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	v1
This version publication date	16 March 2019
First version publication date	16 March 2019

Trial information

Trial identification

Sponsor protocol code	VX16-659-101

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

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
Arm title	Part 1: Placebo

Arm description:

Subjects received placebo matched to VX-659/TEZ/IVA triple combination (TC) for 4 weeks in the TC treatment period.

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

Arm description:

Subjects received VX-659/TEZ/IVA TC low dose for 4 weeks in the TC treatment period.

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 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

Arm description:

Subjects received VX-659/TEZ/IVA TC medium dose for 4 weeks in the TC treatment period.

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

Arm description:

Subjects received VX-659/TEZ/IVA TC high dose for 4 weeks in the TC treatment period.

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

Arm description:

Following run-in period of 4 weeks with TEZ/IVA, subjects received TEZ/IVA and placebo matched to VX-659 for 4 weeks in the TC treatment period.

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 of 4 weeks with TEZ/IVA, subjects received VX-659/TEZ/IVA for 4 weeks in the TC treatment period.

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 TC for 4 weeks in the TC treatment period.

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

Dosage and administration details:

Subjects received placebo matched to VX-561 once daily.

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

Arm description:

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

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

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 triple combination (TC) for 4 weeks in the TC treatment period.	
Reporting group title	Part 1: VX-659/TEZ/IVA TC - Low Dose
Reporting group description:	
Subjects received VX-659/TEZ/IVA TC low dose for 4 weeks in the TC treatment period.	
Reporting group title	Part 1: VX-659/TEZ/IVA TC - Medium Dose
Reporting group description:	
Subjects received VX-659/TEZ/IVA TC medium dose for 4 weeks in the TC treatment period.	
Reporting group title	Part 1: VX-659/TEZ/IVA TC - High Dose
Reporting group description:	
Subjects received VX-659/TEZ/IVA TC high dose for 4 weeks in the TC treatment period.	
Reporting group title	Part 2: TEZ/IVA
Reporting group description:	
Following run-in period of 4 weeks with TEZ/IVA, subjects received TEZ/IVA and placebo matched to VX-659 for 4 weeks in the TC treatment period.	
Reporting group title	Part 2: VX-659/TEZ/IVA TC
Reporting group description:	
Following run-in period of 4 weeks with TEZ/IVA, subjects received VX-659/TEZ/IVA for 4 weeks in the TC treatment period.	
Reporting group title	Part 3: Placebo
Reporting group description:	
Subjects received placebo matched to VX-659/TEZ/VX-561 TC for 4 weeks in the TC treatment period.	
Reporting group title	Part 3: VX-659/TEZ/VX-561 TC
Reporting group description:	
Subjects received VX-659/TEZ/VX-561 TC for 4 weeks in the TC treatment period.	

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	26.6	32.0	31.4
standard deviation	± 6.0	± 11.7	± 9.7
Gender categorical Units: Subjects			
Female	4	7	7
Male	6	4	13

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	27.2	32.5	33.4
standard deviation	± 6.6	± 7.5	± 9.2
Gender categorical Units: Subjects			
Female	12	4	6
Male	10	7	12

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

End points

End points reporting groups

Reporting group title	Part 1: Placebo
Reporting group description:	
Subjects received placebo matched to VX-659/TEZ/IVA triple combination (TC) for 4 weeks in the TC treatment period.	

Reporting group title	Part 1: VX-659/TEZ/IVA TC - Low Dose
Reporting group description:	
Subjects received VX-659/TEZ/IVA TC low dose for 4 weeks in the TC treatment period.	

Reporting group title	Part 1: VX-659/TEZ/IVA TC - Medium Dose
Reporting group description:	
Subjects received VX-659/TEZ/IVA TC medium dose for 4 weeks in the TC treatment period.	

Reporting group title	Part 1: VX-659/TEZ/IVA TC - High Dose
Reporting group description:	
Subjects received VX-659/TEZ/IVA TC high dose for 4 weeks in the TC treatment period.	

Reporting group title	Part 2: TEZ/IVA
Reporting group description:	
Following run-in period of 4 weeks with TEZ/IVA, subjects received TEZ/IVA and placebo matched to VX-659 for 4 weeks in the TC treatment period.	

Reporting group title	Part 2: VX-659/TEZ/IVA TC
Reporting group description:	
Following run-in period of 4 weeks with TEZ/IVA, subjects received VX-659/TEZ/IVA for 4 weeks in the TC treatment period.	

Reporting group title	Part 3: Placebo
Reporting group description:	
Subjects received placebo matched to VX-659/TEZ/VX-561 TC for 4 weeks in the TC treatment period.	

Reporting group title	Part 3: VX-659/TEZ/VX-561 TC
Reporting group description:	
Subjects received VX-659/TEZ/VX-561 TC for 4 weeks in the TC treatment period.	

Primary: Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)[1]
End point description:	
The number of subjects analysed included only subjects who received at least one dose of study drug in the TC treatment period.	

End point type	Primary
End point timeframe:	
From first dose of study drug in TC treatment period up to 28 days after last dose of study drug	

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 AEs	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 AEs	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]

End point description:

The number of subjects analysed included all randomized subjects who carry the intended CFTR allele mutation and received at least 1 dose of study drug in the TC 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: 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 (standard error)	0.4 (± 2.8)	10.2 (± 2.7)	12.0 (± 2.0)	13.3 (± 1.9)

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
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 (standard error)	0.0 (± 1.9)	9.7 (± 1.5)	-5.0 (± 3.4)	12.2 (± 1.9)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug in TC treatment period up to 28 days after last dose of study drug	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Part 1: Placebo
Reporting group description:	
Subjects received placebo matched to VX-659/TEZ/IVA TC for 4 weeks in the TC treatment period.	
Reporting group title	Part 1: VX-659/TEZ/IVA TC - Low Dose
Reporting group description:	
Subjects received VX-659/TEZ/IVA TC low dose for 4 weeks in the TC treatment period.	
Reporting group title	Part 1: VX-659/TEZ/IVA TC - Medium Dose
Reporting group description:	
Subjects received VX-659/TEZ/IVA TC medium dose for 4 weeks in the TC treatment period.	
Reporting group title	Part 1: VX-659/TEZ/IVA TC - High Dose
Reporting group description:	
Subjects received VX-659/TEZ/IVA TC high dose for 4 weeks in the TC treatment period.	
Reporting group title	Part 2: TEZ/IVA
Reporting group description:	
Following run-in period of 4 weeks with TEZ/IVA, subjects received TEZ/IVA and placebo matched to VX-659 for 4 weeks in the TC treatment period.	
Reporting group title	Part 2: VX-659/TEZ/IVA TC
Reporting group description:	
Following run-in period of 4 weeks with TEZ/IVA, subjects received VX-659/TEZ/IVA for 4 weeks in the TC treatment period.	
Reporting group title	Part 3: Placebo
Reporting group description:	
Subjects received placebo matched VX-659/TEZ/VX-561 TC for 4 weeks in the TC treatment period.	
Reporting group title	Part 3: VX-659/TEZ/VX-561 TC
Reporting group description:	
Subjects received VX-659/TEZ/VX-561 TC for 4 weeks in the TC treatment period.	

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	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			

subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 11 (9.09%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)	2 / 11 (18.18%)	2 / 20 (10.00%)
occurrences (all)	0	2	2
Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Application site rash			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Exercise tolerance decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	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	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1

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

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

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

Musculoskeletal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	1 / 10 (10.00%)	2 / 11 (18.18%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	2 / 11 (18.18%)	1 / 20 (5.00%)
occurrences (all)	1	2	2
Upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chronic sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Genital infection fungal			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	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	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 11 (9.09%)	2 / 18 (11.11%)
occurrences (all)	1	1	2
Fatigue			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	1 / 22 (4.55%)	1 / 11 (9.09%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Application site rash			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Exercise tolerance decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	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	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood creatine phosphokinase increased			

subjects affected / exposed	3 / 22 (13.64%)	2 / 11 (18.18%)	1 / 18 (5.56%)
occurrences (all)	3	3	1
Neutrophil count increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	4
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Bacterial test positive			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood glucose increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	1 / 18 (5.56%)
occurrences (all)	0	1	2
International normalised ratio increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Prothrombin time prolonged			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Weight increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	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	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 22 (13.64%)	2 / 11 (18.18%)	2 / 18 (11.11%)
occurrences (all)	3	2	2
Vomiting			

subjects affected / exposed	1 / 22 (4.55%)	2 / 11 (18.18%)	2 / 18 (11.11%)
occurrences (all)	1	2	2
Constipation			
subjects affected / exposed	3 / 22 (13.64%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Diarrhoea			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	2 / 18 (11.11%)
occurrences (all)	1	0	2
Abdominal pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Abdominal pain upper			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Flatulence			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Faeces discoloured			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pancreatic failure			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Parotid gland enlargement			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Salivary hypersecretion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Toothache			

subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	2 / 18 (11.11%)
occurrences (all)	1	0	2
Acne			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Rash erythematous			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Flank pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	3 / 22 (13.64%)	1 / 11 (9.09%)	4 / 18 (22.22%)
occurrences (all)	3	1	4
Nasopharyngitis			
subjects affected / exposed	3 / 22 (13.64%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 22 (9.09%)	0 / 11 (0.00%)	2 / 18 (11.11%)
occurrences (all)	2	0	2
Sinusitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Chronic sinusitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Genital infection fungal			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	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	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	0 / 6 (0.00%)	3 / 19 (15.79%)	
occurrences (all)	0	3	
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Application site rash			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Exercise tolerance decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	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	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Neutrophil count increased			

subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)		
occurrences (all)	2	0		
Aspartate aminotransferase increased				
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)		
occurrences (all)	1	0		
Bacterial test positive				
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)		
occurrences (all)	0	1		
Blood glucose increased				
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)		
occurrences (all)	0	0		
International normalised ratio increased				
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)		
occurrences (all)	0	1		
Lymphocyte count decreased				
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)		
occurrences (all)	1	0		
Prothrombin time prolonged				
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)		
occurrences (all)	0	1		
Weight increased				
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)		
occurrences (all)	0	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	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	2	
Constipation			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Faeces discoloured			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Food poisoning			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Pancreatic failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Parotid gland enlargement			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Salivary hypersecretion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			

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