Clinical trial results:
A Phase 2, Randomized, Double-blind, Placebo-controlled Study of the Efficacy and Safety of VX-864 in PiZZ Subjects

Summary

EudraCT number	2019-004881-16
Trial protocol	IE DE SE GB
Global end of trial date	04 May 2021

Results information

Result version number	v1 (current)
This version publication date	19 May 2022
First version publication date	19 May 2022

Trial information

Trial identification

Sponsor protocol code	VX19-864-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04474197
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 May 2021
Global end of trial reached?	Yes
Global end of trial date	04 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy, safety and pharmacokinetics (PK) of VX-864 in PiZZ subjects.

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	24 July 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 22
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Ireland: 5
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Sweden: 3
Worldwide total number of subjects	44
EEA total number of subjects	11

Notes:

Subjects enrolled per age group

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

From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was conducted in subjects 18 through 80 of years of age, inclusive with the PiZZ genotype.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received placebo matched to VX-864 in the treatment period for 28 days.

Arm type	Placebo
Investigational medicinal product name	Placebo (matched to VX-864)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to VX-864 in the morning and evening.

Arm title	VX-864 100 mg

Arm description:

Subjects received VX-864 100 milligrams (mg) every 12 hours (q12h) in the treatment period for 28 days.

Arm type	Experimental
Investigational medicinal product name	VX-864
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-864 100 mg in the morning and evening.

Arm title	VX-864 300 mg

Arm description:

Subjects received VX-864 300 mg q12h in the treatment period for 28 days.

Arm type	Experimental
Investigational medicinal product name	VX-864
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-864 300 mg in the morning and evening.

Arm title	VX-864 500 mg

Arm description:

Subjects received VX-864 500 mg q12h in the treatment period for 28 days.

Arm type	Experimental
Investigational medicinal product name	VX-864
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-864 500 mg in the morning and evening.

Number of subjects in period 1	Placebo	VX-864 100 mg	VX-864 300 mg
Started	7	10	9
Completed	7	9	9
Not completed	0	1	0
Withdrawal of consent (not due to adverse event)	-	1	-

Number of subjects in period 1	VX-864 500 mg
Started	18
Completed	18
Not completed	0
Withdrawal of consent (not due to adverse event)	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to VX-864 in the treatment period for 28 days.	
Reporting group title	VX-864 100 mg
Reporting group description:	
Subjects received VX-864 100 milligrams (mg) every 12 hours (q12h) in the treatment period for 28 days.	
Reporting group title	VX-864 300 mg
Reporting group description:	
Subjects received VX-864 300 mg q12h in the treatment period for 28 days.	
Reporting group title	VX-864 500 mg
Reporting group description:	
Subjects received VX-864 500 mg q12h in the treatment period for 28 days.	

Reporting group values	Placebo	VX-864 100 mg	VX-864 300 mg
Number of subjects	7	10	9
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	63.4	55.1	53.2
standard deviation	± 10.5	± 5.3	± 16.2
Gender categorical Units: Subjects			
Female	5	6	6
Male	2	4	3
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	7	8	8
Unknown or Not Reported	0	2	1
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	7	10	9
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Plasma Functional Alpha-1 Antitrypsin (AAT) Levels Units: micromole per liter			
arithmetic mean	4.7	4.0	3.8
standard deviation	± 1.3	± 0.7	± 0.9

Reporting group values	VX-864 500 mg	Total	
Number of subjects	18	44	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	57.4		
standard deviation	± 9.9	-	
Gender categorical Units: Subjects			
Female	14	31	
Male	4	13	
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	15	38	
Unknown or Not Reported	2	5	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	18	44	
More than one race	0	0	
Unknown or Not Reported	0	0	
Plasma Functional Alpha-1 Antitrypsin (AAT) Levels Units: micromole per liter			
arithmetic mean	4.1		
standard deviation	± 0.6	-	

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to VX-864 in the treatment period for 28 days.	
Reporting group title	VX-864 100 mg
Reporting group description:	
Subjects received VX-864 100 milligrams (mg) every 12 hours (q12h) in the treatment period for 28 days.	
Reporting group title	VX-864 300 mg
Reporting group description:	
Subjects received VX-864 300 mg q12h in the treatment period for 28 days.	
Reporting group title	VX-864 500 mg
Reporting group description:	
Subjects received VX-864 500 mg q12h in the treatment period for 28 days.	

Primary: Change in Plasma Functional Alpha-1 Antitrypsin (AAT) Levels	
End point title	Change in Plasma Functional Alpha-1 Antitrypsin (AAT) Levels
End point description:	
Full analysis set (FAS) included all randomized subjects who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
From Baseline at Day 28	

End point values	Placebo	VX-864 100 mg	VX-864 300 mg	VX-864 500 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	10	9	18
Units: micromole per liter				
least squares mean (standard error)	-0.1 (± 0.3)	2.3 (± 0.3)	2.3 (± 0.2)	2.1 (± 0.2)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v VX-864 100 mg
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed-effects Model for Repeated Measure
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	2.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	3.1

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v VX-864 300 mg
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed-effects Model for Repeated Measure
Parameter estimate	LS Mean Difference
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	3.1

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v VX-864 500 mg
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed-effects Model for Repeated Measure
Parameter estimate	LS Mean Difference
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	2.9

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

End point title	Safety and Tolerability as Assessed by Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)[1]

End point description:

Safety set included all subjects who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Day 1 up to Week 8

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were planned. No statistical comparisons were planned for this endpoint.

End point values	Placebo	VX-864 100 mg	VX-864 300 mg	VX-864 500 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	10	9	18
Units: subjects				
Subjects with AEs	4	7	7	17
Subjects with SAEs	0	0	0	2

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Plasma Antigenic AAT Levels

End point title	Change in Plasma Antigenic AAT Levels
End point description: FAS.	
End point type	Secondary
End point timeframe: From Baseline at Day 28	

End point values	Placebo	VX-864 100 mg	VX-864 300 mg	VX-864 500 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	10	9	18
Units: micromole per liter				
least squares mean (standard error)	-0.1 (± 0.4)	3.4 (± 0.4)	2.9 (± 0.4)	2.6 (± 0.2)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v VX-864 100 mg

Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed-effects Model for Repeated Measure
Parameter estimate	LS Mean Difference
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4
upper limit	4.6

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v VX-864 300 mg
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed-effects Model for Repeated Measure
Parameter estimate	LS Mean Difference
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.9
upper limit	4

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v VX-864 500 mg
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed-effects Model for Repeated Measure
Parameter estimate	LS Mean Difference
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	3.7

Secondary: Observed Pre-dose Plasma Concentration (Ctrough) of VX-864

End point title	Observed Pre-dose Plasma Concentration (Ctrough) of VX-

End point description:

PK set included subjects who received at least 1 dose of study drug. Here "n" signifies those subjects who were evaluable for this endpoint at specified time points for each reporting group respectively.

End point type	Secondary

End point timeframe:

Pre-dose at Day 7, Day 14, Day 21 and 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: Placebo group was not applicable for this endpoint.

End point values	VX-864 100 mg	VX-864 300 mg	VX-864 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	18	
Units: microgram per milliliter				
arithmetic mean (standard deviation)				
Day 7 (n=9,8,16)	1.13 (± 0.743)	1.62 (± 0.665)	2.74 (± 2.89)	
Day 14 (n=8,9,18)	0.852 (± 0.340)	1.47 (± 0.847)	4.35 (± 5.36)	
Day 21 (n=8,8,18)	0.868 (± 0.503)	1.21 (± 0.770)	1.79 (± 0.922)	
Day 28 (n=9,8,18)	0.797 (± 0.327)	1.29 (± 0.646)	2.55 (± 2.40)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Day 1 up to Week 8	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0
Reporting groups	
Reporting group title	Placebo
Reporting group description: Subjects received placebo matched to VX-864 in the treatment period for 28 days.	
Reporting group title	VX-864 100 mg
Reporting group description: Subjects received VX-864 100 mg q12h in the treatment period for 28 days.	
Reporting group title	VX-864 300 mg
Reporting group description: Subjects received VX-864 300 mg q12h in the treatment period for 28 days.	
Reporting group title	VX-864 500 mg
Reporting group description: Subjects received VX-864 500 mg q12h in the treatment period for 28 days.	

Serious adverse events	Placebo	VX-864 100 mg	VX-864 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (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			
Pneumothorax spontaneous			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (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	VX-864 500 mg		

Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 18 (11.11%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumothorax spontaneous			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	VX-864 100 mg	VX-864 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 7 (57.14%)	7 / 10 (70.00%)	7 / 9 (77.78%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 7 (0.00%)	2 / 10 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Feeling abnormal			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Feeling cold			

subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 10 (20.00%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Reproductive system and breast disorders			
Heavy menstrual bleeding			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Vaginal haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 7 (0.00%)	2 / 10 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Respiration abnormal			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			

subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Sneezing			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Sputum increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Tachypnoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Poor quality sleep			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood cholesterol increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Blood potassium decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood pressure diastolic increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Haemoglobin increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Low density lipoprotein increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	3
Oxygen saturation decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Protein total decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Red blood cell count increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Back injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Muscle strain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Post procedural contusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Post procedural haemorrhage			

subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vaccination complication			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	1 / 7 (14.29%)	1 / 10 (10.00%)	2 / 9 (22.22%)
occurrences (all)	1	1	4
Dysaesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	2 / 9 (22.22%)
occurrences (all)	0	1	2
Tremor			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye allergy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Macular degeneration			

subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Abdominal pain upper			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Flatulence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gingival pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	4
Toothache			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Photosensitivity reaction			

subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Polymorphic light eruption			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Infective exacerbation of bronchiectasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Skin infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			

subjects affected / exposed	1 / 7 (14.29%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	2	1	0

Non-serious adverse events	VX-864 500 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 18 (94.44%)		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	3		
Feeling abnormal			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Feeling cold			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Heavy menstrual bleeding			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Vaginal haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal			

disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Respiration abnormal			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Sinus congestion			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Sneezing			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Sputum increased			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Tachypnoea			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Poor quality sleep			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Blood bicarbonate decreased			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Blood cholesterol increased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Blood potassium decreased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Blood pressure diastolic increased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Blood triglycerides increased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Haemoglobin increased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Low density lipoprotein increased			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Oxygen saturation decreased			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Protein total decreased			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Red blood cell count increased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
White blood cells urine positive			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Back injury			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Muscle strain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Post procedural contusion			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Post procedural haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Skin laceration			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Vaccination complication			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Dizziness			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Dysaesthesia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	4		
Tremor			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Eye disorders			
Eye allergy			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Macular degeneration			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Diarrhoea			

subjects affected / exposed	4 / 18 (22.22%)		
occurrences (all)	4		
Flatulence			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Gingival pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	4 / 18 (22.22%)		
occurrences (all)	4		
Toothache			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Photosensitivity reaction			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Polymorphic light eruption			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Muscle spasms			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Infections and infestations			
Infective exacerbation of bronchiectasis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Skin infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 January 2021	Amended to clarify that the monitoring procedures, consent and re-consent may be conducted through on-site or remote visits due to extenuating circumstances (e.g., events related to COVID-19). Exclusion criteria were updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported