

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

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 0 / 65 (0.00%) 0 |
| Sedation subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 64 (1.56%) 1 | 0 / 65 (0.00%) 0 |
| Hypoaesthesia subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 64 (0.00%) 0 | 0 / 65 (0.00%) 0 |
| Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 0 / 65 (0.00%) 0 |
| Lymphatic Disorder subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 1 / 65 (1.54%) 1 |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 1 / 65 (1.54%) 1 |
| Eye disorders Conjunctivitis subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 64 (1.56%) 1 | 0 / 65 (0.00%) 0 |
| Eye Haemorrhage subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 64 (1.56%) 1 | 0 / 65 (0.00%) 0 |
| Eye Irritation subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 1 / 65 (1.54%) 1 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 64 (0.00%) 0 | 4 / 65 (6.15%) 4 |
| Dry mouth subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 2 / 65 (3.08%) 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 occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 64 (1.56%) 1 | 0 / 65 (0.00%) 0 |
| Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 0 / 65 (0.00%) 0 |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 64 (1.56%) 1 | 0 / 65 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 2 / 64 (3.13%) 3 | 0 / 65 (0.00%) 0 |
| Musculoskeletal Pain subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 2 / 65 (3.08%) 2 |
| Costochondritis subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 1 / 65 (1.54%) 1 |
| Muscle Spasms subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 0 / 65 (0.00%) 0 |
| Neck Pain subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 1 / 65 (1.54%) 1 |
| Osteoarthritis subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 0 / 65 (0.00%) 0 |
| Pain In Extremity subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 1 / 65 (1.54%) 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 occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 1 / 65 (1.54%) 1 |
| Metabolism and nutrition disorders | | | |
| Decreased Appetite | | | |
| subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 64 (0.00%) 0 | 0 / 65 (0.00%) 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 64 (1.56%) 1 | 0 / 65 (0.00%) 0 |
| Gout | | | |
| subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 64 (0.00%) 0 | 0 / 65 (0.00%) 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 occurrences (all) | 1 / 64 (1.56%) 1 | | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | | |
| Fatigue | | | |
| subjects affected / exposed occurrences (all) | 1 / 64 (1.56%) 1 | | |
| Oedema Peripheral | | | |
| subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | | |
| Pyrexia | | | |
| subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | | |
| Immune system disorders | | | |
| Allergy To Chemicals | | | |
| subjects affected / exposed occurrences (all) | 1 / 64 (1.56%) 1 | | |

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

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

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

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