Clinical trial results:
A Phase II, Randomized, Double-Blind, Placebo-Controlled, Dose Finding and Efficacy Study of VPD-737 in the Treatment of Subjects with Chronic Pruritus

Summary

EudraCT number	2014-001581-10
Trial protocol	IE
Global end of trial date	02 December 2014

Results information

Result version number	v1 (current)
This version publication date	29 May 2022
First version publication date	29 May 2022

Trial information

Trial identification

Sponsor protocol code	TCP-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01951274
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Tigercat Pharma, Inc.
Sponsor organisation address	4085 Campbell Avenue, Menlo Park, CA, United States, 94025
Public contact	Nooshin Azimi, PhD, Tigercat Pharma, Inc., +1 6507400343, nooshin@pvd.net
Scientific contact	Nooshin Azimi, PhD, Tigercat Pharma, Inc., +1 6507400343, nooshin@pvd.net

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	02 December 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to compare the efficacy and safety of VPD-737 tablets (at concentrations of 0.25 mg, 1 mg, or 5 mg) and placebo given once daily for 6 weeks for the treatment of chronic pruritus.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki (and amendments), and in compliance with the approved protocol, the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2013
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: 257
Worldwide total number of subjects	257
EEA total number of subjects	0

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)	252
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in United States between 01 October 2013 and 02 December 2014.

Pre-assignment

Screening details:

The Screening period was from Day -44 to Day -1. Informed Consent Forms (ICF) were signed by the participants prior to screening procedures. All the study assessments were performed as per the Schedule of Assessments.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received oral Placebo tablet once daily for 6 weeks.

Arm type	Placebo
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:

Participants received oral Placebo tablet once daily for 6 weeks.

Arm title	VPD-737 0.25mg

Arm description:

Participants received oral VPD-737 0.25 mg tablet once daily for 6 weeks.

Arm type	Experimental
Investigational medicinal product name	Serlopitant
Investigational medicinal product code	VPD-737
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received one tablet per day taken orally at bedtime for 6 weeks.

Arm title	VPD-737 1mg

Arm description:

Participants received oral VPD-737 1 mg tablet once daily for 6 weeks.

Arm type	Experimental

Investigational medicinal product name	Serlopitant
Investigational medicinal product code	VPD-737
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received one tablet per day taken orally at bedtime for 6 weeks.

Arm title	VPD-737 5mg

Arm description:

Participants received oral VPD-737 5 mg tablet once daily for 6 weeks.

Arm type	Experimental
Investigational medicinal product name	Serlopitant
Investigational medicinal product code	VPD-737
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received one tablet per day taken orally at bedtime for 6 weeks.

Number of subjects in period 1	Placebo	VPD-737 0.25mg	VPD-737 1mg
Started	64	64	65
Completed	55	57	56
Not completed	9	7	9
Non-compliance with study	1	-	-
Adverse event, non-fatal	3	-	1
Other	1	1	1
Lost to follow-up	1	2	1
Withdrawal by subject	3	4	5
Protocol deviation	-	-	1

Number of subjects in period 1	VPD-737 5mg
Started	64
Completed	54
Not completed	10
Non-compliance with study	-
Adverse event, non-fatal	1
Other	-
Lost to follow-up	2
Withdrawal by subject	7
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received oral Placebo tablet once daily for 6 weeks.	
Reporting group title	VPD-737 0.25mg
Reporting group description:	
Participants received oral VPD-737 0.25 mg tablet once daily for 6 weeks.	
Reporting group title	VPD-737 1mg
Reporting group description:	
Participants received oral VPD-737 1 mg tablet once daily for 6 weeks.	
Reporting group title	VPD-737 5mg
Reporting group description:	
Participants received oral VPD-737 5 mg tablet once daily for 6 weeks.	

Reporting group values	Placebo	VPD-737 0.25mg	VPD-737 1mg
Number of subjects	64	64	65
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	64	64	63
From 65-84 years	0	0	2
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	44.48	45.09	42.49
standard deviation	± 13.23	± 14.01	± 14.08
Gender categorical Units: Subjects			
Female	39	40	38
Male	25	24	27
Race Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	5	2	2
Black or African American	14	16	21
Other	2	2	3
White	43	43	38
Ethnicity Units: Subjects			
Hispanic or Latino	12	18	17

Not Hispanic or Latino	52	46	48
Atopic Diathesis Units: Subjects			
No	42	40	37
Yes	22	24	28

Reporting group values	VPD-737 5mg	Total	
Number of subjects	64	257	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	61	252	
From 65-84 years	3	5	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	42.94		
standard deviation	± 13.96	-	
Gender categorical Units: Subjects			
Female	39	156	
Male	25	101	
Race Units: Subjects			
American Indian or Alaska Native	0	2	
Asian	1	10	
Black or African American	19	70	
Other	1	8	
White	43	167	
Ethnicity Units: Subjects			
Hispanic or Latino	11	58	
Not Hispanic or Latino	53	199	
Atopic Diathesis Units: Subjects			
No	37	156	
Yes	27	101	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received oral Placebo tablet once daily for 6 weeks.	
Reporting group title	VPD-737 0.25mg
Reporting group description:	
Participants received oral VPD-737 0.25 mg tablet once daily for 6 weeks.	
Reporting group title	VPD-737 1mg
Reporting group description:	
Participants received oral VPD-737 1 mg tablet once daily for 6 weeks.	
Reporting group title	VPD-737 5mg
Reporting group description:	
Participants received oral VPD-737 5 mg tablet once daily for 6 weeks.	

Primary: Percent change from baseline in visual analog scale (VAS) pruritus score

End point title	Percent change from baseline in visual analog scale (VAS) pruritus score
End point description:	
Change from Baseline in VAS pruritus score was measured using a 10- point VAS scale (assessed using participants self-ratings of itch severity). The VAS ranged from no pruritus to worst pruritus on a continuous scale. The intent-to-treat (ITT) population included all randomized participants.	
End point type	Primary
End point timeframe:	
At Week 6	

End point values	Placebo	VPD-737 0.25mg	VPD-737 1mg	VPD-737 5mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	54	55	53
Units: Change in Score				
least squares mean (standard error)				
Week 6	-28.3 (± 4.1)	-34.1 (± 4.1)	-41.4 (± 4.0)	-42.5 (± 4.1)

Statistical analyses

Statistical analysis title	Pairwise comparison of VPD-737 0.25mg and Placebo
Comparison groups	Placebo v VPD-737 0.25mg

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.309
Method	Linear Mixed Effect Model
Parameter estimate	Least square mean difference
Point estimate	5.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	17.1

Statistical analysis title	Pairwise comparison of VPD-737 1mg and Placebo
Comparison groups	Placebo v VPD-737 1mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.022
Method	Linear Mixed Effect Model
Parameter estimate	Least square mean difference
Point estimate	13.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.9
upper limit	24.4

Statistical analysis title	Pairwise comparison of VPD-737 5mg and Placebo
Comparison groups	Placebo v VPD-737 5mg
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.013
Method	Linear Mixed Effect Model
Parameter estimate	Least square mean difference
Point estimate	14.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	3
upper limit	25.5

Secondary: Percent change from baseline in numeric rating scale (NRS) pruritus

score	
End point title	Percent change from baseline in numeric rating scale (NRS) pruritus score

End point description:

Change from Baseline in NRS pruritus score was measured using a 10- point NRS scale (assessed using participants self-ratings of itch severity). The NRS ranged from no pruritus to worst pruritus on a numerical scale from zero to ten. The intent-to-treat (ITT) population included all randomized participants.

End point type	Secondary

End point timeframe:

At Week 6

End point values	Placebo	VPD-737 0.25mg	VPD-737 1mg	VPD-737 5mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	52	55	52
Units: Change in scores				
least squares mean (standard error)				
Week 6	-28.7 (± 3.5)	-35.8 (± 3.5)	-39.4 (± 3.5)	-39.0 (± 3.5)

Statistical analyses

Statistical analysis title	Pairwise comparison of VPD-737 0.25mg and Placebo
Comparison groups	Placebo v VPD-737 0.25mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.153
Method	Linear Mixed Effect Model
Parameter estimate	Least square mean difference
Point estimate	7.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	16.9

Statistical analysis title	Pairwise comparison of VPD-737 1mg and Placebo
Comparison groups	Placebo v VPD-737 1mg

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.031
Method	Linear Mixed Effect Model
Parameter estimate	Least square mean difference
Point estimate	10.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	20.4

Statistical analysis title	Pairwise comparison of VPD-737 5mg and Placebo
Comparison groups	Placebo v VPD-737 5mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.038
Method	Linear Mixed Effect Model
Parameter estimate	Least square mean difference
Point estimate	10.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	20.1

Secondary: Dermatology Life Quality Index (DLQI) total score

End point title	Dermatology Life Quality Index (DLQI) total score

End point description:

DLQI is a dermatology specific quality of life (QoL) instrument designed to assess the impact of the skin disease on a subject's QoL. It is a ten item questionnaire that assesses overall QoL and six aspects that may affect QoL (symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment). Scores range from 0 to 30 with higher scores indicating poor QoL. The intent-to-treat (ITT) population included all randomized participants.

End point type	Secondary

End point timeframe:

At Week 6

End point values	Placebo	VPD-737 0.25mg	VPD-737 1mg	VPD-737 5mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	58	57	55
Units: Score				
least squares mean (standard error)				
Week 6	20.6 (± 2.7)	14.9 (± 2.7)	13.7 (± 2.7)	16.4 (± 2.7)

Statistical analyses

Statistical analysis title	Pairwise comparison of VPD-737 0.25mg and Placebo
Comparison groups	VPD-737 0.25mg v Placebo
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.138
Method	Linear Mixed Effect Model
Parameter estimate	Least square mean difference
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	13.1

Statistical analysis title	Pairwise comparison of VPD-737 1mg and Placebo
Comparison groups	Placebo v VPD-737 1mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.073
Method	Linear Mixed Effect Model
Parameter estimate	Least square mean difference
Point estimate	6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	14.3

Statistical analysis title	Pairwise comparison of VPD-737 5mg and Placebo
Comparison groups	Placebo v VPD-737 5mg

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.277
Method	Linear Mixed Effect Model
Parameter estimate	Linear Mixed Effect Model
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	11.7

Secondary: Subject Global Assessment (SGA)

End point title	Subject Global Assessment (SGA)

End point description:

For SGA, the subjects were asked "In the past 24 hours, please describe your itching," and their responses, rated as 'none', 'mild', 'moderate', or 'severe' were summarized descriptively. The intent-to-treat (ITT) population included all randomized participants.

End point type	Secondary

End point timeframe:

At Week 6

End point values	Placebo	VPD-737 0.25mg	VPD-737 1mg	VPD-737 5mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	58	57	55
Units: Number of Participants				
None	6	13	7	13
Mild Itching	22	21	34	22
Moderate Itching	17	18	11	10
Severe Itching	11	6	5	10

Statistical analyses

Statistical analysis title	Pairwise comparison of VPD-737 0.25mg and Placebo
Comparison groups	Placebo v VPD-737 0.25mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.258
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Pairwise comparison of VPD-737 1mg and Placebo
Comparison groups	Placebo v VPD-737 1mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.106
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Pairwise comparison of VPD-737 5mg and Placebo
Comparison groups	Placebo v VPD-737 5mg
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.222
Method	Cochran-Mantel-Haenszel

Secondary: Physician Global Assessment	
End point title	Physician Global Assessment
End point description:	
Physicians Global Assessment asks physicians to rate change in lesions (if any) from plus 5 (“markedly improved”) to minus 5 (“markedly worse”). The intent-to-treat (ITT) population included all randomized participants.	
End point type	Secondary
End point timeframe:	
At Week 6	

End point values	Placebo	VPD-737 0.25mg	VPD-737 1mg	VPD-737 5mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	58	57	55
Units: Number of participants				
+5 markedly improved	2	7	3	3
+4 largely improved	2	3	7	3
+3 moderately to largely improved	3	2	3	2
+2 moderately improved	9	8	8	8
+1 mildly improved	9	5	7	6
Baseline (no change)	23	25	26	28
-1 mildly worse	5	6	1	3
-2 moderately worse	3	0	2	1
-3 moderately to largely worse	0	2	0	1
-4 largely worse	0	0	0	0

-5 markedly worse	0	0	0	0

Statistical analyses

Statistical analysis title	Pairwise comparison of VPD-737 0.25mg and Placebo
Comparison groups	Placebo v VPD-737 0.25mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.307
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Pairwise comparison of VPD-737 1mg and Placebo
Comparison groups	Placebo v VPD-737 1mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.508
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Pairwise comparison of VPD-737 5mg and Placebo
Comparison groups	Placebo v VPD-737 5mg
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.838
Method	Cochran-Mantel-Haenszel

Secondary: Pittsburgh Sleep Symptom Questionnaire - Insomnia (PSSQ-I)

End point title	Pittsburgh Sleep Symptom Questionnaire - Insomnia (PSSQ-I)

End point description:

The PSSQ-I has 13 patient-rated questions, with three sub-scales, a sleep symptom criteria, duration criteria, and daytime impairment criteria. The instrument scoring produces a binary (1/0) outcome for each domain. The overall scoring of the domains results in a "total" score with values "insomnia disorder" or "No insomnia disorder". The intent-to-treat (ITT) population included all randomized participants.

End point type	Secondary

End point timeframe:

At Week 6

End point values	Placebo	VPD-737 0.25mg	VPD-737 1mg	VPD-737 5mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	58	57	55
Units: Number of participants				
Insomnia disorder	16	10	6	8
No insomnia disorder	40	48	51	47

Statistical analyses

Statistical analysis title	Pairwise comparison of VPD-737 0.25mg and Placebo
Comparison groups	Placebo v VPD-737 0.25mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.151
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Pairwise comparison of VPD-737 1mg and Placebo
Comparison groups	Placebo v VPD-737 1mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.016
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Pairwise comparison of VPD-737 5mg and Placebo
Comparison groups	Placebo v VPD-737 5mg
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.074
Method	Cochran-Mantel-Haenszel

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Baseline (Day 1) up to early termination or follow-up visit (Week 10)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received oral Placebo tablet once daily for 6 weeks.	
Reporting group title	VPD-737 0.25mg
Reporting group description:	
Participants received oral VPD-737 0.25 mg tablet once daily for 6 weeks.	
Reporting group title	VPD-737 1mg
Reporting group description:	
Participants received oral VPD-737 1 mg tablet once daily for 6 weeks.	
Reporting group title	VPD-737 5mg
Reporting group description:	
Participants received oral VPD-737 5 mg tablet once daily for 6 weeks.	

Serious adverse events	Placebo	VPD-737 0.25mg	VPD-737 1mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
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	VPD-737 5mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 64 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Pregnancy, puerperium and perinatal conditions			

Abortion spontaneous			
subjects affected / exposed	0 / 64 (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	Placebo	VPD-737 0.25mg	VPD-737 1mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 63 (25.40%)	21 / 64 (32.81%)	23 / 65 (35.38%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	1	0	0
Oedema Peripheral			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Allergy To Chemicals			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	1	0	1
Nasal Congestion			
subjects affected / exposed	1 / 63 (1.59%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	1	1	0
Pulmonary Congestion			
subjects affected / exposed	1 / 63 (1.59%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	1	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Sinus Congestion			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	1	0	0
Asthma			
subjects affected / exposed	2 / 63 (3.17%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal Pain			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Panic Attack			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	1	0	1
Blood Triglycerides Increased			

subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Weight Increased			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
White Blood Cell Count Decreased			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Excoriation			
subjects affected / exposed	1 / 63 (1.59%)	1 / 64 (1.56%)	1 / 65 (1.54%)
occurrences (all)	1	1	3
Arthropod Bite			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	1 / 65 (1.54%)
occurrences (all)	0	1	1
Contusion			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Rib Fracture			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Supraventricular Extrasystoles			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Somnolence			
subjects affected / exposed	1 / 63 (1.59%)	1 / 64 (1.56%)	3 / 65 (4.62%)
occurrences (all)	1	1	3
Headache			
subjects affected / exposed	4 / 63 (6.35%)	1 / 64 (1.56%)	3 / 65 (4.62%)
occurrences (all)	4	2	3
Dizziness			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Neuropathy Peripheral			

subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Sedation			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Lymphatic Disorder			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Eye Haemorrhage			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Eye Irritation			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	4 / 65 (6.15%)
occurrences (all)	1	0	4
Dry mouth			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	2 / 65 (3.08%)
occurrences (all)	0	0	2
Nausea			

subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	2 / 65 (3.08%)
occurrences (all)	1	0	2
Vomiting			
subjects affected / exposed	1 / 63 (1.59%)	1 / 64 (1.56%)	1 / 65 (1.54%)
occurrences (all)	1	1	1
Abdominal Discomfort			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	1	0	1
Abdominal Distension			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal Pain			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal sounds abnormal			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 63 (1.59%)	2 / 64 (3.13%)	2 / 65 (3.08%)
occurrences (all)	1	2	2
Eczema			
subjects affected / exposed	1 / 63 (1.59%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	1	1	0
Perivascular dermatitis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0

Post Inflammatory Pigmentation Chang			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 63 (1.59%)	2 / 64 (3.13%)	0 / 65 (0.00%)
occurrences (all)	1	3	0
Musculoskeletal Pain			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	2 / 65 (3.08%)
occurrences (all)	0	0	2
Costochondritis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Muscle Spasms			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Neck Pain			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Pain In Extremity			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	2 / 63 (3.17%)	2 / 64 (3.13%)	3 / 65 (4.62%)
occurrences (all)	2	2	3
Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 63 (3.17%)	3 / 64 (4.69%)	0 / 65 (0.00%)
occurrences (all)	2	3	0
Bronchitis			
subjects affected / exposed	1 / 63 (1.59%)	1 / 64 (1.56%)	1 / 65 (1.54%)
occurrences (all)	1	1	1
Urinary tract infection			
subjects affected / exposed	2 / 63 (3.17%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	2	0	0
Candidiasis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	2	0
Gastroenteritis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	1	0	1
Pharyngitis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Staphylococcal Bacteraemia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Tooth Abscess			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Tooth Infection			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Vaginitis Bacterial			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Vulvovaginal mycotic infection			

subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Gout			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	0 / 65 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	VPD-737 5mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 64 (37.50%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Oedema Peripheral			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Allergy To Chemicals			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		

Hypersensitivity			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Nasal Congestion			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Pulmonary Congestion			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Sinus Congestion			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Asthma			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Oropharyngeal Pain			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Panic Attack			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		

Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Blood Triglycerides Increased			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Weight Increased			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
White Blood Cell Count Decreased			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Excoriation			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Arthropod Bite			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Rib Fracture			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Cardiac disorders			
Supraventricular Extrasystoles			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Somnolence			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		

Dizziness subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1		
Neuropathy Peripheral subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1		
Sedation subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0		
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1		
Lymphatic Disorder subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0		
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1		
Eye Haemorrhage subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0		
Eye Irritation subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	2 / 64 (3.13%) 4		

Dry mouth			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Abdominal Discomfort			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Abdominal Distension			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Abdominal Pain			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Gastrointestinal Pain			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	2		
Gastrointestinal sounds abnormal			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Haematochezia			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Eczema			

subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Perivascular dermatitis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Post Inflammatory Pigmentation Chang			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Musculoskeletal Pain			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Costochondritis			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Muscle Spasms			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Neck Pain			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Osteoarthritis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Pain In Extremity			

subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
Candidiasis			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Gastroenteritis viral			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Staphylococcal Bacteraemia			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Tooth Abscess			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Tooth Infection			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		

Vaginitis Bacterial subjects affected / exposed occurrences (all) Vulvovaginal mycotic infection subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0 0 / 64 (0.00%) 0		
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all) Hypocalcaemia subjects affected / exposed occurrences (all) Gout subjects affected / exposed occurrences (all)	 1 / 64 (1.56%) 1 0 / 64 (0.00%) 0 0 / 64 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported