



Clinical trial results:

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

Summary

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

Results information

Result version number	v1
This version publication date	17 May 2020
First version publication date	17 May 2020

Trial information

Trial identification

Sponsor protocol code	VX17-121-001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03768089
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vertex Pharmaceuticals Incorporated
Sponsor organisation address	50 Northern Avenue, Boston, Massachusetts, United States,
Public contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617 341 6777, medicalinfo@vrtx.com
Scientific contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617 341 6777, medicalinfo@vrtx.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 May 2019
Global end of trial reached?	Yes
Global end of trial date	03 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

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

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	115
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

Period 1

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

Arms

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

Arm description:

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

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

Dosage and administration details:

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

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

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

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

Dosage and administration details:

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

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

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

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

Arm description:	
Subjects received placebo matched to VX-121/TEZ/IVA triple combination (TC) for 14 days.	
Arm type	Placebo
Investigational medicinal product name	Placebo (matched to VX-121)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
Subjects received placebo matched to VX-121 suspension once daily.	
Investigational medicinal product name	Placebo (matched to TEZ/IVA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Subjects received placebo matched to TEZ/IVA once daily in the morning.	
Investigational medicinal product name	Placebo (matched to IVA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Subjects received placebo matched to IVA once daily in the evening.	
Arm title	Part C: VX-121/TEZ/IVA TC
Arm description:	
Subjects received VX-121/TEZ/IVA TC for 14 days.	
Arm type	Experimental
Investigational medicinal product name	VX-121
Investigational medicinal product code	VX-121
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
Subjects received VX-121 suspension once daily.	
Investigational medicinal product name	TEZ/IVA
Investigational medicinal product code	VX-661/VX-770
Other name	Tezacaftor/Ivacaftor fixed dose combination
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Subjects received TEZ/IVA once daily in the morning.	
Investigational medicinal product name	IVA
Investigational medicinal product code	VX-770
Other name	Ivacaftor
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Subjects received IVA once daily in the evening.	
Arm title	Part D: Placebo

Arm description:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

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

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

Subjects with CF received VX-121/TEZ/IVA TC for 4 weeks.

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

Dosage and administration details:

Subjects with CF received VX-121 once daily.

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

Dosage and administration details:

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

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

Dosage and administration details:

Subjects with CF received IVA once daily in the evening.

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

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

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

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

Baseline characteristics

Reporting groups^[1]

Reporting group title	Part A: Pooled Placebo (Except Cohorts A3 and A9)
Reporting group description:	
Subjects received single dose of placebo matched to VX-121 in Cohorts A1 to A5 (Except Cohorts A3 and A9).	
Reporting group title	Part A: VX-121 (Except Cohorts A3 and A9)
Reporting group description:	
Subjects received single ascending dose of VX-121 in Cohorts A1 to A5 (except Cohorts A3 and A9).	
Reporting group title	Part A: VX-121 (Cohort A3)
Reporting group description:	
Subjects received single dose VX-121 or placebo without milk, followed by open label VX-121 with milk in Cohort A3.	
Reporting group title	Part A: VX-121 (Cohort A9)
Reporting group description:	
Subjects received single dose of VX-121 suspension, fed on Day 1, VX-121 tablet, fed on Day 9, and then VX-121 tablet, fed with milk on Day 17 in Cohort A9.	
Reporting group title	Part B: Pooled Placebo
Reporting group description:	
Subjects received multiple doses of placebo matched to VX-121 for 10 days.	
Reporting group title	Part B: VX-121
Reporting group description:	
Subjects received multiple ascending doses of VX-121 for 10 days.	
Reporting group title	Part C: Pooled Placebo
Reporting group description:	
Subjects received placebo matched to VX-121/TEZ/IVA triple combination (TC) for 14 days.	
Reporting group title	Part C: VX-121/TEZ/IVA TC
Reporting group description:	
Subjects received VX-121/TEZ/IVA TC for 14 days.	
Reporting group title	Part D: Placebo
Reporting group description:	
Subjects with CF received placebo matched to VX-121/TEZ/IVA TC for 4 weeks.	
Reporting group title	Part D: VX-121/TEZ/IVA TC
Reporting group description:	
Subjects with CF received VX-121/TEZ/IVA TC for 4 weeks.	

Notes:

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

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

Reporting group values	Part A: Pooled Placebo (Except Cohorts A3 and A9)	Part A: VX-121 (Except Cohorts A3 and A9)	Part A: VX-121 (Cohort A3)
Number of subjects	8	23	6
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean	29.8	30.3	25.8

standard deviation	± 10.6	± 11.5	± 4.16
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Gender categorical Units: Subjects			
Female	0	2	0
Male	8	21	6

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

Age continuous Units: years			
arithmetic mean	33.9	31.7	29.6
standard deviation	± 11.5	± 14.0	± 10.5
Gender categorical Units: Subjects			
Female	0	1	0
Male	8	8	24

Reporting group values	Part C: Pooled Placebo	Part C: VX- 121/TEZ/IVA TC	Part D: Placebo
Number of subjects	6	19	3
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	30.3	36.6	22.8
standard deviation	± 12.1	± 13.2	± 4.9
Gender categorical Units: Subjects			
Female	0	1	0
Male	6	18	3

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

Age continuous Units: years			
arithmetic mean	34.8		
standard deviation	± 12.8	-	
Gender categorical Units: Subjects			
Female	1	5	
Male	8	109	

End points

End points reporting groups

Reporting group title	Part A: Pooled Placebo (Except Cohorts A3 and A9)
Reporting group description: Subjects received single dose of placebo matched to VX-121 in Cohorts A1 to A5 (Except Cohorts A3 and A9).	
Reporting group title	Part A: VX-121 (Except Cohorts A3 and A9)
Reporting group description: Subjects received single ascending dose of VX-121 in Cohorts A1 to A5 (except Cohorts A3 and A9).	
Reporting group title	Part A: VX-121 (Cohort A3)
Reporting group description: Subjects received single dose VX-121 or placebo without milk, followed by open label VX-121 with milk in Cohort A3.	
Reporting group title	Part A: VX-121 (Cohort A9)
Reporting group description: Subjects received single dose of VX-121 suspension, fed on Day 1, VX-121 tablet, fed on Day 9, and then VX-121 tablet, fed with milk on Day 17 in Cohort A9.	
Reporting group title	Part B: Pooled Placebo
Reporting group description: Subjects received multiple doses of placebo matched to VX-121 for 10 days.	
Reporting group title	Part B: VX-121
Reporting group description: Subjects received multiple ascending doses of VX-121 for 10 days.	
Reporting group title	Part C: Pooled Placebo
Reporting group description: Subjects received placebo matched to VX-121/TEZ/IVA triple combination (TC) for 14 days.	
Reporting group title	Part C: VX-121/TEZ/IVA TC
Reporting group description: Subjects received VX-121/TEZ/IVA TC for 14 days.	
Reporting group title	Part D: Placebo
Reporting group description: Subjects with CF received placebo matched to VX-121/TEZ/IVA TC for 4 weeks.	
Reporting group title	Part D: VX-121/TEZ/IVA TC
Reporting group description: Subjects with CF received VX-121/TEZ/IVA TC for 4 weeks.	

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:	
End point type	Primary
End point timeframe: From first dose of study drug up to safety follow-up visit OR up to 7 days (except Part D)/28 days (Part D) after the last dose date of study drug for subjects who do not have a safety follow-up visit	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned. No statistical comparisons were planned for primary safety endpoint.

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

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

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to safety follow-up visit OR up to 7 days (except Part D)/28 days (Part D) after the last dose date of study drug for subjects who do not have a safety follow-up visit

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

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

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

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

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

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

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

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

Subjects received single dose of VX-121 suspension, fed on Day 1, VX-121 tablet, fed on Day 9, and then VX-121 tablet, fed with milk on Day 17 in Cohort A9.

Reporting group title	Part B: Pooled Placebo
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Reporting group description:

Subjects received multiple doses of placebo matched to VX-121 for 10 days.

Reporting group title	Part B: VX-121
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Reporting group description:

Subjects received multiple ascending doses of VX-121 for 10 days.

Reporting group title	Part C: Pooled Placebo
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Reporting group description:

Subjects received placebo matched to VX-121/TEZ/IVA triple combination (TC) for 14 days.

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

Subjects received VX-121/TEZ/IVA TC for 14 days.

Reporting group title	Part D: Placebo
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Reporting group description:

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

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

Subjects with CF received VX-121/TEZ/IVA TC for 4 weeks.

Serious adverse events	Part A: Pooled Placebo (Except Cohorts A3 and A9)	Part A: VX-121 (Except Cohorts A3 and A9)	Part A: VX-121 (Cohort A3)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part A: VX-121 (Cohort A9)	Part B: Pooled Placebo	Part B: VX-121
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Serious adverse events	Part D: VX-121/TEZ/IVA TC		
Total subjects affected by serious adverse events			

subjects affected / exposed	0 / 9 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part A: Pooled Placebo (Except Cohorts A3 and A9)	Part A: VX-121 (Except Cohorts A3 and A9)	Part A: VX-121 (Cohort A3)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	9 / 23 (39.13%)	4 / 6 (66.67%)
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Catheter site bruise			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Catheter site erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Catheter site irritation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Catheter site pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 23 (4.35%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Catheter site pruritus			

subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	1 / 23 (4.35%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Feeling cold			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Puncture site pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vessel puncture site pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			

subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 23 (4.35%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Painful respiration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sputum increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Faecal volume decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza A virus test positive			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0	0 / 6 (0.00%) 0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 23 (4.35%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Procedural complication			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness postural			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 8 (12.50%)	2 / 23 (8.70%)	1 / 6 (16.67%)
occurrences (all)	1	2	1
Nerve compression			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ocular hyperaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 23 (4.35%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Defaecation urgency			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 23 (8.70%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Flatulence			
subjects affected / exposed	0 / 8 (0.00%)	1 / 23 (4.35%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral pain			

subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermal cyst			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Papule			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Rash macular subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0	0 / 6 (0.00%) 0
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0	0 / 6 (0.00%) 0
Seborrhoeic dermatitis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0	0 / 6 (0.00%) 0
Skin hypertrophy subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0	0 / 6 (0.00%) 0
Skin hypopigmentation subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0	1 / 6 (16.67%) 2
Skin irritation subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0	0 / 6 (0.00%) 0
Swelling face subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0	0 / 6 (0.00%) 0
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0	0 / 6 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0	0 / 6 (0.00%) 0
Flank pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0	0 / 6 (0.00%) 0
Muscle twitching subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0	1 / 6 (16.67%) 1
Musculoskeletal chest pain			

subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part A: VX-121 (Cohort A9)	Part B: Pooled Placebo	Part B: VX-121
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)	7 / 9 (77.78%)	16 / 24 (66.67%)
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Catheter site bruise			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Catheter site erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Catheter site irritation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2

Catheter site pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	2 / 24 (8.33%)
occurrences (all)	0	2	2
Catheter site pruritus			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Chest discomfort			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	2 / 8 (25.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	5	0	0
Feeling cold			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Feeling hot			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Puncture site pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	3 / 24 (12.50%)
occurrences (all)	0	0	4
Vessel puncture site pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Epistaxis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Painful respiration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Sputum increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	1 / 24 (4.17%)
occurrences (all)	1	1	1
Tension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Faecal volume decreased			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Influenza A virus test positive subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Injury, poisoning and procedural complications			
Arthropod bite subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 9 (11.11%) 2	2 / 24 (8.33%) 2
Contusion subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	2 / 24 (8.33%) 2
Procedural complication subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 9 (0.00%) 0	1 / 24 (4.17%) 1
Dizziness postural subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	4 / 8 (50.00%) 4	2 / 9 (22.22%) 2	3 / 24 (12.50%) 3
Nerve compression subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Somnolence subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1	0 / 24 (0.00%) 0
Blood and lymphatic system disorders			
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Ear and labyrinth disorders			

Ear pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Eye disorders Eye irritation subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Ocular hyperaemia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1	0 / 24 (0.00%) 0
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1	0 / 24 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Defaecation urgency subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Flatulence subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1	1 / 24 (4.17%) 1
Nausea			

subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Oral pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	3 / 24 (12.50%)
occurrences (all)	0	1	3
Dermal cyst			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Papule			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Pruritus generalised			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	2

Rash			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Rash macular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	3
Rash maculo-papular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Skin hypertrophy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Skin hypopigmentation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Swelling face			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 8 (0.00%)	4 / 9 (44.44%)	2 / 24 (8.33%)
occurrences (all)	0	4	2
Flank pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Muscle twitching			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Myalgia subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Infections and infestations Infective pulmonary exacerbation of cystic fibrosis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0
Periodontitis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0	0 / 24 (0.00%) 0

Non-serious adverse events	Part C: Pooled Placebo	Part C: VX- 121/TEZ/IVA TC	Part D: Placebo
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 6 (66.67%)	12 / 19 (63.16%)	2 / 3 (66.67%)
Vascular disorders Phlebitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	0 / 3 (0.00%) 0
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	0 / 3 (0.00%) 0
Catheter site bruise subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	3 / 19 (15.79%) 3	0 / 3 (0.00%) 0
Catheter site erythema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	0 / 3 (0.00%) 0

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

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

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

Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	0 / 3 (0.00%) 0
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	0 / 3 (0.00%) 0
Eye disorders Eye irritation subjects affected / exposed occurrences (all) Ocular hyperaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	1 / 19 (5.26%) 1 1 / 19 (5.26%) 1	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Defaecation urgency subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Flatulence	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1	1 / 19 (5.26%) 2 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 1 / 19 (5.26%) 1 2 / 19 (10.53%) 4 2 / 19 (10.53%) 2	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0

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

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

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

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

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

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

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported