



Clinical trial results:

A Phase 2, Randomized, Double-blind, Controlled Study to Evaluate the Safety and Efficacy of VX-659 Combination Therapy in Subjects Aged 18 Years and Older With Cystic Fibrosis

Summary

EudraCT number	2016-003585-11
Trial protocol	IE GB
Global end of trial date	28 February 2018

Results information

Result version number	v2 (current)
This version publication date	16 July 2021
First version publication date	16 March 2019
Version creation reason	<ul style="list-style-type: none">• New data added to full data set Secondary endpoints results need to be added

Trial information

Trial identification

Sponsor protocol code	VX16-659-101
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03224351
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, +1 877 634 8789, medicalinfo@vrtx.com
Scientific contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 877 634 8789, 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 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2018
Global end of trial reached?	Yes
Global end of trial date	28 February 2018
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-659 in triple combination (TC) with Tezacaftor/Ivacaftor (TEZ/IVA) or with TEZ/VX-561.

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	08 August 2017
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 Kingdom: 29
Country: Number of subjects enrolled	Ireland: 11
Country: Number of subjects enrolled	United States: 77
Country: Number of subjects enrolled	Israel: 7
Worldwide total number of subjects	124
EEA total number of subjects	40

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)	124
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study included 3 parts and was conducted in adult subjects with cystic fibrosis (CF).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Part 1: Placebo
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Arm description:

Subjects received placebo matched to VX-659/TEZ/IVA in TC treatment period for 4 weeks and placebo matched to TEZ/IVA in washout period for 4 days.

Arm type	Placebo
Investigational medicinal product name	Placebo (matched to VX-659)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to VX-659 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 1: VX-659/TEZ/IVA TC - Low Dose
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Arm description:

Subjects received VX-659 80 milligram (mg) once daily (qd)/TEZ 100 mg qd/IVA 150 mg every 12 hours (q12h) in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 days.

Arm type	Experimental
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Investigational medicinal product name	VX-659
Investigational medicinal product code	VX-659
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-659 low dose 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 1: VX-659/TEZ/IVA TC - Medium Dose
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Arm description:

Subjects received VX-659 240 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks
and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 days.

Arm type	Experimental
Investigational medicinal product name	VX-659
Investigational medicinal product code	VX-659
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-659 medium dose 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 1: VX-659/TEZ/IVA TC - High Dose
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Arm description:

Subjects received VX-659 400 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks

and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 days.

Arm type	Experimental
Investigational medicinal product name	VX-659
Investigational medicinal product code	VX-659
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-659 high dose 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 2: TEZ/IVA
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Arm description:

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

Arm type	Active comparator
Investigational medicinal product name	Placebo (matched to VX-659)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to VX-659 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 2: VX-659/TEZ/IVA TC
Arm description: Following run-in period with TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks, subjects received VX-659 400 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 weeks.	
Arm type	Experimental
Investigational medicinal product name	VX-659
Investigational medicinal product code	VX-659
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received VX-659 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 3: Placebo
Arm description: Subjects received placebo matched to VX-659/TEZ/VX-561 in TC treatment period for 4 weeks.	
Arm type	Placebo
Investigational medicinal product name	Placebo (matched to VX-659)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received placebo matched to VX-659 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
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Dosage and administration details:

Subjects received placebo matched to VX-561 once daily.

Arm title	Part 3: VX-659/TEZ/VX-561 TC
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Arm description:

Subjects received VX-659 400 mg qd/TEZ 100 mg qd/VX-561 200 mg qd in TC treatment period for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	VX-659
Investigational medicinal product code	VX-659
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-659 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	VX-561
Other name	CTP-656
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-561 once daily.

Number of subjects in period 1 ^[1]	Part 1: Placebo	Part 1: VX-659/TEZ/IVA TC - Low Dose	Part 1: VX-659/TEZ/IVA TC - Medium Dose
Started	10	11	20
Completed	10	11	20

Number of subjects in period 1 ^[1]	Part 1: VX-659/TEZ/IVA TC - High Dose	Part 2: TEZ/IVA	Part 2: VX-659/TEZ/IVA TC
Started	22	11	18
Completed	22	11	18

Number of subjects in period 1 ^[1]	Part 3: Placebo	Part 3: VX-659/TEZ/VX-561 TC
Started	6	19

Completed	6	19
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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: There were 117 subjects dosed in the TC treatment period for all 3 parts. 7 subjects were dosed in the run-in period in part 2 but were not dosed in TC treatment period. Therefore, the total enrolled subjects are 124 where as the subjects reported in disposition and baseline are 117.

Baseline characteristics

Reporting groups

Reporting group title	Part 1: Placebo
Reporting group description: Subjects received placebo matched to VX-659/TEZ/IVA in TC treatment period for 4 weeks and placebo matched to TEZ/IVA in washout period for 4 days.	
Reporting group title	Part 1: VX-659/TEZ/IVA TC - Low Dose
Reporting group description: Subjects received VX-659 80 milligram (mg) once daily (qd)/TEZ 100 mg qd/IVA 150 mg every 12 hours (q12h) in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 days.	
Reporting group title	Part 1: VX-659/TEZ/IVA TC - Medium Dose
Reporting group description: Subjects received VX-659 240 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 days.	
Reporting group title	Part 1: VX-659/TEZ/IVA TC - High Dose
Reporting group description: Subjects received VX-659 400 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 days.	
Reporting group title	Part 2: TEZ/IVA
Reporting group description: Following run-in period with TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks, subjects received TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 weeks.	
Reporting group title	Part 2: VX-659/TEZ/IVA TC
Reporting group description: Following run-in period with TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks, subjects received VX-659 400 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 weeks.	
Reporting group title	Part 3: Placebo
Reporting group description: Subjects received placebo matched to VX-659/TEZ/VX-561 in TC treatment period for 4 weeks.	
Reporting group title	Part 3: VX-659/TEZ/VX-561 TC
Reporting group description: Subjects received VX-659 400 mg qd/TEZ 100 mg qd/VX-561 200 mg qd in TC treatment period for 4 weeks.	

Reporting group values	Part 1: Placebo	Part 1: VX-659/TEZ/IVA TC - Low Dose	Part 1: VX-659/TEZ/IVA TC - Medium Dose
Number of subjects	10	11	20
Age categorical			
Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	26.6 ± 6.0	32.0 ± 11.7	31.4 ± 9.7
Gender categorical Units: Subjects			
Female	4	7	7
Male	6	4	13
Ethnicity (NIH/ OMB) Units: Subjects			
Hispanic or Latino	0	0	2
Not Hispanic or Latino	10	11	18
Unknown or Not Reported	0	0	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	10	11	20
More than one race	0	0	0
Unknown or Not Reported	0	0	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	2	0	1
≥40 to <70 percent	6	9	13
≥70 to ≤90 percent	2	2	6
>90 percent	0	0	0

Reporting group values	Part 1: VX-659/TEZ/IVA TC - High Dose	Part 2: TEZ/IVA	Part 2: VX-659/TEZ/IVA TC
Number of subjects	22	11	18
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	27.2 ± 6.6	32.5 ± 7.5	33.4 ± 9.2
Gender categorical Units: Subjects			
Female	12	4	6
Male	10	7	12
Ethnicity (NIH/ OMB) Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	22	10	17
Unknown or Not Reported	0	0	0

Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	22	11	16
More than one race	0	0	0
Unknown or Not Reported	0	0	1
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	2	0	1
>=40 to <70 percent	13	8	12
>=70 to <=90 percent	7	3	5
>90 percent	0	0	0

Reporting group values	Part 3: Placebo	Part 3: VX-659/TEZ/VX-561 TC	Total
Number of subjects	6	19	117
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	24.5	32.5	
standard deviation	± 5.3	± 9.4	-
Gender categorical			
Units: Subjects			
Female	3	11	54
Male	3	8	63
Ethnicity (NIH/ OMB)			
Units: Subjects			
Hispanic or Latino	1	1	6
Not Hispanic or Latino	5	18	111
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	2	2
White	6	17	113
More than one race	0	0	0
Unknown or Not Reported	0	0	1
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	2	8
>=40 to <70 percent	5	13	79
>=70 to <=90 percent	1	4	30
>90 percent	0	0	0

End points

End points reporting groups

Reporting group title	Part 1: Placebo
Reporting group description: Subjects received placebo matched to VX-659/TEZ/IVA in TC treatment period for 4 weeks and placebo matched to TEZ/IVA in washout period for 4 days.	
Reporting group title	Part 1: VX-659/TEZ/IVA TC - Low Dose
Reporting group description: Subjects received VX-659 80 milligram (mg) once daily (qd)/TEZ 100 mg qd/IVA 150 mg every 12 hours (q12h) in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 days.	
Reporting group title	Part 1: VX-659/TEZ/IVA TC - Medium Dose
Reporting group description: Subjects received VX-659 240 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 days.	
Reporting group title	Part 1: VX-659/TEZ/IVA TC - High Dose
Reporting group description: Subjects received VX-659 400 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 days.	
Reporting group title	Part 2: TEZ/IVA
Reporting group description: Following run-in period with TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks, subjects received TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 weeks.	
Reporting group title	Part 2: VX-659/TEZ/IVA TC
Reporting group description: Following run-in period with TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks, subjects received VX-659 400 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 weeks.	
Reporting group title	Part 3: Placebo
Reporting group description: Subjects received placebo matched to VX-659/TEZ/VX-561 in TC treatment period for 4 weeks.	
Reporting group title	Part 3: VX-659/TEZ/VX-561 TC
Reporting group description: Subjects received VX-659 400 mg qd/TEZ 100 mg qd/VX-561 200 mg qd in TC treatment period for 4 weeks.	

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

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

End point timeframe:

Day 1 Through Safety Follow-up (up to Day 61 for Part 1, Day 85 for Part 2 and Day 57 for Part 3)

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 1: Placebo	Part 1: VX-659/TEZ/IVA TC - Low Dose	Part 1: VX-659/TEZ/IVA TC - Medium Dose	Part 1: VX-659/TEZ/IVA TC - High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	20	22
Units: subjects				
Subjects with TEAEs	9	10	15	17
Subjects with SAEs	3	1	4	1

End point values	Part 2: TEZ/IVA	Part 2: VX-659/TEZ/IVA TC	Part 3: Placebo	Part 3: VX-659/TEZ/VX-561 TC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	18	6	19
Units: subjects				
Subjects with TEAEs	9	15	6	18
Subjects with SAEs	2	1	3	2

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]
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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. Full Analysis Set (FAS) included all randomized subjects with an eligible cystic fibrosis transmembrane conductance regulator protein (CFTR) genotype and received at least 1 dose of study drug.

End point type	Primary
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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: The study is not designed to perform between treatment group comparisons.

End point values	Part 1: Placebo	Part 1: VX-659/TEZ/IVA TC - Low Dose	Part 1: VX-659/TEZ/IVA TC - Medium Dose	Part 1: VX-659/TEZ/IVA TC - High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	20	22
Units: percentage points				
least squares mean (confidence interval 95%)	0.4 (-5.3 to 6.1)	10.2 (4.8 to 15.5)	12.0 (8.0 to 16.0)	13.3 (9.5 to 17.1)

End point values	Part 2: TEZ/IVA	Part 2: VX-659/TEZ/IVA TC	Part 3: Placebo	Part 3: VX-659/TEZ/VX-561 TC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	18	6	19
Units: percentage points				
least squares mean (confidence interval 95%)	0.0 (-3.9 to 3.9)	9.7 (6.6 to 12.7)	-5.0 (-12.2 to 2.1)	12.2 (8.3 to 16.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change in Sweat Chloride Concentrations

End point title	Absolute Change in Sweat Chloride 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	Part 1: VX-659/TEZ/IVA TC - Low Dose	Part 1: VX-659/TEZ/IVA TC - Medium Dose	Part 1: VX-659/TEZ/IVA TC - High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	20	22
Units: millimole per liter (mmol/L)				
least squares mean (confidence interval 95%)	2.9 (-6.3 to 12.2)	-45.7 (-54.4 to -37.0)	-43.8 (-50.7 to -37.0)	-51.4 (-57.8 to -44.9)

End point values	Part 2: TEZ/IVA	Part 2: VX-659/TEZ/IVA TC	Part 3: Placebo	Part 3: VX-659/TEZ/VX-561 TC
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Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	18	6	19
Units: millimole per liter (mmol/L)				
least squares mean (confidence interval 95%)	3.0 (-2.8 to 8.9)	-42.2 (-46.8 to -37.7)	-1.3 (-12.4 to 9.8)	-38.1 (-44.4 to -31.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Relative Change in ppFEV1

End point title	Relative Change in ppFEV1
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
End point timeframe: From Baseline Through Day 29	

End point values	Part 1: Placebo	Part 1: VX-659/TEZ/IVA TC - Low Dose	Part 1: VX-659/TEZ/IVA TC - Medium Dose	Part 1: VX-659/TEZ/IVA TC - High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	20	22
Units: percent change				
least squares mean (confidence interval 95%)	0.0 (-10.5 to 10.4)	18.8 (8.9 to 28.7)	21.1 (13.8 to 28.5)	24.6 (17.6 to 31.6)

End point values	Part 2: TEZ/IVA	Part 2: VX-659/TEZ/IVA TC	Part 3: Placebo	Part 3: VX-659/TEZ/VX-561 TC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	18	6	19
Units: percent change				
least squares mean (confidence interval 95%)	0.1 (-7.1 to 7.3)	17.3 (11.7 to 23.0)	-11.3 (-23.7 to 1.1)	21.5 (14.6 to 28.4)

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
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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	Part 1: VX-659/TEZ/IVA TC - Low Dose	Part 1: VX-659/TEZ/IVA TC - Medium Dose	Part 1: VX-659/TEZ/IVA TC - High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	20	22
Units: units on a scale				
least squares mean (confidence interval 95%)	4.7 (-7.5 to 16.8)	24.6 (13.0 to 36.2)	19.8 (11.0 to 28.6)	21.8 (13.6 to 30.0)

End point values	Part 2: TEZ/IVA	Part 2: VX-659/TEZ/IVA TC	Part 3: Placebo	Part 3: VX-659/TEZ/VX-561 TC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	18	6	19
Units: units on a scale				
least squares mean (confidence interval 95%)	2.9 (-5.2 to 11.1)	19.5 (13.1 to 25.9)	-4.1 (-17.8 to 9.6)	14.7 (7.1 to 22.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Pre-dose Concentration (Ctough) of VX-659, TEZ, M1-TEZ, IVA, M1-IVA, and VX-561

End point title

Observed Pre-dose Concentration (Ctough) of VX-659, TEZ, M1-TEZ, IVA, M1-IVA, and VX-561^[3]

End point description:

Pharmacokinetic Set (PK) included all subjects who have received at least 1 dose of study drug in TC treatment period. Here "n" signifies those subjects who were evaluable at specified time points and "99999" represents "not applicable" for particular category for Ctough assessments. VX-659 category was not applicable for Part 2: TEZ/IVA group. VX-561 category was applicable for Part 3: TC group only. IVA and M1-IVA categories were not applicable for Part 3: TC group.

End point type

Secondary

End point timeframe:

Pre-dose at Day 15 and Day 29

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: Parts 1 and 3: Placebo arms were not applicable for this endpoint.

End point values	Part 1: VX-659/TEZ/IVA TC - Low Dose	Part 1: VX-659/TEZ/IVA TC - Medium Dose	Part 1: VX-659/TEZ/IVA TC - High Dose	Part 2: TEZ/IVA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	20	22	11
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
VX-659: Day 15 (n=10, 16, 19, 0, 17, 17)	393 (± 604)	622 (± 429)	1100 (± 731)	99999 (± 99999)
VX-659: Day 29 (n=11, 19, 22, 0, 18, 19)	566 (± 861)	699 (± 489)	1080 (± 582)	99999 (± 99999)
TEZ: Day 15 (n=10, 16, 19, 7, 17, 17)	1910 (± 1360)	1250 (± 907)	1110 (± 455)	1050 (± 473)
TEZ: Day 29 (n=11, 19, 22, 11, 18, 19)	1910 (± 1230)	1050 (± 553)	1010 (± 479)	1150 (± 480)
M1-TEZ: Day 15 (n=10, 16, 19, 7, 17, 19)	4390 (± 949)	3710 (± 1230)	4280 (± 1190)	4160 (± 1260)
M1-TEZ: Day 29 (n=11, 19, 22, 11, 18, 19)	4300 (± 774)	3650 (± 1280)	3870 (± 1020)	3790 (± 1080)
IVA: Day 15 (n=10, 16, 19, 7, 17, 0)	824 (± 781)	522 (± 567)	423 (± 261)	458 (± 239)
IVA: Day 29 (n=11, 19, 22, 11, 18, 0)	719 (± 604)	443 (± 398)	371 (± 220)	490 (± 179)
M1-IVA: Day 15 (n=10, 16, 19, 7, 17, 0)	1200 (± 711)	1050 (± 852)	1170 (± 674)	1310 (± 684)
M1-IVA Day 29 (n=11, 19, 22, 11, 18, 0)	1130 (± 682)	1140 (± 950)	1030 (± 460)	1240 (± 321)
VX-561: Day 15 (n=0, 0, 0, 0, 0, 17)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
VX-561: Day 15 (n=0, 0, 0, 0, 0, 19)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Part 2: VX-659/TEZ/IVA TC	Part 3: VX-659/TEZ/VX-561 TC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	19		
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
VX-659: Day 15 (n=10, 16, 19, 0, 17, 17)	835 (± 474)	1140 (± 646)		
VX-659: Day 29 (n=11, 19, 22, 0, 18, 19)	1070 (± 914)	923 (± 582)		
TEZ: Day 15 (n=10, 16, 19, 7, 17, 17)	1350 (± 1440)	1000 (± 305)		
TEZ: Day 29 (n=11, 19, 22, 11, 18, 19)	955 (± 422)	776 (± 321)		
M1-TEZ: Day 15 (n=10, 16, 19, 7, 17, 19)	4010 (± 1210)	4060 (± 660)		
M1-TEZ: Day 29 (n=11, 19, 22, 11, 18, 19)	3810 (± 1120)	3660 (± 1190)		
IVA: Day 15 (n=10, 16, 19, 7, 17, 0)	313 (± 158)	99999 (± 99999)		
IVA: Day 29 (n=11, 19, 22, 11, 18, 0)	296 (± 175)	99999 (± 99999)		

M1-IVA: Day 15 (n=10, 16, 19, 7, 17, 0)	844 (\pm 622)	99999 (\pm 99999)		
M1-IVA Day 29 (n=11, 19, 22, 11, 18, 0)	866 (\pm 691)	99999 (\pm 99999)		
VX-561: Day 15 (n=0, 0, 0, 0, 0, 17)	99999 (\pm 99999)	380 (\pm 240)		
VX-561: Day 15 (n=0, 0, 0, 0, 0, 19)	99999 (\pm 99999)	288 (\pm 165)		

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 61 for Part 1, Day 85 for Part 2 and Day 57 for Part 3)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	Part 1: Placebo
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Reporting group description:

Subjects received placebo matched to VX-659/TEZ/IVA in TC treatment period for 4 weeks and placebo matched to TEZ/IVA in washout period for 4 days.

Reporting group title	Part 1: VX-659/TEZ/IVA TC - Low Dose
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Reporting group description:

Subjects received VX-659 80 mg qd/TEZ 100 mg qd/IVA 150 mg every 12 q12h in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 days.

Reporting group title	Part 1: VX-659/TEZ/IVA TC - Medium Dose
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Reporting group description:

Subjects received VX-659 240 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 days.

Reporting group title	Part 1: VX-659/TEZ/IVA TC - High Dose
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Reporting group description:

Subjects received VX-659 400 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 days.

Reporting group title	Part 2: TEZ/IVA
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Reporting group description:

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

Reporting group title	Part 2: VX-659/TEZ/IVA TC
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Reporting group description:

Following run-in period with TEZ 100 mg qd/IVA 150 mg q12h for 4 weeks, subjects received VX-659 400 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in TC treatment period for 4 weeks and TEZ 100 mg qd/IVA 150 mg q12h in washout period for 4 weeks.

Reporting group title	Part 3: Placebo
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Reporting group description:

Subjects received placebo matched to VX-659/TEZ/VX-561 in TC treatment period for 4 weeks.

Reporting group title	Part 3: VX-659/TEZ/VX-561 TC
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Reporting group description:

Subjects received VX-659 400 mg qd/TEZ 100 mg qd/VX-561 200 mg qd in TC treatment period for 4 weeks.

Serious adverse events	Part 1: Placebo	Part 1: VX-659/TEZ/IVA TC - Low Dose	Part 1: VX-659/TEZ/IVA TC - Medium Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)	1 / 11 (9.09%)	4 / 20 (20.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Pulmonary function test decreased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 20 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (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
Pleuritic pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (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	2 / 10 (20.00%)	1 / 11 (9.09%)	2 / 20 (10.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral			

subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (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 1: VX-659/TEZ/IVA TC - High Dose	Part 2: TEZ/IVA	Part 2: VX-659/TEZ/IVA TC
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 22 (4.55%)	2 / 11 (18.18%)	1 / 18 (5.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Pulmonary function test decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (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
Pleuritic pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (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	1 / 22 (4.55%)	2 / 11 (18.18%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (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
Respiratory tract infection viral			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (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
Pneumonia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (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

Serious adverse events	Part 3: Placebo	Part 3: VX-659/TEZ/VX-561 TC	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	2 / 19 (10.53%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Pulmonary function test decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	3 / 6 (50.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part 1: Placebo	Part 1: VX-659/TEZ/IVA TC - Low Dose	Part 1: VX-659/TEZ/IVA TC - Medium Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 10 (80.00%)	10 / 11 (90.91%)	15 / 20 (75.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Fibroadenoma of breast subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 20 (5.00%) 1
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 11 (9.09%) 1	1 / 20 (5.00%) 1
Fatigue subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	2 / 11 (18.18%) 2	2 / 20 (10.00%) 2
Pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Application site rash subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Asthenia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Exercise tolerance decreased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Influenza like illness subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 20 (5.00%) 1
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Reproductive system and breast disorders Testicular pain			

subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vaginal discharge			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 10 (10.00%)	3 / 11 (27.27%)	6 / 20 (30.00%)
occurrences (all)	1	3	6
Sputum increased			
subjects affected / exposed	0 / 10 (0.00%)	2 / 11 (18.18%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Oropharyngeal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	3
Haemoptysis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 11 (18.18%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Respiration abnormal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Nasal congestion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Sinus congestion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)	1 / 11 (9.09%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Lower respiratory tract congestion			

subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 10 (0.00%)	2 / 11 (18.18%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Wheezing			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	3
Paranasal sinus discomfort			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Rales			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sinus pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sputum discoloured			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Bronchospasm			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Nasal discharge discolouration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Throat tightness			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Psychiatric disorders Irritability subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 20 (5.00%) 1
Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	1 / 20 (5.00%) 1
Neutrophil count increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 11 (9.09%) 1	0 / 20 (0.00%) 0
Bacterial test positive subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Blood glucose increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
International normalised ratio increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Lymphocyte count decreased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Prothrombin time prolonged subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Weight increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Activated partial thromboplastin time			

prolonged			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Blood glucose decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pulmonary function test decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood chloride decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood creatinine decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood glucose fluctuation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			

subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Coronavirus test positive			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Crystal urine present			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Forced expiratory volume decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Glucose urine present			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Monocyte count increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Red blood cells urine positive			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Urinary sediment present			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
White blood cell count increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural			

complications			
Laceration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	4 / 20 (20.00%)
occurrences (all)	0	1	4
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sinus headache			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Ear congestion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Motion sickness subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 20 (5.00%) 1
Diarrhoea subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	0 / 20 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	1 / 20 (5.00%) 1
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Flatulence subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Faeces discoloured subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 20 (5.00%) 1
Food poisoning subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 20 (5.00%) 1
Pancreatic failure			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Parotid gland enlargement subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Salivary hypersecretion subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 20 (5.00%) 1
Toothache subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 20 (5.00%) 1
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Acne subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Dermatitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Rash erythematous subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 20 (5.00%) 1
Skin disorder subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Renal and urinary disorders			
Micturition urgency subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 20 (5.00%) 1
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 20 (5.00%) 1
Flank pain			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Intervertebral disc protrusion subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	2 / 11 (18.18%) 2	1 / 20 (5.00%) 1
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	2 / 11 (18.18%) 2	1 / 20 (5.00%) 2
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Sinusitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Influenza subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Cellulitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Chronic sinusitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Genital infection fungal subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 20 (0.00%) 0
Lower respiratory tract infection			

subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Abnormal loss of weight			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 1: VX-659/TEZ/IVA TC - High Dose	Part 2: TEZ/IVA	Part 2: VX-659/TEZ/IVA TC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 22 (77.27%)	8 / 11 (72.73%)	15 / 18 (83.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Fibroadenoma of breast subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	1 / 11 (9.09%) 1	2 / 18 (11.11%) 2
Fatigue subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	0 / 18 (0.00%) 0
Pain subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	1 / 11 (9.09%) 1	0 / 18 (0.00%) 0
Application site rash subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Asthenia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Exercise tolerance decreased subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Influenza like illness subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Reproductive system and breast disorders Testicular pain			

subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vaginal discharge			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 22 (18.18%)	2 / 11 (18.18%)	4 / 18 (22.22%)
occurrences (all)	5	2	4
Sputum increased			
subjects affected / exposed	3 / 22 (13.64%)	1 / 11 (9.09%)	3 / 18 (16.67%)
occurrences (all)	4	2	3
Oropharyngeal pain			
subjects affected / exposed	4 / 22 (18.18%)	0 / 11 (0.00%)	2 / 18 (11.11%)
occurrences (all)	4	0	2
Haemoptysis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Respiration abnormal			
subjects affected / exposed	3 / 22 (13.64%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Nasal congestion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	4 / 18 (22.22%)
occurrences (all)	0	0	4
Sinus congestion			
subjects affected / exposed	2 / 22 (9.09%)	1 / 11 (9.09%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
Dyspnoea			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract congestion			

subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	2 / 18 (11.11%)
occurrences (all)	0	1	2
Productive cough			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Paranasal sinus discomfort			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Rales			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Sinus pain			
subjects affected / exposed	2 / 22 (9.09%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Sputum discoloured			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Bronchospasm			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nasal discharge discolouration			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Throat tightness			

subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	1 / 18 (5.56%) 1
Psychiatric disorders Irritability subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	2 / 11 (18.18%) 3	1 / 18 (5.56%) 1
Neutrophil count increased subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	1 / 18 (5.56%) 4
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	1 / 18 (5.56%) 1
Bacterial test positive subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	1 / 18 (5.56%) 1
Blood glucose increased subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	1 / 18 (5.56%) 2
International normalised ratio increased subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	1 / 18 (5.56%) 1
Lymphocyte count decreased subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	1 / 18 (5.56%) 2
Prothrombin time prolonged subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	1 / 18 (5.56%) 1
Weight increased subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	1 / 18 (5.56%) 1
Activated partial thromboplastin time			

prolonged			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood glucose decreased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Pulmonary function test decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood chloride decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood creatinine decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood glucose fluctuation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Blood potassium increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Blood sodium decreased			

subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Coronavirus test positive			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Crystal urine present			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Forced expiratory volume decreased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Glucose urine present			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Haemoglobin decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Monocyte count increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Red blood cells urine positive			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Urinary sediment present			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural			

complications			
Laceration			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 22 (18.18%)	0 / 11 (0.00%)	3 / 18 (16.67%)
occurrences (all)	4	0	3
Dizziness			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Sinus headache			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ear congestion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Motion sickness subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	2 / 11 (18.18%) 2	2 / 18 (11.11%) 2
Vomiting subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	2 / 11 (18.18%) 2	2 / 18 (11.11%) 2
Constipation subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	2 / 18 (11.11%) 2
Abdominal pain subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	1 / 18 (5.56%) 1
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	2 / 18 (11.11%) 2
Flatulence subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Faeces discoloured subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Food poisoning subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	0 / 18 (0.00%) 0
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Pancreatic failure			

subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	0 / 18 (0.00%) 0
Parotid gland enlargement subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	1 / 18 (5.56%) 1
Salivary hypersecretion subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Toothache subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	2 / 18 (11.11%) 2
Acne subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	1 / 18 (5.56%) 1
Dermatitis subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	0 / 18 (0.00%) 0
Rash erythematous subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Skin disorder subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	1 / 18 (5.56%) 1
Renal and urinary disorders			
Micturition urgency subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	1 / 18 (5.56%) 1
Flank pain			

subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Intervertebral disc protrusion subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	1 / 11 (9.09%) 1	4 / 18 (22.22%) 4
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	0 / 11 (0.00%) 0	2 / 18 (11.11%) 2
Sinusitis subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	1 / 18 (5.56%) 1
Influenza subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Cellulitis subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	0 / 18 (0.00%) 0
Chronic sinusitis subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	0 / 18 (0.00%) 0
Genital infection fungal subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	1 / 18 (5.56%) 1
Lower respiratory tract infection			

subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Respiratory tract infection viral			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Abnormal loss of weight			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 3: Placebo	Part 3: VX-659/TEZ/VX-561 TC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	18 / 19 (94.74%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Fibroadenoma of breast subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Application site rash subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all) Exercise tolerance decreased subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0	3 / 19 (15.79%) 3 0 / 19 (0.00%) 0 2 / 19 (10.53%) 2 1 / 19 (5.26%) 1 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0	
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	
Reproductive system and breast disorders Testicular pain			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Vaginal discharge			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 6 (33.33%)	4 / 19 (21.05%)	
occurrences (all)	2	5	
Sputum increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Haemoptysis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Respiration abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Sinus congestion			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Lower respiratory tract congestion			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	1
Productive cough		
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0
Wheezing		
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0
Paranasal sinus discomfort		
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0
Rales		
subjects affected / exposed	2 / 6 (33.33%)	0 / 19 (0.00%)
occurrences (all)	2	0
Rhinorrhoea		
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0
Sinus pain		
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0
Sputum discoloured		
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0
Bronchospasm		
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	1
Epistaxis		
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0
Nasal discharge discolouration		
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0
Throat irritation		
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0
Throat tightness		

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Psychiatric disorders Irritability subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Neutrophil count increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2	0 / 19 (0.00%) 0	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 19 (0.00%) 0	
Bacterial test positive subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	
Blood glucose increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
International normalised ratio increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	
Lymphocyte count decreased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 19 (0.00%) 0	
Prothrombin time prolonged subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	
Weight increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Activated partial thromboplastin time			

prolonged			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Blood glucose decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Blood triglycerides increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Pulmonary function test decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Blood chloride decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Blood creatinine decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Blood glucose fluctuation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Blood potassium increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Blood sodium decreased			

subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Body temperature increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Coronavirus test positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Crystal urine present			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Forced expiratory volume decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Glucose urine present			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Haemoglobin decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Monocyte count increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Red blood cells urine positive			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Urinary sediment present			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
White blood cell count increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural			

complications			
Laceration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Wound			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	2	
Lethargy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Migraine			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Sinus headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	2	
Ear congestion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	

Motion sickness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 19 (10.53%) 2	
Vomiting subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 2	
Constipation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	
Diarrhoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	
Abdominal pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Flatulence subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	
Faeces discoloured subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Food poisoning subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Pancreatic failure			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Parotid gland enlargement subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Salivary hypersecretion subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Toothache subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 19 (10.53%) 2	
Acne subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	
Dermatitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Rash erythematous subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Skin disorder subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Renal and urinary disorders			
Micturition urgency subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	
Flank pain			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Chronic sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Genital infection fungal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Lower respiratory tract infection			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Abnormal loss of weight			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Increased appetite			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2017	Added study drug doses, revised elements of the study design including treatment arms, sample size, and study duration, and revised inclusion/exclusion criteria.
01 September 2017	Added Part 3 to evaluate VX-659 in triple combination with TEZ/VX-561.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported