3	0
Feeling abnormal			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pain			

subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 20 (5.00%)	2 / 10 (20.00%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 20 (45.00%)	7 / 10 (70.00%)	5 / 18 (27.78%)
occurrences (all)	13	9	6
Dysphonia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	3 / 20 (15.00%)	2 / 10 (20.00%)	0 / 18 (0.00%)
occurrences (all)	3	3	0
Epistaxis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	2 / 20 (10.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
Lower respiratory tract congestion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	3 / 20 (15.00%)	2 / 10 (20.00%)	1 / 18 (5.56%)
occurrences (all)	3	2	1
Nasal obstruction			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			

subjects affected / exposed	2 / 20 (10.00%)	0 / 10 (0.00%)	3 / 18 (16.67%)
occurrences (all)	2	0	3
Painful respiration			
subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Paranasal sinus hypersecretion			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Pleuritic pain			
subjects affected / exposed	1 / 20 (5.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Productive cough			
subjects affected / exposed	3 / 20 (15.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Rales			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Respiration abnormal			
subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	1 / 20 (5.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	3	2	0
Sneezing			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sputum increased			
subjects affected / exposed	4 / 20 (20.00%)	3 / 10 (30.00%)	5 / 18 (27.78%)
occurrences (all)	7	3	5
Throat clearing			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Wheezing			

subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Mood swings			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Panic attack			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Sleep disorder			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Somnambulism			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			

subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin unconjugated increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	2 / 18 (11.11%)
occurrences (all)	1	0	2
Blood glucose increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood pressure diastolic increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood pressure increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Crystal urine present			
subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Eosinophil count increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Forced expiratory volume decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Glucose urine present			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	2 / 20 (10.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	1
Dysgeusia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	6 / 20 (30.00%)	1 / 10 (10.00%)	2 / 18 (11.11%)
occurrences (all)	9	1	2
Paraesthesia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Thrombocytopenia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Swelling of eyelid			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	1 / 20 (5.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	1	2	0

Abdominal pain			
subjects affected / exposed	2 / 20 (10.00%)	1 / 10 (10.00%)	1 / 18 (5.56%)
occurrences (all)	2	1	1
Abdominal pain upper			
subjects affected / exposed	2 / 20 (10.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Constipation			
subjects affected / exposed	2 / 20 (10.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	5 / 20 (25.00%)	1 / 10 (10.00%)	2 / 18 (11.11%)
occurrences (all)	6	1	2
Dyspepsia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	2 / 20 (10.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Frequent bowel movements			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Post-tussive vomiting			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Salivary hypersecretion			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Acne			

subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Exfoliative rash			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Pruritus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Rash			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	3 / 18 (16.67%)
occurrences (all)	1	0	3
Rash pruritic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Skin lesion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Back pain			

subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 10 (20.00%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Neck pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Tendon pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Infective pulmonary exacerbation of cystic fibrosis			

subjects affected / exposed	3 / 20 (15.00%)	2 / 10 (20.00%)	0 / 18 (0.00%)
occurrences (all)	4	2	0
Nasopharyngitis			
subjects affected / exposed	2 / 20 (10.00%)	2 / 10 (20.00%)	2 / 18 (11.11%)
occurrences (all)	2	3	2
Oral candidiasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Sinusitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 10 (10.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Viral rash			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 20 (5.00%)	2 / 10 (20.00%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
Hyperglycaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Hypoglycaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 10 (0.00%)	2 / 18 (11.11%)
occurrences (all)	1	0	2
Polydipsia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 10 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 November 2018	Amended to include study drug doses and dosing regimen.
04 March 2019	Amended to include clarification on PK sampling and study conduct.
09 May 2019	Amended to update acceptable methods of contraception.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported