Clinical trial results:
A Phase 2, Multicenter, Double-Blinded, Placebo-Controlled Study to Evaluate Safety, Efficacy, Pharmacokinetics, and Pharmacodynamics of VX-661 Monotherapy and VX-661/Ivacaftor Cotherapy in Subjects with Cystic Fibrosis, Homozygous or Heterozygous for the F508del-CFTR Mutation

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2011-003821-93
Trial protocol	DE GB
Global end of trial date	25 March 2014

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	13 July 2016

Trial information

Trial identification

Sponsor protocol code	VX11-661-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01531673
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vertex Pharmaceuticals Incorporated
Sponsor organisation address	50 Northern Avenue, Boston, Massachusetts, United States, 02210-1862
Public contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, 1 617-341-6777, medicalinfo@vrtx.com
Scientific contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, 1 617-341-6777, medicalinfo@vrtx.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 April 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of VX-661 monotherapy and VX-661/ivacaftor (also known as VX-770; commercially available as Kalydeco) cotherapy and to evaluate the effect of VX-661 monotherapy and VX-661/ivacaftor cotherapy on cystic fibrosis transmembrane conductance regulator (CFTR) function.

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	14 February 2012
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: 15
Country: Number of subjects enrolled	Germany: 42
Country: Number of subjects enrolled	Canada: 18
Country: Number of subjects enrolled	United States: 115
Worldwide total number of subjects	190
EEA total number of subjects	57

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)	1
Adults (18-64 years)	189
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 194 subjects were randomized of which 190 subjects were treated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1-6d Combined: Placebo

Arm description:

All subjects in group 1, 2a, 2b, 3a, 3b, 4, 5a, 5b, 6a and 6d who received placebo matched to VX-661 tablet and/or placebo matched to ivacaftor tablet for up to 28 days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to VX-661 tablet orally once daily (qd) for up to 28 days (for Group 1, 2a, 2b, 3a, 3b, 4, 5a, 5b and 6a) and placebo matched to VX-661 tablet orally every 12 hours (q12h) for up to 28 days (for Group 6d) .

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to ivacaftor tablet orally q12h for up to 28 days (for Group 2a, 2b, 3a, 3b, 4, 5a, 5b, 6a, 6d).

Arm title	Group 1: VX-661 10 mg qd

Arm description:

All subjects in group 1 who received VX-661 10 milligram (mg) tablet orally qd for up to 28 days.

Arm type	Experimental
Investigational medicinal product name	VX-661
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-661 10 mg tablet orally qd for up to 28 days.

Arm title	Group 2a: VX-661 30 mg qd

Arm description:

All subjects in group 2a who received VX-661 30 mg tablet orally qd and placebo matched to Ivacaftor tablet q12h for up to 28 days.

Arm type	Experimental
Investigational medicinal product name	VX-661
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-661 30 mg tablet orally qd for up to 28 days.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to ivacaftor tablet orally q12h for up to 28 days.

Arm title	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h

Arm description:

All subjects in group 2b who received VX-661 10 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.

Arm type	Experimental
Investigational medicinal product name	VX-661
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-661 10 mg tablet orally qd for up to 28 days.

Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	VX-770
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ivacaftor 150 mg tablet administered orally q12h for up to 28 days.

Arm title	Group 3a: VX-661 100 mg qd

Arm description:

All subjects in group 3a who received VX-661 100 mg tablet orally qd and placebo matched to Ivacaftor tablet q12h for up to 28 days.

Arm type	Experimental
Investigational medicinal product name	VX-661
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-661 100 mg tablet orally qd for up to 28 days.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to ivacaftor tablet orally q12h for up to 28 days.

Arm title	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h

Arm description:

All subjects in group 3b who received VX-661 30 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.

Arm type	Experimental
Investigational medicinal product name	VX-661
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-661 30 mg tablet orally qd for up to 28 days.

Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	VX-770
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ivacaftor 150 mg tablet administered orally q12h for up to 28 days.

Arm title	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h

Arm description:

All subjects in group 4 who received VX-661 100 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.

Arm type	Experimental
Investigational medicinal product name	VX-661
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-661 100 mg tablet orally qd for up to 28 days.

Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	VX-770
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ivacaftor 150 mg tablet administered orally q12h for up to 28 days.

Arm title	Group 5a: VX-661 150 mg qd

Arm description:

All subjects in group 5a who received VX-661 150 mg tablet orally qd for up to 28 days.

Arm type	Experimental

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

Dosage and administration details:

VX-661 150 mg tablet orally qd for up to 28 days.

Arm title	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h

Arm description:

All subjects in group 5b who received VX-661 150 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.

Arm type	Experimental
Investigational medicinal product name	VX-661
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-661 150 mg tablet orally qd for up to 28 days.

Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	VX-770
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ivacaftor 150 mg tablet administered orally q12h for up to 28 days.

Arm title	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h

Arm description:

All subjects in group 6a who received VX-661 100 mg tablet qd and Ivacaftor 50 mg tablet q12h orally for up to 28 days.

Arm type	Experimental
Investigational medicinal product name	VX-661
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-661 100 mg tablet orally qd for up to 28 days.

Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	VX-770
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ivacaftor 50 mg tablet orally q12h for up to 28 days.

Arm title	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h

Arm description:

All subjects in group 6d who received VX-661 50 mg tablet and Ivacaftor 150 mg tablet q12h orally for up to 28 days.

Arm type	Experimental

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

Dosage and administration details:

VX-661 50 mg tablet orally q12h for up to 28 days.

Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	VX-770
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ivacaftor 150 mg tablet administered orally q12h for up to 28 days.

Arm title	Group 7: Placebo

Arm description:

All subjects in group 7 who received placebo matched to VX-661 tablet orally qd in combination with physician-prescribed Kalydeco for up to 28 days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to VX-661 tablet orally qd for up to 28 days.

Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	VX-770
Other name	Kalydeco
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ivacaftor 150 mg tablet administered orally q12h for up to 28 days.

Arm title	Group 7: VX-661 100 mg qd

Arm description:

All subjects in group 7 who received VX-661 100 mg tablet orally qd in combination with physician-prescribed Kalydeco for up to 28 days.

Arm type	Experimental
Investigational medicinal product name	VX-661
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-661 100 mg tablet orally qd for up to 28 days.

Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	VX-770
Other name	Kalydeco
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ivacaftor 150 mg tablet administered orally q12h for up to 28 days.

Number of subjects in period 1	Group 1-6d Combined: Placebo	Group 1: VX-661 10 mg qd	Group 2a: VX-661 30 mg qd
Started	33	8	8
Completed	33	7	8
Not completed	0	1	0
Non-Compliance	-	-	-
Adverse Event	-	1	-
Unspecified	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h	Group 3a: VX-661 100 mg qd	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h
Started	18	8	19
Completed	17	7	18
Not completed	1	1	1
Non-Compliance	-	-	1
Adverse Event	-	-	-
Unspecified	1	-	-
Lost to follow-up	-	1	-

Number of subjects in period 1	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h	Group 5a: VX-661 150 mg qd	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h
Started	17	9	17
Completed	17	9	17
Not completed	0	0	0
Non-Compliance	-	-	-
Adverse Event	-	-	-
Unspecified	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h	Group 7: Placebo
Started	19	16	4
Completed	18	16	4
Not completed	1	0	0
Non-Compliance	-	-	-
Adverse Event	-	-	-
Unspecified	1	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Group 7: VX-661

	100 mg qd
Started	14
Completed	14
Not completed	0
Non-Compliance	-
Adverse Event	-
Unspecified	-
Lost to follow-up	-

Baseline characteristics

Reporting groups

Reporting group title	Group 1-6d Combined: Placebo
Reporting group description:	
All subjects in group 1, 2a, 2b, 3a, 3b, 4, 5a, 5b, 6a and 6d who received placebo matched to VX-661 tablet and/or placebo matched to ivacaftor tablet for up to 28 days.	
Reporting group title	Group 1: VX-661 10 mg qd
Reporting group description:	
All subjects in group 1 who received VX-661 10 milligram (mg) tablet orally qd for up to 28 days.	
Reporting group title	Group 2a: VX-661 30 mg qd
Reporting group description:	
All subjects in group 2a who received VX-661 30 mg tablet orally qd and placebo matched to Ivacaftor tablet q12h for up to 28 days.	
Reporting group title	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h
Reporting group description:	
All subjects in group 2b who received VX-661 10 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.	
Reporting group title	Group 3a: VX-661 100 mg qd
Reporting group description:	
All subjects in group 3a who received VX-661 100 mg tablet orally qd and placebo matched to Ivacaftor tablet q12h for up to 28 days.	
Reporting group title	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h
Reporting group description:	
All subjects in group 3b who received VX-661 30 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.	
Reporting group title	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h
Reporting group description:	
All subjects in group 4 who received VX-661 100 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.	
Reporting group title	Group 5a: VX-661 150 mg qd
Reporting group description:	
All subjects in group 5a who received VX-661 150 mg tablet orally qd for up to 28 days.	
Reporting group title	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h
Reporting group description:	
All subjects in group 5b who received VX-661 150 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.	
Reporting group title	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h
Reporting group description:	
All subjects in group 6a who received VX-661 100 mg tablet qd and Ivacaftor 50 mg tablet q12h orally for up to 28 days.	
Reporting group title	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h
Reporting group description:	
All subjects in group 6d who received VX-661 50 mg tablet and Ivacaftor 150 mg tablet q12h orally for up to 28 days.	
Reporting group title	Group 7: Placebo
Reporting group description:	
All subjects in group 7 who received placebo matched to VX-661 tablet orally qd in combination with physician-prescribed Kalydeco for up to 28 days.	
Reporting group title	Group 7: VX-661 100 mg qd
Reporting group description:	
All subjects in group 7 who received VX-661 100 mg tablet orally qd in combination with physician-prescribed Kalydeco for up to 28 days.	

Reporting group values	Group 1-6d Combined: Placebo	Group 1: VX-661 10 mg qd	Group 2a: VX-661 30 mg qd
Number of subjects	33	8	8
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	30.7	35.3	30.8
standard deviation	± 8.42	± 8.26	± 6.63
Gender categorical Units: Subjects			
Female	13	4	4
Male	20	4	4

Reporting group values	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h	Group 3a: VX-661 100 mg qd	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h
Number of subjects	18	8	19
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	28.3	29.1	29.2
standard deviation	± 7.05	± 7.12	± 6.39
Gender categorical Units: Subjects			
Female	6	3	6
Male	12	5	13

Reporting group values	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h	Group 5a: VX-661 150 mg qd	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h
Number of subjects	17	9	17
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	31	28.2	28.2
standard deviation	± 9.3	± 8.6	± 6.46
Gender categorical Units: Subjects			
Female	11	3	10
Male	6	6	7

Reporting group values	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h	Group 7: Placebo
Number of subjects	19	16	4

Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	27.9	32.8	34.5
standard deviation	± 5.58	± 11.92	± 7.59
Gender categorical Units: Subjects			
Female	7	7	3
Male	12	9	1

Reporting group values	Group 7: VX-661 100 mg qd	Total	
Number of subjects	14	190	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	26.6		
standard deviation	± 7.01	-	
Gender categorical Units: Subjects			
Female	6	83	
Male	8	107	

End points reporting groups

Reporting group title	Group 1-6d Combined: Placebo
Reporting group description:	
All subjects in group 1, 2a, 2b, 3a, 3b, 4, 5a, 5b, 6a and 6d who received placebo matched to VX-661 tablet and/or placebo matched to ivacaftor tablet for up to 28 days.	
Reporting group title	Group 1: VX-661 10 mg qd
Reporting group description:	
All subjects in group 1 who received VX-661 10 milligram (mg) tablet orally qd for up to 28 days.	
Reporting group title	Group 2a: VX-661 30 mg qd
Reporting group description:	
All subjects in group 2a who received VX-661 30 mg tablet orally qd and placebo matched to Ivacaftor tablet q12h for up to 28 days.	
Reporting group title	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h
Reporting group description:	
All subjects in group 2b who received VX-661 10 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.	
Reporting group title	Group 3a: VX-661 100 mg qd
Reporting group description:	
All subjects in group 3a who received VX-661 100 mg tablet orally qd and placebo matched to Ivacaftor tablet q12h for up to 28 days.	
Reporting group title	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h
Reporting group description:	
All subjects in group 3b who received VX-661 30 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.	
Reporting group title	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h
Reporting group description:	
All subjects in group 4 who received VX-661 100 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.	
Reporting group title	Group 5a: VX-661 150 mg qd
Reporting group description:	
All subjects in group 5a who received VX-661 150 mg tablet orally qd for up to 28 days.	
Reporting group title	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h
Reporting group description:	
All subjects in group 5b who received VX-661 150 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.	
Reporting group title	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h
Reporting group description:	
All subjects in group 6a who received VX-661 100 mg tablet qd and Ivacaftor 50 mg tablet q12h orally for up to 28 days.	
Reporting group title	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h
Reporting group description:	
All subjects in group 6d who received VX-661 50 mg tablet and Ivacaftor 150 mg tablet q12h orally for up to 28 days.	
Reporting group title	Group 7: Placebo
Reporting group description:	
All subjects in group 7 who received placebo matched to VX-661 tablet orally qd in combination with physician-prescribed Kalydeco for up to 28 days.	
Reporting group title	Group 7: VX-661 100 mg qd
Reporting group description:	
All subjects in group 7 who received VX-661 100 mg tablet orally qd in combination with physician-prescribed Kalydeco for up to 28 days.	

Subject analysis set title	Group 1-5b Combined Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in group 1, 2a, 2b, 3a, 3b, 4, 5a and 5b who received placebo matched to VX-661 tablet and/or placebo matched to ivacaftor tablet for up to 28 days.

Subject analysis set title	Group 4 and 6 Combined: Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in group 4, 6a and 6d who received placebo matched to VX-661 tablet and/or placebo matched to ivacaftor tablet for up to 28 days.

Primary: Safety as Determined by Adverse Events

End point title	Safety as Determined by Adverse Events[1]

End point description:

An AE is defined as any untoward medical occurrence in a subject during the study; the event does not necessarily have a causal relationship with the treatment. This includes any newly occurring event or previous condition that has increased in severity or frequency after the Informed Consent Form is signed. An SAE is any AE that results in any of the following: death; life-threatening condition; inpatient hospitalization or prolongation of hospitalization; persistent or significant disability or incapacity; congenital anomaly or birth defect; or other important medical event. Treatment-emergent adverse events are defined as adverse events that were reported or worsened on or after start of study drug through the Follow-up Visit or premature discontinuation. The analysis was done using safety set which included all subjects who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Start of study drug through the 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: No statistical analysis was planned for safety endpoint.

End point values	Group 1-6d Combined: Placebo	Group 1: VX-661 10 mg qd	Group 2a: VX-661 30 mg qd	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	8	8	18
Units: subjects				
number (not applicable)				
Subjects with AEs	30	8	7	15
Subjects with SAEs	5	1	1	1

End point values	Group 3a: VX-661 100 mg qd	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h	Group 5a: VX-661 150 mg qd
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	19	17	9
Units: subjects				
number (not applicable)				
Subjects with AEs	7	18	10	8
Subjects with SAEs	0	2	2	0

End point values	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h	Group 7: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	19	16	4
Units: subjects				
number (not applicable)				
Subjects with AEs	17	16	16	2
Subjects with SAEs	0	1	2	0

End point values	Group 7: VX-661 100 mg qd			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: subjects				
number (not applicable)				
Subjects with AEs	12			
Subjects with SAEs	1			

Statistical analyses

No statistical analyses for this end point

Primary: Change in Sweat Chloride From Baseline Through Study Day 28

End point title	Change in Sweat Chloride From Baseline Through Study Day

End point description:

Sweat samples were collected using an approved collection device. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug. The analysis was done using Full Analysis Set (FAS) which included all randomized subjects who received at least 1 dose of study drug. Here 'Number of subjects analysed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline through Day 28

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 1: VX-661 10 mg qd	Group 2a: VX-661 30 mg qd	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h	Group 3a: VX-661 100 mg qd
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	6	18	8
Units: millimole per liter (mmol/L)				
least squares mean (confidence interval 95%)	3.92 (-0.5 to 8.34)	-4.76 (-9.75 to 0.22)	-5.06 (-8.02 to -2.09)	-20.43 (-24.75 to -16.12)

End point values	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h	Group 5a: VX-661 150 mg qd	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	17	9	17
Units: millimole per liter (mmol/L)				
least squares mean (confidence interval 95%)	-6 (-8.98 to 3.02)	-6.04 (-9.12 to -2.96)	-10.46 (-14.53 to -6.39)	-2.63 (-5.67 to 0.41)

End point values	Group 1-5b Combined Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: millimole per liter (mmol/L)				
least squares mean (confidence interval 95%)	-0.86 (-3.36 to 1.65)			

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Group 1: VX-661 10 mg qd v Group 1-5b Combined Placebo
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0647
Method	Mixed-effect repeated measure (MMRM)
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	4.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	9.84

Statistical analysis title	Statistical Analysis 2
Comparison groups	Group 2a: VX-661 30 mg qd v Group 1-5b Combined Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1686
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-3.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.5
upper limit	1.68

Statistical analysis title	Statistical Analysis 3
Comparison groups	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h v Group 1-5b Combined Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0348
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.1
upper limit	-0.31

Statistical analysis title	Statistical Analysis 4
Comparison groups	Group 3a: VX-661 100 mg qd v Group 1-5b Combined Placebo
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-19.58

Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.57
upper limit	-14.59

Statistical analysis title	Statistical Analysis 5
Comparison groups	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h v Group 1-5b Combined Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0101
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-5.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.03
upper limit	-1.25

Statistical analysis title	Statistical Analysis 6
Comparison groups	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h v Group 1-5b Combined Placebo
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-5.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.16
upper limit	-1.21

Statistical analysis title	Copy of Statistical Analysis 7
Comparison groups	Group 5a: VX-661 150 mg qd v Group 1-5b Combined Placebo

Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-9.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.38
upper limit	-4.82

Statistical analysis title	Copy of Copy of Statistical Analysis 8
Comparison groups	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h v Group 1-5b Combined Placebo
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3745
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.71
upper limit	2.17

Primary: Change in Sweat Chloride From Baseline Through Study Day 28 for Group 6

End point title	Change in Sweat Chloride From Baseline Through Study Day 28 for Group 6[3]

End point description:

Sweat samples were collected using an approved collection device. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug. The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug. Here 'Number of subjects analysed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline through Day 28

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h	Group 4 and 6 Combined: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	14	
Units: mmol/L				
least squares mean (confidence interval 95%)	-6.07 (-10.84 to -1.31)	-7.89 (-12.3 to -3.48)	-1.19 (-5.5 to 3.12)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h v Group 4 and 6 Combined: Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0357
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-6.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.94
upper limit	-0.46

Primary: Change in Sweat Chloride From Baseline Through Study Day 28 for Group 7

End point title	Change in Sweat Chloride From Baseline Through Study Day 28 for Group 7[4]

End point description:

Sweat samples were collected using an approved collection device. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug. The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug. Here 'Number of subjects analysed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline through Day 28

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 7: Placebo	Group 7: VX-661 100 mg qd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	13		
Units: mmol/L				
least squares mean (confidence interval 95%)	10.18 (-2.48 to 22.84)	-7.02 (-14.15 to 0.11)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Group 7: VX-661 100 mg qd v Group 7: Placebo
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0238
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-17.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.75
upper limit	-2.65

Secondary: Change in Sweat Chloride From Baseline to Each Visit up to Study Day 28

End point title	Change in Sweat Chloride From Baseline to Each Visit up to Study Day 28[5]

End point description:

Sweat samples were collected using an approved collection device. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug. The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug. Here 'Number of subjects analysed' signifies those subjects who were evaluable for this endpoint and 'n' signifies those subjects who were evaluable for this endpoint at the specified time points for each group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Day 7, Day 14, Day 21, Day 28

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 1: VX-661 10 mg qd	Group 2a: VX-661 30 mg qd	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h	Group 3a: VX-661 100 mg qd
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	18	8
Units: mmol/L				
least squares mean (confidence interval 95%)				
Day 7 (n= 8, 6, 16, 8, 16, 16, 9, 17, 23)	1.73 (-3.82 to 7.29)	-3.13 (-9.5 to 3.25)	-5.37 (-9.24 to -1.49)	-19.48 (-25 to -13.97)
Day 14 (n= 8, 6, 17, 8, 14, 14, 9, 15, 24)	0.91 (-4.64 to 6.46)	-7.88 (-14.25 to -1.5)	-6.55 (-10.34 to -2.76)	-28.23 (-33.75 to -22.72)
Day 21 (n= 7, 6, 17, 8, 15, 13, 9, 15, 23)	4.84 (-0.99 to 10.66)	-4.61 (-10.98 to 1.76)	-3.7 (-7.48 to 0.09)	-18.78 (-24.3 to -13.27)
Day 28 (n= 7, 6, 17, 8, 16, 14, 9, 15, 22)	8.19 (2.37 to 14.02)	-3.44 (-9.82 to 2.93)	-4.62 (-8.41 to -0.83)	-15.23 (-20.75 to -9.72)

End point values	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h	Group 5a: VX-661 150 mg qd	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	17	9	17
Units: mmol/L				
least squares mean (confidence interval 95%)				
Day 7 (n= 8, 6, 16, 8, 16, 16, 9, 17, 23)	-5.02 (-8.85 to -1.19)	-6.85 (-10.72 to -2.99)	-13.89 (-19.09 to -8.69)	-0.59 (-4.38 to 3.2)
Day 14 (n= 8, 6, 17, 8, 14, 14, 9, 15, 24)	-6.77 (-10.81 to -2.74)	-7.37 (-11.44 to -3.3)	-10.28 (-15.48 to -5.08)	-2.4 (-6.38 to 1.58)
Day 21 (n= 7, 6, 17, 8, 15, 13, 9, 15, 23)	-5.83 (-9.77 to -1.89)	-4.26 (-8.44 to -0.08)	-12.17 (-17.37 to -6.97)	-3.9 (-7.88 to 0.08)
Day 28 (n= 7, 6, 17, 8, 16, 14, 9, 15, 22)	-6.37 (-10.22 to -2.52)	-5.68 (-9.76 to -1.61)	-5.5 (-10.7 to 0.3)	-3.62 (-7.6 to 0.36)

End point values	Group 1-5b Combined Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: mmol/L				
least squares mean (confidence interval 95%)				
Day 7 (n= 8, 6, 16, 8, 16, 16, 9, 17, 23)	0.22 (-3.01 to 3.45)			
Day 14 (n= 8, 6, 17, 8, 14, 14, 9, 15, 24)	-1.32 (-4.5 to 1.87)			
Day 21 (n= 7, 6, 17, 8, 15, 13, 9, 15, 23)	-1.05 (-4.29 to 2.18)			
Day 28 (n= 7, 6, 17, 8, 16, 14, 9, 15, 22)	-1.27 (-4.55 to 2.01)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Sweat Chloride From Baseline to Each Visit up to Study Day 28 for Group 6

End point title	Change in Sweat Chloride From Baseline to Each Visit up to Study Day 28 for Group 6[6]

End point description:

Sweat samples were collected using an approved collection device. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug. The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies those subjects who were evaluable for this endpoint at the specified time points for each group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Day 7, Day 14, Day 21, Day 28

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h	Group 4 and 6 Combined: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	19	16	14	
Units: mmol/L				
least squares mean (confidence interval 95%)				
Day 7 (n= 15, 13, 13)	-6.61 (-12.06 to -1.16)	-11.04 (-16.37 to -5.7)	-0.36 (-5.54 to 4.83)	
Day 14 (n= 17, 14, 14)	-7.9 (-13.25 to -2.55)	-7.11 (-12.34 to -1.88)	-2.1 (-7.19 to 2.98)	
Day 21 (n= 13, 14, 13)	-6.34 (-12 to 0.68)	-6.98 (-12.2 to -1.76)	-2.47 (-7.67 to 2.72)	
Day 28 (n= 16, 15, 13)	-3.44 (-8.85 to 1.97)	-6.43 (-11.55 to -1.31)	0.19 (-5.01 to 5.39)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Sweat Chloride From Baseline to Each Visit up to Study Day 28 for Group 7

End point title	Change in Sweat Chloride From Baseline to Each Visit up to Study Day 28 for Group 7[7]

End point description:

Sweat samples were collected using an approved collection device. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug. The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies those subjects who were evaluable for this endpoint at the specified time points for each group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Day 7, Day 14, Day 21, Day 28

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 7: Placebo	Group 7: VX-661 100 mg qd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: mmol/L				
least squares mean (confidence interval 95%)				
Day 7 (n= 4, 12)	4.87 (-8.32 to 18.06)	-7.28 (-14.76 to 0.2)		
Day 14 (n= 4, 11)	10.75 (-2.44 to 23.94)	-8.95 (-16.54 to -1.35)		
Day 21 (n= 4, 10)	9.37 (-3.82 to 22.56)	-4.14 (-11.86 to 3.58)		
Day 28 (n= 3, 11)	15.73 (1.85 to 29.61)	-7.72 (-15.31 to -0.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1) From Baseline to Each Visit and From Baseline Through Study Day 28

End point title	Change in Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1) From Baseline to Each Visit and From Baseline Through Study Day 28[8]

End point description:

FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies those subjects who were evaluable for the specified time point for each group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Day 7, Day 14, Day 21, Day 28

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 1: VX-661 10 mg qd	Group 2a: VX-661 30 mg qd	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h	Group 3a: VX-661 100 mg qd
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8[9]	8	18	8
Units: percent predicted of FEV1				
least squares mean (confidence interval 95%)				
PB Through Day 28 (n= 8,8,18,8,19,17,9,17,24)	3.49 (0.21 to 6.77)	1.63 (-1.62 to 4.87)	1.3 (-0.87 to 3.47)	1.6 (-1.64 to 4.85)
Day 7 (n= 8, 8, 18, 8, 19, 17, 9, 17, 24)	2.72 (-1.17 to 6.62)	0.8 (-3.09 to 4.69)	0.47 (-2.13 to 3.06)	3 (-0.89 to 6.89)
Day 14 (n= 8, 8, 18, 8, 18, 15, 8, 16, 24)	5.25 (1.35 to 9.15)	3.72 (-0.17 to 7.61)	0.91 (-1.69 to 3.5)	1.61 (-2.28 to 5.5)
Day 21 (n= 7, 8, 18, 8, 17, 15, 9, 16, 24)	2.71 (-1.34 to 6.76)	1.8 (-2.09 to 5.69)	1.84 (-0.75 to 4.44)	0.25 (-3.64 to 4.15)
Day 28 (n= 7, 8, 17, 8, 17, 15, 9, 16, 23)	3.26 (-0.79 to 7.32)	0.19 (-3.7 to 4.08)	1.99 (-0.65 to 4.63)	1.55 (-2.34 to 5.45)

Notes:

[9] - PB= Post-Baseline

End point values	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h	Group 5a: VX-661 150 mg qd	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	17	9	17
Units: percent predicted of FEV1				
least squares mean (confidence interval 95%)				
PB Through Day 28 (n= 8,8,18,8,19,17,9,17,24)	2.9 (0.76 to 5.03)	3.75 (1.47 to 6.02)	2.54 (-0.53 to 5.61)	3.61 (1.36 to 5.86)
Day 7 (n= 8, 8, 18, 8, 19, 17, 9, 17, 24)	2.9 (0.37 to 5.42)	2.66 (-0.01 to 5.33)	0.5 (-3.17 to 4.18)	2.51 (-0.16 to 5.18)
Day 14 (n= 8, 8, 18, 8, 18, 15, 8, 16, 24)	1.79 (-0.78 to 4.36)	4.52 (1.73 to 7.3)	2.79 (-1 to 6.59)	3.72 (1 to 6.44)
Day 21 (n= 7, 8, 18, 8, 17, 15, 9, 16, 24)	3.88 (1.27 to 6.5)	3.37 (0.58 to 6.15)	4.52 (0.85 to 8.19)	4.08 (1.36 to 6.8)
Day 28 (n= 7, 8, 17, 8, 17, 15, 9, 16, 23)	3.02 (0.4 to 5.63)	4.44 (1.66 to 7.23)	2.34 (-1.33 to 6.01)	4.13 (1.41 to 6.86)

End point values	Group 1-5b Combined Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: percent predicted of FEV1				
least squares mean (confidence interval 95%)				
PB Through Day 28 (n= 8,8,18,8,19,17,9,17,24)	-0.14 (-2.02 to 1.74)			
Day 7 (n= 8, 8, 18, 8, 19, 17, 9, 17, 24)	-0.41 (-2.66 to 1.84)			
Day 14 (n= 8, 8, 18, 8, 18, 15, 8, 16, 24)	0.03 (-2.21 to 2.28)			

Day 21 (n= 7, 8, 18, 8, 17, 15, 9, 16, 24)	0.18 (-2.07 to 2.43)			
Day 28 (n= 7, 8, 17, 8, 17, 15, 9, 16, 23)	-0.36 (-2.63 to 1.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1) From Baseline to Each Visit and From Baseline Through Study Day 28 for Group 6

End point title	Change in Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1) From Baseline to Each Visit and From Baseline Through Study Day 28 for Group 6[10]

End point description:

FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies those subjects who were evaluable for the specified time point for each group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Day 7, Day 14, Day 21, Day 28

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h	Group 4 and 6 Combined: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	19	16	14	
Units: percent predicted of FEV1				
least squares mean (confidence interval 95%)				
Post-Baseline Through Day 28 (n= 18, 16, 14)	0.94 (-1.42 to 3.3)	2.31 (-0.19 to 4.8)	1.47 (-1.2 to 4.13)	
Day 7 (n= 18, 16, 14)	1.37 (-1.33 to 4.08)	1.95 (-0.93 to 4.82)	1.09 (-1.97 to 4.15)	
Day 14 (n= 17, 16, 14)	1.2 (-1.55 to 3.95)	2.52 (-0.36 to 5.4)	1.37 (-1.69 to 4.44)	
Day 21 (n= 17, 16, 13)	0.36 (-2.38 to 3.11)	3.21 (0.33 to 6.08)	1.73 (-1.39 to 4.85)	
Day 28 (n= 16, 16, 13)	0.81 (-1.97 to 3.6)	1.56 (-1.32 to 4.44)	1.67 (-1.45 to 4.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1) From Baseline to Each Visit and From Baseline Through Study Day 28 for Group 7

End point title	Change in Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1) From Baseline to Each Visit and From Baseline Through Study Day 28 for Group 7[11]

End point description:

FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies those subjects who were evaluable at the specified time point for each group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Day 7, Day 14, Day 21, Day 28

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 7: Placebo	Group 7: VX-661 100 mg qd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: percent predicted of FEV1				
least squares mean (confidence interval 95%)				
Post-Baseline Through Day 28	1.4 (-5.04 to 7.83)	4.6 (1.17 to 8.03)		
Day 7	3 (-3.55 to 9.55)	4.14 (0.65 to 7.63)		
Day 14	0.98 (-5.56 to 7.53)	5.22 (1.73 to 8.71)		
Day 21	2.72 (-3.83 to 9.27)	3.88 (0.39 to 7.38)		
Day 28	-1.12 (-7.66 to 5.43)	5.16 (1.67 to 8.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in FEV1 (Liter [L]) From Baseline to Each Visit and From Baseline Through Study Day 28

End point title	Change in FEV1 (Liter [L]) From Baseline to Each Visit and From Baseline Through Study Day 28[12]

End point description:

FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies those subjects who were evaluable at the specified time point for each group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Day 7, Day 14, Day 21, Day 28

Notes:

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

Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 1: VX-661 10 mg qd	Group 2a: VX-661 30 mg qd	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h	Group 3a: VX-661 100 mg qd
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8[13]	8	18	8
Units: Liters				
least squares mean (confidence interval 95%)				
PB Through Day 28 (n=8,8,18,8,19,17,9,17, 24)	0.14 (0.02 to 0.26)	0.07 (-0.05 to 0.19)	0.05 (-0.03 to 0.13)	0.04 (-0.08 to 0.16)
Day 7 (n= 8, 8, 18, 8, 19, 17, 9, 17, 24)	0.11 (-0.04 to 0.25)	0.02 (-0.13 to 0.16)	0.02 (-0.08 to 0.12)	0.09 (-0.06 to 0.24)
Day 14 (n= 8, 8, 18, 8, 18, 15, 8, 16, 24)	0.2 (0.05 to 0.34)	0.14 (-0.01 to 0.28)	0.03 (-0.07 to 0.12)	0.04 (-0.11 to 0.19)
Day 21 (n= 7, 8, 18, 8, 17, 15, 9, 16, 24)	0.12 (-0.03 to 0.27)	0.08 (-0.06 to 0.23)	0.07 (-0.03 to 0.17)	0 (-0.15 to 0.15)
Day 28 (n= 7, 8, 17, 8, 17, 15, 9, 16, 23)	0.13 (-0.02 to 0.28)	0.03 (-0.11 to 0.18)	0.08 (-0.02 to 0.18)	0.04 (-0.11 to 0.18)

Notes:

[13] - PB=Post-Baseline

End point values	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h	Group 5a: VX-661 150 mg qd	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	17	9	17
Units: Liters				
least squares mean (confidence interval 95%)				
PB Through Day 28 (n=8,8,18,8,19,17,9,17, 24)	0.1 (0.02 to 0.18)	0.14 (0.06 to 0.23)	0.1 (-0.01 to 0.21)	0.12 (0.04 to 0.21)
Day 7 (n= 8, 8, 18, 8, 19, 17, 9, 17, 24)	0.1 (0 to 0.19)	0.11 (0.01 to 0.21)	0.02 (-0.12 to 0.16)	0.08 (-0.02 to 0.18)
Day 14 (n= 8, 8, 18, 8, 18, 15, 8, 16, 24)	0.05 (-0.04 to 0.15)	0.17 (0.06 to 0.27)	0.11 (-0.03 to 0.25)	0.12 (0.02 to 0.23)
Day 21 (n= 7, 8, 18, 8, 17, 15, 9, 16, 24)	0.14 (0.04 to 0.23)	0.13 (0.02 to 0.23)	0.18 (0.04 to 0.31)	0.14 (0.04 to 0.24)
Day 28 (n= 7, 8, 17, 8, 17, 15, 9, 16, 23)	0.1 (0.01 to 0.2)	0.16 (0.06 to 0.27)	0.09 (-0.05 to 0.23)	0.15 (0.05 to 0.26)

End point values	Group 1-5b Combined Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Liters				
least squares mean (confidence interval 95%)				

PB Through Day 28 (n=8,8,18,8,19,17,9,17, 24)	0.01 (-0.06 to 0.08)			
Day 7 (n= 8, 8, 18, 8, 19, 17, 9, 17, 24)	-0.01 (-0.09 to 0.08)			
Day 14 (n= 8, 8, 18, 8, 18, 15, 8, 16, 24)	0.02 (-0.07 to 0.1)			
Day 21 (n= 7, 8, 18, 8, 17, 15, 9, 16, 24)	0.02 (-0.06 to 0.1)			
Day 28 (n= 7, 8, 17, 8, 17, 15, 9, 16, 23)	0.01 (-0.08 to 0.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in FEV1 (L) From Baseline to Each Visit and From Baseline Through Study Day 28 for Group 6

End point title	Change in FEV1 (L) From Baseline to Each Visit and From Baseline Through Study Day 28 for Group 6[14]

End point description:

FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies those subjects who were evaluable at the specified time point for each group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Day 7, Day 14, Day 21, Day 28

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h	Group 4 and 6 Combined: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	19	16	14	
Units: Liters				
least squares mean (confidence interval 95%)				
Post-Baseline Through Day 28 (n= 18, 16, 14)	0.02 (-0.07 to 0.11)	0.09 (-0.01 to 0.18)	0.07 (-0.04 to 0.17)	
Day 7 (n= 18, 16, 14)	0.04 (-0.07 to 0.14)	0.06 (-0.05 to 0.17)	0.05 (-0.06 to 0.17)	
Day 14 (n= 17, 16, 14)	0.03 (-0.07 to 0.14)	0.1 (-0.01 to 0.21)	0.06 (-0.05 to 0.18)	
Day 21 (n= 17, 16, 13)	-0.01 (-0.11 to 0.1)	0.13 (0.02 to 0.24)	0.08 (-0.04 to 0.2)	
Day 28 (n= 16, 16, 13)	0.02 (-0.08 to 0.13)	0.06 (-0.05 to 0.17)	0.08 (-0.04 to 0.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in FEV1 (L) From Baseline to Each Visit and From Baseline Through Study Day 28 for Group 7

End point title	Change in FEV1 (L) From Baseline to Each Visit and From Baseline Through Study Day 28 for Group 7[15]

End point description:

FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, Day 7, Day 14, Day 21, Day 28

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 7: Placebo	Group 7: VX-661 100 mg qd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: Liters				
least squares mean (confidence interval 95%)				
Post-Baseline Through Day 28	0.09 (-0.16 to 0.34)	0.16 (0.03 to 0.29)		
Day 7	0.14 (-0.11 to 0.39)	0.15 (0.01 to 0.28)		
Day 14	0.08 (-0.17 to 0.33)	0.18 (0.05 to 0.32)		
Day 21	0.14 (-0.11 to 0.4)	0.13 (-0.01 to 0.26)		
Day 28	-0.01 (-0.26 to 0.25)	0.19 (0.05 to 0.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Respiratory Domain Score From Baseline to Each Visit up to Study Day 28

End point title	Change in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Respiratory Domain Score From Baseline to Each Visit up to Study Day 28[16]

End point description:

The CFQ-R is a validated patient-reported outcome measuring health-related quality of life for subjects with cystic fibrosis. Respiratory domain assessed respiratory symptoms (for example, coughing, congestion, wheezing), score range: 0-100; higher scores indicating fewer symptoms and better health-related quality of life.The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies those subjects who were evaluable at the specified time point for each group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Day 14, Day 28

Notes:

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

Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 1: VX-661 10 mg qd	Group 2a: VX-661 30 mg qd	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h	Group 3a: VX-661 100 mg qd
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8[17]	8	18	8
Units: units on a scale				
least squares mean (confidence interval 95%)				
PB Through Day 28 (n=8,8,18,8,18,15,9,16,24)	4.02 (-4.38 to 12.43)	5.54 (-2.72 to 13.79)	3.8 (-1.74 to 9.35)	0.61 (-7.64 to 8.86)
Day 14 (n= 8, 8, 18, 8, 18, 15, 9, 16, 24)	6.67 (-2.9 to 16.25)	4.84 (-4.73 to 14.41)	4.29 (-2.09 to 10.67)	0.27 (-9.3 to 9.83)
Day 28 (n= 7, 8, 17, 8, 17, 15, 9, 16, 23)	1.38 (-8.7 to 11.45)	6.23 (-3.34 to 15.8)	3.31 (-3.21 to 9.84)	0.95 (-8.61 to 10.52)

Notes:

[17] - PB= Post-Baseline

End point values	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h	Group 5a: VX-661 150 mg qd	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	17	9	17
Units: units on a scale				
least squares mean (confidence interval 95%)				
PB Through Day 28 (n=8,8,18,8,18,15,9,16,24)	3.52 (-2.02 to 9.06)	5.15 (-0.88 to 11.19)	2.58 (-5.21 to 10.37)	7.62 (1.78 to 13.45)
Day 14 (n= 8, 8, 18, 8, 18, 15, 9, 16, 24)	2.81 (-3.56 to 9.19)	4.41 (-2.58 to 11.4)	4.13 (-4.9 to 13.16)	7.13 (0.37 to 13.89)
Day 28 (n= 7, 8, 17, 8, 17, 15, 9, 16, 23)	4.22 (-2.29 to 10.74)	5.9 (-1.1 to 12.89)	1.03 (-8 to 10.06)	8.1 (1.34 to 14.87)

End point values	Group 1-5b Combined Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: units on a scale				
least squares mean (confidence interval 95%)				
PB Through Day 28 (n=8,8,18,8,18,15,9,16,24)	1.69 (-3.1 to 6.48)			
Day 14 (n= 8, 8, 18, 8, 18, 15, 9, 16, 24)	0.53 (-4.99 to 6.05)			

Day 28 (n= 7, 8, 17, 8, 17, 15, 9, 16, 23)	2.85 (-2.76 to 8.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Respiratory Domain Score From Baseline to Each Visit up to Study Day 28 for Group 6

End point title	Change in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Respiratory Domain Score From Baseline to Each Visit up to Study Day 28 for Group 6[18]

End point description:

The CFQ-R is a validated patient-reported outcome measuring health-related quality of life for subjects with cystic fibrosis. Respiratory domain assessed respiratory symptoms (for example, coughing, congestion, wheezing), score range: 0-100; higher scores indicating fewer symptoms and better health-related quality of life. The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies those subjects who were evaluable at the specified time point for each group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Day 14, Day 28

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h	Group 4 and 6 Combined: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	19	16	14	
Units: units on a scale				
least squares mean (confidence interval 95%)				
Post-Baseline Through Day 28 (n= 17, 16, 14)	0.87 (-4.44 to 6.19)	1.91 (-3.5 to 7.33)	1.65 (-4.18 to 7.49)	
Day 14 (n= 17, 16, 14)	2.02 (-3.97 to 8.02)	0.87 (-5.25 to 6.99)	2.78 (-3.76 to 9.32)	
Day 28 (n= 17, 16, 13)	-0.27 (-6.27 to 5.72)	2.96 (-3.16 to 9.08)	0.53 (-6.18 to 7.23)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Respiratory Domain Score From Baseline to Each Visit up to Study Day 28 for Group 7

End point title	Change in Cystic Fibrosis Questionnaire-Revised (CFQ-R)

	Respiratory Domain Score From Baseline to Each Visit up to Study Day 28 for Group 7[19]

End point description:

The CFQ-R is a validated patient-reported outcome measuring health-related quality of life for subjects with cystic fibrosis. Respiratory domain assessed respiratory symptoms (for example, coughing, congestion, wheezing), score range: 0-100; higher scores indicating fewer symptoms and better health-related quality of life. The analysis was done using FAS which included all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies those subjects who were evaluable at the specified time point for each group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Day 14, Day 28

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only arms which are applicable to the endpoint are reported.

End point values	Group 7: Placebo	Group 7: VX-661 100 mg qd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: units on a scale				
least squares mean (confidence interval 95%)				
Post-Baseline Through Day 28 (n= 4, 14)	-3.02 (-13.52 to 7.47)	3.79 (-1.78 to 9.36)		
Day 14 (n= 4, 13)	1.83 (-10.64 to 14.3)	5.24 (-1.56 to 12.04)		
Day 28 (n= 4, 14)	-7.87 (-20.34 to 4.6)	2.33 (-4.24 to 8.91)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Start of study drug through the Follow-up Visit (28 days after last dose) or premature discontinuation

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Group 1-6d Combined: Placebo

Reporting group description:

All subjects in group 1, 2a, 2b, 3a, 3b, 4, 5a, 5b, 6a and 6d who received placebo matched to VX-661 tablet and/or placebo matched to ivacaftor tablet for up to 28 days.

Reporting group title	Group 1: VX-661 10 mg qd

Reporting group description:

All subjects in group 1 who received VX661 10 milligram tablet orally qd for up to 28 days.

Reporting group title	Group 2a: VX-661 30 mg qd

Reporting group description:

All subjects in group 2a who received VX661 30 mg tablet orally qd and placebo matched to Ivacaftor tablet q12h for up to 28 days.

Reporting group title	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h

Reporting group description:

All subjects in group 2b who received VX661 10 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.

Reporting group title	Group 3a: VX-661 100 mg qd

Reporting group description:

All subjects in group 3a who received VX661 100 mg tablet orally qd and placebo matched to Ivacaftor tablet q12h for up to 28 days.

Reporting group title	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h

Reporting group description:

All subjects in group 3b who received VX661 30 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.

Reporting group title	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h

Reporting group description:

All subjects in group 4 who received VX661 100 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.

Reporting group title	Group 5a: VX-661 150 mg qd

Reporting group description:

All subjects in group 5a who received VX661 150 mg tablet orally qd for up to 28 days.

Reporting group title	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h

Reporting group description:

All subjects in group 5b who received VX661 150 mg tablet qd and Ivacaftor 150 mg tablet q12h orally for up to 28 days.

Reporting group title	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h

Reporting group description:

All subjects in group 6a who received VX661 100 mg tablet qd and Ivacaftor 50 mg tablet q12h orally for up to 28 days.

Reporting group title	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h

Reporting group description:

All subjects in group 6d who received VX661 50 mg tablet and Ivacaftor 150 mg tablet q12h orally for up to 28 days.

Reporting group title	Group 7: Placebo

Reporting group description:

All subjects in group 7 who received placebo matched to VX-661 tablet orally qd in combination with physician-prescribed Kalydeco for up to 28 days.

Reporting group title	Group 7: VX-661 100 mg qd

Reporting group description:

All subjects in group 7 who received VX-661 100 mg tablet orally qd in combination with physician-prescribed Kalydeco for up to 28 days.

Serious adverse events	Group 1-6d Combined: Placebo	Group 1: VX-661 10 mg qd	Group 2a: VX-661 30 mg qd
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 33 (15.15%)	1 / 8 (12.50%)	1 / 8 (12.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			

subjects affected / exposed	5 / 33 (15.15%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 5	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h	Group 3a: VX-661 100 mg qd	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	2 / 19 (10.53%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (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			
Haemoptysis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (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 / 18 (5.56%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (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	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h	Group 5a: VX-661 150 mg qd	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 17 (11.76%)	0 / 9 (0.00%)	0 / 17 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (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			
Haemoptysis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (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
Musculoskeletal and connective tissue disorders			
Arthritis			

subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (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 / 17 (11.76%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (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	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h	Group 7: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 19 (5.26%)	2 / 16 (12.50%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (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			
Haemoptysis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (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

Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (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 / 19 (5.26%)	2 / 16 (12.50%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (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	Group 7: VX-661 100 mg qd		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 14 (7.14%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 14 (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: 0 %

Non-serious adverse events	Group 1-6d Combined: Placebo	Group 1: VX-661 10 mg qd	Group 2a: VX-661 30 mg qd
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 33 (90.91%)	8 / 8 (100.00%)	7 / 8 (87.50%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 33 (9.09%)	4 / 8 (50.00%)	1 / 8 (12.50%)
occurrences (all)	4	4	1
Pyrexia			
subjects affected / exposed	2 / 33 (6.06%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	2	2	0

Application site rash			
subjects affected / exposed	1 / 33 (3.03%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Pain			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Thirst			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Application site erythema			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Catheter site haematoma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Disease progression			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Feeling abnormal			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infusion site pain			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Infusion site swelling			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Medical device complication			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site haematoma			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Vessel puncture site reaction			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Drug hypersensitivity			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Menstrual disorder			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Metrorrhagia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			

subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 33 (18.18%)	3 / 8 (37.50%)	3 / 8 (37.50%)
occurrences (all)	7	3	3
Sputum increased			
subjects affected / exposed	2 / 33 (6.06%)	2 / 8 (25.00%)	2 / 8 (25.00%)
occurrences (all)	2	2	2
Haemoptysis			
subjects affected / exposed	2 / 33 (6.06%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	2	3	0
Oropharyngeal pain			
subjects affected / exposed	3 / 33 (9.09%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	3	0	1
Nasal congestion			
subjects affected / exposed	1 / 33 (3.03%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	2	3	0
Rales			
subjects affected / exposed	0 / 33 (0.00%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Respiration abnormal			
subjects affected / exposed	2 / 33 (6.06%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Respiratory tract congestion			
subjects affected / exposed	2 / 33 (6.06%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Sinus congestion			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Rhinorrhoea			

subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	1 / 33 (3.03%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Dysphonia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Increased viscosity of bronchial secretion			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Productive cough			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Sputum discoloured			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Asthma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bronchial obstruction			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Bronchial secretion retention			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bronchiectasis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

Increased bronchial secretion			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nasal obstruction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nasal oedema			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Painful respiration			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Paranasal sinus hypersecretion			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Respiratory tract irritation			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Thinking abnormal			

subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Investigations			
Pulmonary function test decreased			
subjects affected / exposed	1 / 33 (3.03%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Weight decreased			
subjects affected / exposed	1 / 33 (3.03%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Blood glucose decreased			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	2 / 33 (6.06%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Liver function test abnormal			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin unconjugated increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus increased			

subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal examination abnormal			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Transaminases increased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Urinary casts present			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Urine colour abnormal			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vitamin D decreased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			

Muscle strain			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Concussion			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Excoriation			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Post concussion syndrome			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skeletal injury			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Sunburn			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

Congenital, familial and genetic disorders			
Cystic fibrosis related diabetes			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 33 (24.24%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	9	1	1
Sinus headache			
subjects affected / exposed	2 / 33 (6.06%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Dizziness			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	3 / 8 (37.50%)
occurrences (all)	0	0	3
Lethargy			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Neuralgia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Partial seizures			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Syncope			

subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ear discomfort			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Conjunctival irritation			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 33 (3.03%)	1 / 8 (12.50%)	2 / 8 (25.00%)
occurrences (all)	1	1	3
Diarrhoea			
subjects affected / exposed	2 / 33 (6.06%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	2	2	1
Vomiting			

subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Abdominal pain			
subjects affected / exposed	2 / 33 (6.06%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Abdominal distension			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Abdominal discomfort			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Change of bowel habit			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Enteritis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Faecaloma			

subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Paraesthesia oral			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	2 / 33 (6.06%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Rash			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cold sweat			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Nail disorder			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash follicular			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Red man syndrome			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urine odour abnormal			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	3 / 33 (9.09%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	3	1	0
Musculoskeletal chest pain			

subjects affected / exposed	2 / 33 (6.06%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Back pain			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Arthritis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	8 / 33 (24.24%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	10	0	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 33 (9.09%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	4	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Sinusitis			
subjects affected / exposed	3 / 33 (9.09%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	3	2	0
Viral upper respiratory tract infection			

subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Acute sinusitis			
subjects affected / exposed	1 / 33 (3.03%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Gastroenteritis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	2 / 33 (6.06%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Gastroenteritis viral			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Otitis media			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	2 / 33 (6.06%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection viral			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

Paronychia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 33 (3.03%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Vitamin E deficiency			

subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Vitamin K deficiency			
subjects affected / exposed	1 / 33 (3.03%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Group 2b: VX-661 10 mg qd/Ivacaftor 150 mg q12h	Group 3a: VX-661 100 mg qd	Group 3b: VX-661 30 mg qd/Ivacaftor 150 mg q12h
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 18 (83.33%)	7 / 8 (87.50%)	18 / 19 (94.74%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 18 (5.56%)	1 / 8 (12.50%)	3 / 19 (15.79%)
occurrences (all)	1	1	3
Pyrexia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Application site rash			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Thirst			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Application site erythema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Catheter site haematoma			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Chest pain			

subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Disease progression			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Feeling abnormal			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Infusion site pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Infusion site swelling			
subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Medical device complication			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site reaction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Drug hypersensitivity			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hypersensitivity			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Menstrual disorder			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Metrorrhagia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 18 (11.11%)	2 / 8 (25.00%)	3 / 19 (15.79%)
occurrences (all)	3	2	3
Sputum increased			
subjects affected / exposed	2 / 18 (11.11%)	1 / 8 (12.50%)	1 / 19 (5.26%)
occurrences (all)	2	1	1
Haemoptysis			
subjects affected / exposed	0 / 18 (0.00%)	2 / 8 (25.00%)	1 / 19 (5.26%)
occurrences (all)	0	2	2
Oropharyngeal pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Nasal congestion			

subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Rales			
subjects affected / exposed	2 / 18 (11.11%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	2
Respiration abnormal			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Respiratory tract congestion			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Sinus congestion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Increased viscosity of bronchial secretion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Sputum discoloured			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Bronchial obstruction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Bronchial secretion retention			
subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Bronchiectasis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Increased bronchial secretion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nasal obstruction			
subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Nasal oedema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Painful respiration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory tract irritation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract congestion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Thinking abnormal			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Investigations			
Pulmonary function test decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
Weight decreased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood glucose decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal			

subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin unconjugated increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood phosphorus increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastrointestinal examination abnormal			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Urinary casts present			

subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Urine colour abnormal			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vitamin D decreased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Concussion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Excoriation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Limb injury			

subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Post concussion syndrome			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skeletal injury			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Sunburn			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Cystic fibrosis related diabetes			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 18 (11.11%)	1 / 8 (12.50%)	4 / 19 (21.05%)
occurrences (all)	3	2	4
Sinus headache			
subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Migraine			

subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Partial seizures			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Ear discomfort			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

Conjunctival haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Conjunctival irritation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 18 (11.11%)	1 / 8 (12.50%)	2 / 19 (10.53%)
occurrences (all)	2	1	4
Diarrhoea			
subjects affected / exposed	2 / 18 (11.11%)	1 / 8 (12.50%)	1 / 19 (5.26%)
occurrences (all)	2	1	1
Vomiting			
subjects affected / exposed	1 / 18 (5.56%)	1 / 8 (12.50%)	2 / 19 (10.53%)
occurrences (all)	1	1	2
Abdominal pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			

subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Abdominal discomfort			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Change of bowel habit			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Enteritis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Faecaloma			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Paraesthesia oral			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Toothache			

subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Cold sweat			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Rash erythematous			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Rash follicular			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Rash macular			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Rash papular			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Red man syndrome			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Urine odour abnormal			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	2 / 18 (11.11%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 18 (5.56%)	2 / 8 (25.00%)	0 / 19 (0.00%)
occurrences (all)	2	2	0
Back pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Arthralgia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Joint swelling			

subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	4 / 18 (22.22%)	1 / 8 (12.50%)	4 / 19 (21.05%)
occurrences (all)	4	1	5
Upper respiratory tract infection			
subjects affected / exposed	2 / 18 (11.11%)	1 / 8 (12.50%)	2 / 19 (10.53%)
occurrences (all)	2	1	3
Nasopharyngitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	2
Sinusitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Oral candidiasis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Acute sinusitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Bronchitis			

subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 8 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Increased appetite			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vitamin E deficiency			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vitamin K deficiency			
subjects affected / exposed	0 / 18 (0.00%)	0 / 8 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Group 4: VX-661 100 mg qd/Ivacaftor 150 mg q12h	Group 5a: VX-661 150 mg qd	Group 5b: VX-661 150 mg qd/Ivacaftor 150 mg q12h
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 17 (52.94%)	8 / 9 (88.89%)	17 / 17 (100.00%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	2 / 17 (11.76%)
occurrences (all)	0	2	4
Pyrexia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Application site rash			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Application site erythema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Catheter site haematoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Disease progression			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Feeling abnormal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Infusion site pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Infusion site swelling			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Medical device complication			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site reaction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Drug hypersensitivity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Menstrual disorder			

subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Metrorrhagia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 17 (11.76%)	2 / 9 (22.22%)	3 / 17 (17.65%)
occurrences (all)	2	3	5
Sputum increased			
subjects affected / exposed	2 / 17 (11.76%)	2 / 9 (22.22%)	1 / 17 (5.88%)
occurrences (all)	2	3	1
Haemoptysis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Rales			
subjects affected / exposed	2 / 17 (11.76%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
Respiration abnormal			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	4	0
Respiratory tract congestion			
subjects affected / exposed	1 / 17 (5.88%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Sinus congestion			

subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	2 / 17 (11.76%)
occurrences (all)	1	0	2
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Epistaxis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Dysphonia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dyspnoea exertional			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Increased viscosity of bronchial secretion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Sputum discoloured			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Asthma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Bronchial obstruction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Bronchial secretion retention			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Bronchiectasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Increased bronchial secretion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nasal obstruction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nasal oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Painful respiration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Respiratory tract irritation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Depression			

subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Thinking abnormal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Investigations			
Pulmonary function test decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Blood glucose decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin unconjugated increased			

subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal examination abnormal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Neutrophil count decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Urinary casts present			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Urine colour abnormal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vitamin D decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
White blood cell count decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

White blood cells urine positive			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Concussion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Excoriation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Post concussion syndrome			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Skeletal injury			

subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Sunburn			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Cystic fibrosis related diabetes			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	2 / 17 (11.76%)
occurrences (all)	0	1	3
Sinus headache			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Dizziness			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Lethargy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Partial seizures			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Presyncope			

subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Ear discomfort			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Conjunctival irritation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	1 / 17 (5.88%)	4 / 9 (44.44%)	0 / 17 (0.00%)
occurrences (all)	1	4	0
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)	2 / 9 (22.22%)	1 / 17 (5.88%)
occurrences (all)	0	2	1
Abdominal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Constipation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Flatulence			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Abdominal pain lower			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Change of bowel habit			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Dental caries			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Enteritis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Faecaloma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Faeces discoloured			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Paraesthesia oral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Retching			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	1
Cold sweat			

subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rash follicular			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Rash papular			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Red man syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Urine odour abnormal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Arthralgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Arthritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	3 / 17 (17.65%)	1 / 9 (11.11%)	2 / 17 (11.76%)
occurrences (all)	3	1	3
Upper respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Nasopharyngitis			

subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	3 / 17 (17.65%)
occurrences (all)	0	0	3
Sinusitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Oral candidiasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Acute sinusitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Bronchitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Cellulitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			

subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vitamin E deficiency			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vitamin K deficiency			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Group 6a: VX-661 100 mg qd/Ivacaftor 50 mg q12h	Group 6d: VX-661 50 mg q12h/Ivacaftor 150 mg q12h	Group 7: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 19 (84.21%)	16 / 16 (100.00%)	2 / 4 (50.00%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Application site rash			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Application site erythema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Catheter site haematoma			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Disease progression			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Feeling abnormal			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Feeling hot			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Infusion site pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infusion site swelling			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Medical device complication			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Vessel puncture site reaction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Drug hypersensitivity			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Menstrual disorder			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metrorrhagia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 19 (21.05%)	3 / 16 (18.75%)	0 / 4 (0.00%)
occurrences (all)	6	4	0
Sputum increased			
subjects affected / exposed	2 / 19 (10.53%)	3 / 16 (18.75%)	0 / 4 (0.00%)
occurrences (all)	3	3	0

Haemoptysis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 19 (5.26%)	2 / 16 (12.50%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
Nasal congestion			
subjects affected / exposed	2 / 19 (10.53%)	1 / 16 (6.25%)	1 / 4 (25.00%)
occurrences (all)	2	1	1
Rales			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Respiration abnormal			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Respiratory tract congestion			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			
subjects affected / exposed	1 / 19 (5.26%)	1 / 16 (6.25%)	1 / 4 (25.00%)
occurrences (all)	2	1	1
Dyspnoea			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Increased viscosity of bronchial secretion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Sputum discoloured			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Bronchial obstruction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bronchial secretion retention			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bronchiectasis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Increased bronchial secretion			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Nasal obstruction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasal oedema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Painful respiration			

subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory tract irritation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Thinking abnormal			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Investigations			
Pulmonary function test decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			

subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood glucose decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin unconjugated increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood potassium increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal examination abnormal			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			

subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Platelet count decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urinary casts present			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urine colour abnormal			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Vitamin D decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
White blood cells urine positive			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Concussion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Excoriation			

subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Laceration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Post concussion syndrome			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Scratch			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Skeletal injury			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Sunburn			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Cystic fibrosis related diabetes			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 19 (21.05%)	4 / 16 (25.00%)	0 / 4 (0.00%)
occurrences (all)	5	7	0
Sinus headache			

subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Lethargy			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Neuralgia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Partial seizures			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			

subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ear discomfort			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Vertigo			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Conjunctival irritation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 19 (5.26%)	5 / 16 (31.25%)	0 / 4 (0.00%)
occurrences (all)	1	8	0
Diarrhoea			
subjects affected / exposed	0 / 19 (0.00%)	2 / 16 (12.50%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Vomiting			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Abdominal pain			
subjects affected / exposed	3 / 19 (15.79%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	3	2	0
Abdominal pain upper			

subjects affected / exposed	2 / 19 (10.53%)	0 / 16 (0.00%)	1 / 4 (25.00%)
occurrences (all)	2	0	1
Constipation			
subjects affected / exposed	0 / 19 (0.00%)	2 / 16 (12.50%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Flatulence			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Change of bowel habit			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dental caries			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Enteritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Faecaloma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			

subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Paraesthesia oral			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cold sweat			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Nail disorder			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Rash erythematous			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash follicular			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Red man syndrome			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Urine odour abnormal			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 19 (0.00%)	2 / 16 (12.50%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			

subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	2 / 19 (10.53%)	3 / 16 (18.75%)	1 / 4 (25.00%)
occurrences (all)	2	3	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 19 (10.53%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 19 (0.00%)	3 / 16 (18.75%)	1 / 4 (25.00%)
occurrences (all)	0	4	1
Sinusitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Oral candidiasis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Acute sinusitis			

subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 19 (0.00%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Respiratory syncytial virus infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 19 (5.26%)	1 / 16 (6.25%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hypoglycaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Dehydration			
subjects affected / exposed	1 / 19 (5.26%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitamin E deficiency			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitamin K deficiency			
subjects affected / exposed	0 / 19 (0.00%)	0 / 16 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Group 7: VX-661 100 mg qd		

Total subjects affected by non-serious adverse events subjects affected / exposed	12 / 14 (85.71%)		
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Application site rash subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Thirst subjects affected / exposed occurrences (all) Application site erythema subjects affected / exposed occurrences (all) Catheter site haematoma subjects affected / exposed occurrences (all) Chest pain subjects affected / exposed occurrences (all) Disease progression subjects affected / exposed occurrences (all) Feeling abnormal	 1 / 14 (7.14%) 1 2 / 14 (14.29%) 2 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0		

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Feeling hot			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Infusion site pain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Infusion site swelling			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Medical device complication			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Vessel puncture site haematoma			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Vessel puncture site reaction			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Drug hypersensitivity			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Hypersensitivity			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		

Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Dysmenorrhoea			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Menstrual disorder			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Metrorrhagia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Vaginal haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 14 (28.57%)		
occurrences (all)	4		
Sputum increased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Haemoptysis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Nasal congestion			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Rales			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Respiration abnormal			

subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Respiratory tract congestion				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Sinus congestion				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Dyspnoea				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Rhinorrhoea				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Epistaxis				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Dysphonia				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Dyspnoea exertional				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Increased viscosity of bronchial secretion				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Productive cough				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Sputum discoloured				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Wheezing				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			

Asthma				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Bronchial obstruction				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Bronchial secretion retention				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Bronchiectasis				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Increased bronchial secretion				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Nasal obstruction				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Nasal oedema				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Painful respiration				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Paranasal sinus hypersecretion				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Respiratory tract irritation				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Upper respiratory tract congestion				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Psychiatric disorders				
Abnormal dreams				

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Thinking abnormal			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Investigations			
Pulmonary function test decreased			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Blood glucose decreased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Hepatic enzyme increased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Liver function test abnormal			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Blood bilirubin increased				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Blood bilirubin unconjugated increased				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Blood creatinine increased				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Blood phosphorus increased				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Blood potassium increased				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Gastrointestinal examination abnormal				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Neutrophil count decreased				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Platelet count decreased				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Transaminases increased				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Urinary casts present				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Urine colour abnormal				

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Vitamin D decreased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
White blood cells urine positive			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Concussion			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Excoriation			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Laceration			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Ligament sprain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Limb injury			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Post concussion syndrome			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Scratch			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Skeletal injury			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Sunburn			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Congenital, familial and genetic disorders			
Cystic fibrosis related diabetes			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	4		
Sinus headache			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Lethargy			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Neuralgia			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Partial seizures			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Ear discomfort			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Vertigo			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Conjunctival irritation			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Dry eye			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	6		
Diarrhoea			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		

Abdominal discomfort				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Abdominal pain lower				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Change of bowel habit				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Dental caries				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Enteritis				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Faecaloma				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Faeces discoloured				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Frequent bowel movements				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Paraesthesia oral				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Retching				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Toothache				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Skin and subcutaneous tissue disorders				
Pruritus				

subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Night sweats				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Rash				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Cold sweat				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Dry skin				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Eczema				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Nail disorder				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Photosensitivity reaction				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Rash erythematous				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Rash follicular				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Rash macular				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Rash papular				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Red man syndrome				

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Urine odour abnormal			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Arthritis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Acute sinusitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Otitis media			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Paronychia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Dehydration			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Increased appetite			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Vitamin E deficiency			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Vitamin K deficiency			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 November 2011	Changed the maximum dose level of VX-661 from 200 mg to "to be determined (TBD)" based on pharmacokinetics (PK), pharmacodynamics (PD), and safety data.
04 April 2012	Added provision to discontinue subjects who developed life-threatening adverse events or serious adverse events (SAEs) from the study.
24 January 2013	Addition of Group 6a: VX-661 100 mg qd/ivacaftor 50 mg q12h. Addition of Group 7 to include subjects hetereozygous for the F508del-CFTR mutation.
08 July 2013	Addition of groups to investigate ivacaftor 100 mg and 50 mg qd in combination with 100 mg VX-661 qd. Addition of group to investigate 50 mg VX-661 q12h in combination with 150 mg ivacaftor q12h. Change in the study population in Group 7 to include subjects who were 12 years or older.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Pharmacokinetic final data are not yet available. Once the data are available for PK endpoints, the posting will be updated to include the same.

Notes: