



Clinical trial results:

A Phase 2, Randomized, Double-blind, Placebo-controlled, 6-Week, Parallel-design Study of the Efficacy and Safety of VX-150 in Treating Subjects With Pain Caused by Small Fiber Neuropathy

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2017-001042-10 |
| Trial protocol | DE NL IT |
| Global end of trial date | 08 November 2018 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 13 December 2021 |
| First version publication date | 27 November 2019 |
| Version creation reason | <ul style="list-style-type: none">• New data added to full data set Secondary endpoints data will be added |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | VX16-150-102 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03304522 |
| 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 | 05 December 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 12 October 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 November 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of VX-150 for the treatment of pain caused by small fiber neuropathy.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 20 September 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Italy: 10 |
| Country: Number of subjects enrolled | Netherlands: 6 |
| Country: Number of subjects enrolled | United States: 71 |
| Country: Number of subjects enrolled | Germany: 2 |
| Worldwide total number of subjects | 89 |
| EEA total number of subjects | 18 |

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) | 66 |
| From 65 to 84 years | 23 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 89 subjects were enrolled and randomized in the study.

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 | VX-150 |

Arm description:

Subjects received VX-150 once daily for 6 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | VX-150 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received VX-150 1250 milligrams (mg) once daily.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Subjects received placebo matched to VX-150 once daily for 6 weeks.

| | |
|--|-----------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo (matched to VX-150) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received placebo matched to VX-150 once daily.

| Number of subjects in period 1 | VX-150 | Placebo |
|--------------------------------|--------|---------|
| Started | 46 | 43 |
| Completed | 45 | 35 |
| Not completed | 1 | 8 |
| Other | - | 1 |

| | | |
|---|---|---|
| Withdrawal of consent (for other reason) | - | 2 |
| Adverse event | - | 4 |
| Withdrawal of consent (due to lack of efficacy) | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|---|---------|
| Reporting group title | VX-150 |
| Reporting group description: | |
| Subjects received VX-150 once daily for 6 weeks. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received placebo matched to VX-150 once daily for 6 weeks. | |

| Reporting group values | VX-150 | Placebo | Total |
|--|---------|---------|-------|
| Number of subjects | 46 | 43 | 89 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years | | | |
| arithmetic mean | 55.1 | 58.1 | |
| standard deviation | ± 12.34 | ± 11.86 | - |
| Gender categorical Units: Subjects | | | |
| Female | 22 | 21 | 43 |
| Male | 24 | 22 | 46 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 3 | 5 | 8 |
| Not Hispanic or Latino | 43 | 38 | 81 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 1 | 1 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 6 | 4 | 10 |
| White | 39 | 34 | 73 |
| More than one race | 1 | 2 | 3 |
| Unknown or Not Reported | 0 | 2 | 2 |
| Pain Intensity at Baseline on 11-point Numeric Rating Scale (NRS) | | | |
| Pain intensity was evaluated using the 11-point NRS (where 0 signified no pain and 10 signified worst imaginable pain). Higher score indicates greater level of pain. Baseline score was average of daily pain scores from Day -7 to Day -1. | | | |
| Units: units on a scale | | | |
| arithmetic mean | 6.433 | 5.990 | |
| standard deviation | ± 1.440 | ± 1.413 | - |

End points

End points reporting groups

| | |
|---|---------|
| Reporting group title | VX-150 |
| Reporting group description: | |
| Subjects received VX-150 once daily for 6 weeks. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received placebo matched to VX-150 once daily for 6 weeks. | |

Primary: Change in Weekly Average of Daily Pain Intensity on the 11 Point NRS

| | |
|---|--|
| End point title | Change in Weekly Average of Daily Pain Intensity on the 11 Point NRS |
| End point description: | |
| Pain intensity was evaluated using the 11-point NRS (where 0 signified no pain and 10 signified worst imaginable pain) during the last 24 hours on the NRS each evening. Higher score indicates greater level of pain. 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 Week 6 | |

| End point values | VX-150 | Placebo | | |
|-------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 46 | 43 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | -2.018 (\pm 0.274) | -0.933 (\pm 0.287) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical Analysis |
| Comparison groups | VX-150 v Placebo |
| Number of subjects included in analysis | 89 |
| 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 | -1.085 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.876 |
| upper limit | -0.293 |

Secondary: Percentage of Subjects With Greater Than or Equal to (\geq) 30 Percent (%) Reduction in the Weekly Average of Daily Pain Intensity on the 11-Point NRS

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Greater Than or Equal to (\geq) 30 Percent (%) Reduction in the Weekly Average of Daily Pain Intensity on the 11-Point NRS |
|-----------------|--|

End point description:

Pain intensity was evaluated using the 11-point NRS (where 0 signified no pain and 10 signified worst imaginable pain) during the last 24 hours on the NRS each evening. Higher score indicates greater level of pain. Percentage of subjects \geq 30% reduction in the weekly average of daily pain intensity on the 11-Point NRS were reported. FAS. Here, 'number of subjects analysed' signifies subjects who were evaluable for this endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline at Week 6

| End point values | VX-150 | Placebo | | |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 34 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 45.0 | 26.5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With \geq 50% Reduction in the Weekly Average of Daily Pain Intensity on the 11-Point NRS

| | |
|-----------------|--|
| End point title | Percentage of Subjects With \geq 50% Reduction in the Weekly Average of Daily Pain Intensity on the 11-Point NRS |
|-----------------|--|

End point description:

Pain intensity was evaluated using the 11-point NRS (where 0 signified no pain and 10 signified worst imaginable pain) during the last 24 hours on the NRS each evening. Higher score indicates greater level of pain. Percentage of subjects \geq 50% reduction in the weekly average of daily pain intensity on the 11-Point NRS were reported. FAS. Here, 'number of subjects analysed' signifies subjects who were evaluable for this endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline at Week 6

| End point values | VX-150 | Placebo | | |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 34 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 32.5 | 17.6 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the Daily Sleep Interference Scale (DSIS)

| | |
|--|---|
| End point title | Change in the Daily Sleep Interference Scale (DSIS) |
| End point description: Pain-associated sleep interference was assessed using DSIS, based on an 11-point scale (where 0 signified none: pain does not interfere with sleep and 10 signified severe: pain completely interferes with sleep, unable to sleep). Higher score indicates greater pain associated sleep interference. FAS. | |
| End point type | Secondary |
| End point timeframe: From Baseline at Week 6 | |

| End point values | VX-150 | Placebo | | |
|-------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 46 | 43 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | -1.777 (\pm 0.276) | -0.665 (\pm 0.289) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | VX-150 vs Placebo |
| Comparison groups | VX-150 v Placebo |
| Number of subjects included in analysis | 89 |
| 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 | -1.111 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.911 |
| upper limit | -0.312 |

Secondary: Percentage of Subjects Categorized as Improved on the Patient Global Impression of Change (PGIC) Scale

| | |
|---|--|
| End point title | Percentage of Subjects Categorized as Improved on the Patient Global Impression of Change (PGIC) Scale |
| End point description: | |
| PGIC scale evaluated the change in activity limitations, symptoms, emotions, and overall quality of life (QoL) related to the subjects painful condition on 7-point scale from 1 (improved) to 7 (worse). Subjects were categorized as following: scale from 1 - 2 were categorized as "improved", scale from 3 - 4 as "no change" and scale from 5 - 7 were categorized as "worse". Percentage of subjects categorized as improved on PGIC scale at week 6 were reported for this outcome measure. FAS. Here, 'number of subjects analysed' signifies subjects who were evaluable for this endpoint. | |
| End point type | Secondary |
| End point timeframe: | |
| At Week 6 | |

| End point values | VX-150 | Placebo | | |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 46 | 43 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 39.5 | 13.5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Pain Intensity on the 11-Point NRS

| | |
|---|--|
| End point title | Change in Pain Intensity on the 11-Point NRS |
| End point description: | |
| Pain intensity was evaluated using the 11-point NRS (where 0 signified no pain and 10 signified worst imaginable pain) during the last 24 hours on the NRS each evening. Higher score indicates greater level of pain. FAS. | |
| End point type | Secondary |
| End point timeframe: | |
| From Baseline at Week 6 | |

| End point values | VX-150 | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 46 | 43 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | -18.4 (± 3.1) | -5.0 (± 3.1) | | |

Statistical analyses

| Statistical analysis title | VX-150 vs Placebo |
|---|--|
| Comparison groups | Placebo v VX-150 |
| Number of subjects included in analysis | 89 |
| 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 | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.5 |
| upper limit | 0.3 |

Secondary: Pre-dose Plasma Concentration (Ctough) of VRT-1207355 and the Metabolite VRT-1268114

| | |
|-----------------|---|
| End point title | Pre-dose Plasma Concentration (Ctough) of VRT-1207355 and the Metabolite VRT-1268114 ^[1] |
|-----------------|---|

End point description:

Pharmacokinetic (PK) set included subjects who received at least 1 dose of study drug and for whom the primary PK data was considered to be sufficient and interpretable.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Pre-dose at Day 7

Notes:

[1] - 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: This endpoint was applicable for VX-150 arm. Therefore, data are reported for this arm only.

| End point values | VX-150 | | | |
|--|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: microgram per milliliter (mcg/mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| VRT-1207355 | 3.89 (± 2.73) | | | |
| VRT-1268114 | 1.35 (± 0.752) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Meaningful Findings in Columbia Suicide Severity Rating Scale (C-SSRS) Responses

| | |
|-----------------|---|
| End point title | Number of Subjects With Clinically Meaningful Findings in Columbia Suicide Severity Rating Scale (C-SSRS) Responses |
|-----------------|---|

End point description:

The C-SSRS is an interview-based rating scale was evaluated through a series of questions about suicidal thoughts and behaviors with the possible answers yes or no. Yes represents a worse outcome. Clinically Meaningfulness of C-SSRS responses were judged by investigator based on answers received from subjects. Here "99999" represents that no subject had any clinically meaningful findings in C-SSRS responses. Safety Set included all subjects who have received at least 1 dose of study drug.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 up to Week 10

| End point values | VX-150 | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 46 | 43 | | |
| Units: subjects | 99999 | 99999 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and Tolerability as Assessed by Number of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

| | |
|-----------------|--|
| End point title | Safety and Tolerability as Assessed by Number of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs) |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 up to Week 10

| | | | | |
|-----------------------------|-----------------|-----------------|--|--|
| End point values | VX-150 | Placebo | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 46 | 43 | | |
| Units: subjects | | | | |
| Subjects with AEs | 29 | 24 | | |
| Subjects with SAEs | 0 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Week 10

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received placebo matched to VX-150 once daily for 6 weeks.

| | |
|-----------------------|--------|
| Reporting group title | VX-150 |
|-----------------------|--------|

Reporting group description:

Subjects received VX-150 once daily for 6 weeks.

| Serious adverse events | Placebo | VX-150 | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | 0 / 46 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Tendon rupture | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Placebo | VX-150 | |
|---|-----------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 43 (16.28%) | 16 / 46 (34.78%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | 11 / 46 (23.91%) | |
| occurrences (all) | 6 | 14 | |
| Gastrointestinal disorders | | | |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 3 / 46 (6.52%) | |
| occurrences (all) | 1 | 3 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 3 / 46 (6.52%) | |
| occurrences (all) | 1 | 3 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 3 / 46 (6.52%) | |
| occurrences (all) | 1 | 3 | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 3 / 46 (6.52%) | |
| occurrences (all) | 0 | 3 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 21 April 2017 | Amended inclusion criteria to clarify the study population and Body Mass Index (BMI) |
| 19 May 2017 | Amended the dose limit of VX-150 |
| 11 August 2017 | Allowed inclusion of women of childbearing potential; updated the upper limit of BMI and the visit requirements |
| 13 April 2018 | Updated inclusion and exclusion criteria to facilitate subject recruitment |
| 25 May 2018 | The protocol was amended to enable timely assessment of study data to support continued development |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported