



Clinical trial results:

A Clinical Study of Two Doses of a Selective p38 MAP Kinase Inhibitor, VX-745, to Evaluate the Effects of 12-Week Oral Twice-Daily Dosing on Amyloid Plaque Load as Assessed by Quantitative Dynamic 11C-PiB Positive Emission Tomography (PET) Amyloid Scanning

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2014-002855-25 |
| Trial protocol | NL |
| Global end of trial date | 14 September 2016 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 14 October 2017 |
| First version publication date | 14 October 2017 |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | EIP-VX00-745-302 |
|-----------------------|------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02423122 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | EIP Pharma, LLC |
| Sponsor organisation address | 11 Channing Street, Cambridge, MA, United States, 02138 |
| Public contact | Clinical Trial Operations, Voisin Consulting, clinicaltrialinformation@voisinconsulting.com |
| Scientific contact | Clinical Trial Operations, Voisin Consulting, clinicaltrialinformation@voisinconsulting.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 | 10 March 2017 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 September 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the effects on amyloid plaque burden of administration of VX-745 for 12-weeks, as assessed by Dynamic 11C-PiB PET amyloid scanning in patients with MCI due to AD or mild AD

Protection of trial subjects:

Dosimetry for the neuroimaging studies were prospectively defined and the radiation burden were assured to be within International Committee for Radiation Protection (ICRP) and World Health Organization (WHO) guidelines. Otherwise, the usual and customary safety measures for an early phase 2 clinical trial were conducted, and, as the only invasive assessments were routine blood tests, no specific additional measures to protect trial subjects needed to be taken.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 04 May 2015 |
| 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 | Netherlands: 16 |
| Worldwide total number of subjects | 16 |
| EEA total number of subjects | 16 |

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) | 5 |
| From 65 to 84 years | 11 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|------------------------------|-------------------|
| Number of subjects started | 21 ^[1] |
| Number of subjects completed | 16 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|---------------------------------|
| Reason: Number of subjects | Screen failure: 4 |
| Reason: Number of subjects | Consent withdrawn by subject: 1 |

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The worldwide number corresponds to the number of patients randomized (16) and not to the number of patients screened (21).

Period 1

| | |
|------------------------------|-----------------------------------|
| Period 1 title | Treatment period (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 | VX-745 40 mg |
|------------------|--------------|

Arm description: -

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | VX-745 |
| Investigational medicinal product code | VX-745 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

VX-745 capsule(s) will be administered orally, twice daily with food for 12 weeks. Doses should be taken within 30 minutes following a meal or snack. Doses should be taken approximately 12 hours apart at the same times each day throughout the study.

| | |
|------------------|---------------|
| Arm title | VX-745 125 mg |
|------------------|---------------|

Arm description: -

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | VX-745 |
| Investigational medicinal product code | VX-745 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

VX-745 capsule(s) will be administered orally, twice daily with food for 12 weeks. Doses should be taken within 30 minutes following a meal or snack. Doses should be taken approximately 12 hours apart at the

same times each day throughout the study.

| Number of subjects in period 1 | VX-745 40 mg | VX-745 125 mg |
|---------------------------------------|--------------|---------------|
| Started | 9 | 7 |
| Completed | 8 | 7 |
| Not completed | 1 | 0 |
| PET-scan failure | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | VX-745 40 mg |
|-----------------------|--------------|

| |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

| | |
|-----------------------|---------------|
| Reporting group title | VX-745 125 mg |
|-----------------------|---------------|

| |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

| Reporting group values | VX-745 40 mg | VX-745 125 mg | Total |
|------------------------|--------------|---------------|-------|
| Number of subjects | 9 | 7 | 16 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 2 | 3 | 5 |
| From 65-84 years | 7 | 4 | 11 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 68.33 | 65.29 | |
| full range (min-max) | 60 to 76 | 60 to 75 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 2 | 4 | 6 |
| Male | 7 | 3 | 10 |

End points

End points reporting groups

| | |
|------------------------------|---------------|
| Reporting group title | VX-745 40 mg |
| Reporting group description: | - |
| Reporting group title | VX-745 125 mg |
| Reporting group description: | - |

Primary: PET Metrics - Global (change from baseline)

| | |
|--|---|
| End point title | PET Metrics - Global (change from baseline) |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Dynamic PET scanning with full quantitative analysis will be performed at baseline and at the end of treatment | |

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|--|-----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 7 | | |
| Units: N/A | | | | |
| arithmetic mean (full range (min-max)) | -0.02 (-0.27 to 0.17) | 0.03 (-0.03 to 0.09) | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Wilcoxon Signed Rank Test |
| Comparison groups | VX-745 40 mg v VX-745 125 mg |
| Number of subjects included in analysis | 15 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.619 |
| Method | Wilcoxon (Mann-Whitney) |

Primary: PET Metrics - Global (number of responders)

| | |
|------------------------|--|
| End point title | PET Metrics - Global (number of responders) ^[1] |
| End point description: | |
| End point type | Primary |

End point timeframe:

Dynamic PET scanning with full quantitative analysis will be performed at baseline and at the end of treatment

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics, i.e. number and percentage of responders by dose group were tabulated.

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 7 | | |
| Units: Number of responders | 3 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: WMS - Overall Score (change from baseline)

| | |
|-----------------|--|
| End point title | WMS - Overall Score (change from baseline) |
|-----------------|--|

End point description:

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

End point timeframe:

WMS (immediate and delayed recall) were performed at Days 1, 28 and 84

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|--|-----------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 7 | | |
| Units: N/A | | | | |
| arithmetic mean (full range (min-max)) | 9.5 (-11 to 19) | 37.57 (-7 to 76) | | |

Statistical analyses

| | |
|----------------------------|---------------------------|
| Statistical analysis title | Wilcoxon signed rank test |
|----------------------------|---------------------------|

Statistical analysis description:

P-value is based on Wilcoxon signed rank test that tested for improvement (1-sided)

| | |
|-------------------|------------------------------|
| Comparison groups | VX-745 40 mg v VX-745 125 mg |
|-------------------|------------------------------|

| | |
|---|-------------------------|
| Number of subjects included in analysis | 15 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.002 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: WMS - Overall Composite (number of responders)

| | |
|--|--|
| End point title | WMS - Overall Composite (number of responders) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| WMS (immediate and delayed recall) were performed at Days 1, 28 and 84 | |

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 7 | | |
| Units: Number of responders | 6 | 6 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: MMSE - Composite Score (Day 7)

| | |
|--|--------------------------------|
| End point title | MMSE - Composite Score (Day 7) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| MMSE scores were evaluated during 6 visits, including screening, Days 1, 28, 56, 84 and follow-up visits | |

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|--|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 7 | | |
| Units: N/A | | | | |
| arithmetic mean (full range (min-max)) | 23.88 (18 to 28) | 24.29 (20 to 30) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: VX-745 Plasma Concentration - <3 hours

End point title VX-745 Plasma Concentration - <3 hours

End point description:

End point type Secondary

End point timeframe:

On Days 14, 28, 56 and 84, a 5 mL sample of whole blood will be collected.

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|--|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: ng.hr/mL | | | | |
| arithmetic mean (full range (min-max)) | 9.77 (5.43 to 19.1) | 24.97 (9.88 to 50.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: VX-745 Plasma Concentration - 3 to 4 hours

End point title VX-745 Plasma Concentration - 3 to 4 hours

End point description:

End point type Secondary

End point timeframe:

On Days 14, 28, 56 and 84, a 5 mL sample of whole blood will be collected.

| | | | | |
|--|----------------------|----------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: ng.hr/mL | | | | |
| arithmetic mean (full range (min-max)) | 11.62 (6.18 to 22.1) | 24.16 (17.7 to 36.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: VX-745 Plasma Concentration - >4 to <6 hours

| | |
|--|--|
| End point title | VX-745 Plasma Concentration - >4 to <6 hours |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| On Days 14, 28, 56 and 84, a 5 mL sample of whole blood will be collected. | |

| | | | | |
|--|---------------------|----------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: ng.hr/mL | | | | |
| arithmetic mean (full range (min-max)) | 7.59 (2.35 to 18.2) | 15.37 (1.84 to 35.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: VX-745 Plasma Concentration - ≥6 hours

| | |
|--|--|
| End point title | VX-745 Plasma Concentration - ≥6 hours |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| On Days 14, 28, 56 and 84, a 5 mL sample of whole blood will be collected. | |

| | | | | |
|--|---------------------|----------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: ng.hr/mL | | | | |
| arithmetic mean (full range (min-max)) | 4.95 (3.01 to 8.38) | 12.02 (5.96 to 20.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Adverse Events (AE)

| | |
|-----------------|--------------------------------|
| End point title | Summary of Adverse Events (AE) |
|-----------------|--------------------------------|

End point description:

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

End point timeframe:

Adverse events that occur from the first dose of study drug on Day 1 through the Follow-up Visit will be considered treatment-emergent adverse events

| | | | | |
|-----------------------------|-----------------|-----------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: Subjects with any AE | 19 | 9 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Basophils (change from baseline)

| | |
|-----------------|---|
| End point title | Absolute Basophils (change from baseline) |
|-----------------|---|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|--|----------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: X10 ⁹ /L | | | | |
| arithmetic mean (full range (min-max)) | 0.01 (-0.01 to 0.03) | 0 (-0.04 to 0.06) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Eosinophils (change from baseline)

| | |
|-----------------|---|
| End point title | Absolute Eosinophils (change from baseline) |
|-----------------|---|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|--|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: X10 ⁹ /L | | | | |
| arithmetic mean (full range (min-max)) | 0.04 (-0.01 to 0.09) | 0.01 (-0.11 to 0.07) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Lymphocytes (change from baseline)

| | |
|-----------------|---|
| End point title | Absolute Lymphocytes (change from baseline) |
|-----------------|---|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|----------------------|----------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: X10 ⁹ /L | | | | |
| arithmetic mean (full range (min-max)) | 0.29 (-0.23 to 0.75) | 0.11 (-0.39 to 0.49) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Monocytes (change from baseline)

| | |
|-----------------|---|
| End point title | Absolute Monocytes (change from baseline) |
|-----------------|---|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|-----------------------|----------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: X10 ⁹ /L | | | | |
| arithmetic mean (full range (min-max)) | -0.03 (-0.45 to 0.12) | 0.02 (-0.42 to 0.26) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Neutrophils (change from baseline)

| | |
|-----------------|---|
| End point title | Absolute Neutrophils (change from baseline) |
|-----------------|---|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|-----------------------|-----------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: X10 ⁹ /L | | | | |
| arithmetic mean (full range (min-max)) | -0.11 (-3.61 to 1.41) | -0.66 (-2.07 to 0.41) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Basophils Percentage (change from baseline)

| | |
|-----------------|---|
| End point title | Basophils Percentage (change from baseline) |
|-----------------|---|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|--------------------|---------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: percent | | | | |
| arithmetic mean (full range (min-max)) | 0.08 (-0.5 to 0.7) | -0.03 (-0.8 to 0.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Eosinophils Percentage (change from baseline)

| | |
|-----------------|---|
| End point title | Eosinophils Percentage (change from baseline) |
|-----------------|---|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|-------------------|--------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: percent | | | | |
| arithmetic mean (full range (min-max)) | 0.3 (-0.7 to 1.6) | 0.15 (-1.5 to 1.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Lymphocytes Percentage (change from baseline)

| | |
|-----------------|---|
| End point title | Lymphocytes Percentage (change from baseline) |
|-----------------|---|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|---------------------|--------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: percent | | | | |
| arithmetic mean (full range (min-max)) | 3.68 (-2.6 to 19.6) | 2.03 (-5.3 to 9.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Monocytes Percentage (change from baseline)

| | |
|-----------------|---|
| End point title | Monocytes Percentage (change from baseline) |
|-----------------|---|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|--|---------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: percent | | | | |
| arithmetic mean (full range (min-max)) | -0.91 (-4.8 to 0.6) | 0.48 (-6.2 to 3.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Neutrophils Percentage (change from baseline)

| | |
|-----------------|---|
| End point title | Neutrophils Percentage (change from baseline) |
|-----------------|---|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|--|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: percent | | | | |
| arithmetic mean (full range (min-max)) | -3.1 (-20.1 to 2.7) | -4.43 (-13.6 to 5.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Erythrocytes (change from baseline)

| | |
|-----------------|-------------------------------------|
| End point title | Erythrocytes (change from baseline) |
|-----------------|-------------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|-----------------------|----------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: X10 ¹² /L | | | | |
| arithmetic mean (full range (min-max)) | -0.05 (-0.39 to 0.37) | 0.03 (-0.31 to 0.33) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: MCH (change from baseline)

| | |
|-----------------|----------------------------|
| End point title | MCH (change from baseline) |
|-----------------|----------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|--------------------|-----------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: AMOL/CEL | | | | |
| arithmetic mean (full range (min-max)) | 51.67 (-81 to 211) | 30 (-43 to 130) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: MCHC (change from baseline)

| | |
|-----------------|-----------------------------|
| End point title | MCHC (change from baseline) |
|-----------------|-----------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|--------------------|-----------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | 0.52 (-0.9 to 2.4) | 0 (-0.8 to 1.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: MCV (change from baseline)

| | |
|-----------------|----------------------------|
| End point title | MCV (change from baseline) |
|-----------------|----------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|-----------------|-----------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: FL | | | | |
| arithmetic mean (full range (min-max)) | 0.22 (-1 to 1) | 1.43 (0 to 3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Hemoglobin (change from baseline)

| | |
|-----------------|-----------------------------------|
| End point title | Hemoglobin (change from baseline) |
|-----------------|-----------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|--|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | 0.14 (-0.8 to 0.9) | 0.21 (-0.4 to 0.5) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Leukocytes (change from baseline)

| | |
|-----------------|-----------------------------------|
| End point title | Leukocytes (change from baseline) |
|-----------------|-----------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|--|--------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: X10 ⁹ /L | | | | |
| arithmetic mean (full range (min-max)) | 0.18 (-3.2 to 1.8) | -0.27 (-1.5 to 1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Platelets (change from baseline)

| | |
|-----------------|----------------------------------|
| End point title | Platelets (change from baseline) |
|-----------------|----------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|------------------|---------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: X10 ⁹ /L | | | | |
| arithmetic mean (full range (min-max)) | 10.67 (-9 to 40) | -24.71 (-145 to 33) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Albumin (change from baseline)

| | |
|-----------------|--------------------------------|
| End point title | Albumin (change from baseline) |
|-----------------|--------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|--------------------|---------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: G/L | | | | |
| arithmetic mean (full range (min-max)) | 0.31 (-2.6 to 3.7) | -1.14 (-4.7 to 1.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Alkaline Phosphatase (change from baseline)

| | |
|-----------------|---|
| End point title | Alkaline Phosphatase (change from baseline) |
|-----------------|---|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|----------------------|----------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: U/L | | | | |
| arithmetic mean (full range (min-max)) | -1.08 (-21.6 to 9.1) | 0.39 (-10.2 to 14.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: ALT (change from baseline)

| | |
|-----------------|----------------------------|
| End point title | ALT (change from baseline) |
|-----------------|----------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|---------------------|-----------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: U/L | | | | |
| arithmetic mean (full range (min-max)) | 2.52 (-4.8 to 10.1) | 1.6 (-7 to 6.5) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: AST (change from baseline)

| | |
|-----------------|----------------------------|
| End point title | AST (change from baseline) |
|-----------------|----------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|-------------------|--------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: U/L | | | | |
| arithmetic mean (full range (min-max)) | 0.3 (-4.6 to 6.7) | 0.93 (-8.5 to 6.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Total Bilirubin (change from baseline)

| | |
|-----------------|--|
| End point title | Total Bilirubin (change from baseline) |
|-----------------|--|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|---------------------|---------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MICROMOL/L | | | | |
| arithmetic mean (full range (min-max)) | -0.18 (-1.8 to 1.7) | -0.91 (-8.2 to 2.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Glucose (change from baseline)

| | |
|-----------------|--------------------------------|
| End point title | Glucose (change from baseline) |
|-----------------|--------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|---------------------|----------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | 0.69 (-2.33 to 4.1) | -1.2 (-5.18 to 2.23) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Blood Urea Nitrogen (change from baseline)

| | |
|-----------------|--|
| End point title | Blood Urea Nitrogen (change from baseline) |
|-----------------|--|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|--------------------|------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | 0.22 (-1.2 to 2.2) | 0.06 (-1 to 1.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Calcium (change from baseline)

| | |
|-----------------|--------------------------------|
| End point title | Calcium (change from baseline) |
|-----------------|--------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|---------------------|----------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | 0.01 (-0.1 to 0.08) | -0.02 (-0.1 to 0.07) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Bicarbonate (change from baseline)

| | |
|-----------------|------------------------------------|
| End point title | Bicarbonate (change from baseline) |
|-----------------|------------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|--------------------|--------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | -0.6 (-3.9 to 1.7) | -0.2 (-2.6 to 2.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Chloride (change from baseline)

| | |
|-----------------|---------------------------------|
| End point title | Chloride (change from baseline) |
|-----------------|---------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|--------------------|------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 6 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | -0.7 (-3.6 to 3.6) | 1.45 (-2 to 4.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Total cholesterol (change from baseline)

| | |
|-----------------|--|
| End point title | Total cholesterol (change from baseline) |
|-----------------|--|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|----------------------|---------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | 0.03 (-1.02 to 1.32) | 0.4 (-0.19 to 0.79) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Triglycerides (change from baseline)

| | |
|-----------------|--------------------------------------|
| End point title | Triglycerides (change from baseline) |
|-----------------|--------------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|----------------------|-----------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | -0.2 (-15.6 to 17.3) | 4 (0.7 to 6.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Creatinine (change from baseline)

| | |
|-----------------|-----------------------------------|
| End point title | Creatinine (change from baseline) |
|-----------------|-----------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|----------------------|-----------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MICROMOL/L | | | | |
| arithmetic mean (full range (min-max)) | -0.2 (-15.6 to 17.3) | 4 (0.7 to 6.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: GGT (change from baseline)

| | |
|-----------------|----------------------------|
| End point title | GGT (change from baseline) |
|-----------------|----------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|---------------------|-------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: U/L | | | | |
| arithmetic mean (full range (min-max)) | 4.63 (-7.4 to 22.2) | 10.07 (0.4 to 37) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: LDH (change from baseline)

| | |
|-----------------|----------------------------|
| End point title | LDH (change from baseline) |
|-----------------|----------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|---------------------|-----------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 5 | | |
| Units: U/L | | | | |
| arithmetic mean (full range (min-max)) | -3.84 (-18.6 to 30) | -0.26 (-14.7 to 14.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phosphate (change from baseline)

| | |
|-----------------|----------------------------------|
| End point title | Phosphate (change from baseline) |
|-----------------|----------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|--|-----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | -0.02 (-0.37 to 0.49) | 0.07 (-0.08 to 0.19) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Potassium (change from baseline)

| | |
|-----------------|----------------------------------|
| End point title | Potassium (change from baseline) |
|-----------------|----------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| End point values | VX-745 40 mg | VX-745 125 mg | | |
|--|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | 0.11 (-0.33 to 0.69) | -0.05 (-1.19 to 0.44) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Sodium (change from baseline)

| | |
|-----------------|-------------------------------|
| End point title | Sodium (change from baseline) |
|-----------------|-------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|---------------------|--------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | -0.73 (-4.8 to 3.2) | 1.01 (-0.6 to 2.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Total protein (change from baseline)

| | |
|-----------------|--------------------------------------|
| End point title | Total protein (change from baseline) |
|-----------------|--------------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|--------------------|--------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: G/L | | | | |
| arithmetic mean (full range (min-max)) | 1.28 (-3.6 to 5.2) | -0.8 (-6.2 to 4.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Uric acid (change from baseline)

| | |
|-----------------|----------------------------------|
| End point title | Uric acid (change from baseline) |
|-----------------|----------------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|------------------------|------------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: MICROMOL/L | | | | |
| arithmetic mean (full range (min-max)) | -13.86 (-50.3 to 22.6) | -11.34 (-20.2 to -6.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: HDL (change from baseline)

| | |
|-----------------|----------------------------|
| End point title | HDL (change from baseline) |
|-----------------|----------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|-----------------------|------------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 1 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | -0.05 (-0.16 to 0.06) | -0.09 (-0.09 to -0.09) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: LDL (change from baseline)

| | |
|-----------------|----------------------------|
| End point title | LDL (change from baseline) |
|-----------------|----------------------------|

End point description:

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

End point timeframe:

Clinical laboratory sampling performed at screening, at each treatment period study visits (from Day 1 to 84) and at the follow-up visit

| | | | | |
|--|-----------------|------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 1 | | |
| Units: MMOL/L | | | | |
| arithmetic mean (full range (min-max)) | 0.1 (0 to 0.2) | 0.3 (0.3 to 0.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Systolic Blood Pressure (change from baseline)

| | |
|---|--|
| End point title | Systolic Blood Pressure (change from baseline) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Vital signs measurements performed at screening and at Day 84 | |

| | | | | |
|--|------------------|------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: mmHg | | | | |
| arithmetic mean (full range (min-max)) | -4.3 (-28 to 36) | -6.6 (-26 to 30) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Diastolic Blood Pressure (change from baseline)

| | |
|---|---|
| End point title | Diastolic Blood Pressure (change from baseline) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Vital signs measurements performed at screening and at Day 84 | |

| | | | | |
|--|------------------|-----------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: mmHg | | | | |
| arithmetic mean (full range (min-max)) | -1.1 (-15 to 17) | -5.3 (-15 to 2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Heart Rate (change from baseline)

| | |
|---|-----------------------------------|
| End point title | Heart Rate (change from baseline) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Vital signs measurements performed at screening and at Day 84 | |

| | | | | |
|--|-----------------|-----------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: beats/min | | | | |
| arithmetic mean (full range (min-max)) | 7.1 (-6 to 23) | 4.3 (-8 to 19) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Weight (change from baseline)

| | |
|---|-------------------------------|
| End point title | Weight (change from baseline) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Vital signs measurements performed at screening and at Day 84 | |

| | | | | |
|--|-----------------|-------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: kg | | | | |
| arithmetic mean (full range (min-max)) | 1.5 (0 to 5) | 0.5 (-0.4 to 1.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Temperature (change from baseline)

| | |
|---|------------------------------------|
| End point title | Temperature (change from baseline) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Vital signs measurements performed at screening and at Day 84 | |

| | | | | |
|--|--------------------|-------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: celsius | | | | |
| arithmetic mean (full range (min-max)) | -0.2 (-1.5 to 0.7) | 0.2 (-0.4 to 0.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: BMI (change from baseline)

| | |
|---|----------------------------|
| End point title | BMI (change from baseline) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Vital signs measurements performed at screening and at Day 84 | |

| | | | | |
|--|-----------------|---------------------|--|--|
| End point values | VX-745 40 mg | VX-745 125 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: kg/m ² | | | | |
| arithmetic mean (full range (min-max)) | 0.5 (0 to 1.79) | 0.2 (-0.12 to 0.59) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events that occur from the first dose of study drug on Day 1 through the Follow-up Visit will be considered treatment-emergent adverse events.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | VX-745 40 mg |
|-----------------------|--------------|

| | |
|------------------------------|---|
| Reporting group description: | - |
|------------------------------|---|

| | |
|-----------------------|---------------|
| Reporting group title | VX-745 125 mg |
|-----------------------|---------------|

| | |
|------------------------------|---|
| Reporting group description: | - |
|------------------------------|---|

| Serious adverse events | VX-745 40 mg | VX-745 125 mg | |
|---|---------------|---------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 7 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | VX-745 40 mg | VX-745 125 mg | |
|---|-----------------|----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 9 (100.00%) | 5 / 7 (71.43%) | |
| Vascular disorders | | | |
| VASCULAR DISORDERS NEC | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 7 (14.29%) | |
| occurrences (all) | 19 | 9 | |
| VASCULAR HYPERTENSIVE DISORDERS | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 7 (14.29%) | |
| occurrences (all) | 19 | 9 | |
| General disorders and administration site conditions | | | |
| GENERAL SYSTEM DISORDERS NEC | | | |

| | | | |
|--|--|---|--|
| subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 19 | 1 / 7 (14.29%) 9 | |
| Respiratory, thoracic and mediastinal disorders RESPIRATORY DISORDERS NEC subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 19 | 0 / 7 (0.00%) 9 | |
| Psychiatric disorders ANXIETY DISORDERS AND SYMPTOMS subjects affected / exposed occurrences (all) PERSONALITY DISORDERS AND DISTURBANCES IN BEHAVIOUR subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 19 1 / 9 (11.11%) 19 | 0 / 7 (0.00%) 9 0 / 7 (0.00%) 9 | |
| Investigations WATER, ELECTROLYTE AND MINERAL INVESTIGATIONS subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 19 | 0 / 7 (0.00%) 9 | |
| Injury, poisoning and procedural complications BONE AND JOINT INJURIES subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 19 | 0 / 7 (0.00%) 9 | |
| Nervous system disorders NEUROLOGICAL DISORDERS NEC subjects affected / exposed occurrences (all) SPINAL CORD AND NERVE ROOT DISORDERS subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 19 1 / 9 (11.11%) 19 | 1 / 7 (14.29%) 9 0 / 7 (0.00%) 9 | |
| Blood and lymphatic system disorders ANAEMIAS NONHAEMOLYTIC AND MARROW DEPRESSION subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 19 | 0 / 7 (0.00%) 9 | |
| Ear and labyrinth disorders | | | |

| | | | |
|--|---|--|--|
| <p>INNER EAR AND VIIIITH CRANIAL NERVE DISORDERS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 9 (11.11%)</p> <p>19</p> | <p>0 / 7 (0.00%)</p> <p>9</p> | |
| <p>Gastrointestinal disorders</p> <p>GASTROINTESTINAL MOTILITY AND DEFAECATION CONDITIONS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>GASTROINTESTINAL SIGNS AND SYMPTOMS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 9 (44.44%)</p> <p>19</p> <p>1 / 9 (11.11%)</p> <p>19</p> | <p>0 / 7 (0.00%)</p> <p>9</p> <p>1 / 7 (14.29%)</p> <p>9</p> | |
| <p>Skin and subcutaneous tissue disorders</p> <p>EPIDERMAL AND DERMAL CONDITIONS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 9 (0.00%)</p> <p>19</p> | <p>3 / 7 (42.86%)</p> <p>9</p> | |
| <p>Endocrine disorders</p> <p>HYPOTHALAMUS AND PITUITARY GLAND DISORDERS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>THYROID GLAND DISORDERS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 9 (11.11%)</p> <p>19</p> <p>1 / 9 (11.11%)</p> <p>19</p> | <p>0 / 7 (0.00%)</p> <p>9</p> <p>0 / 7 (0.00%)</p> <p>9</p> | |
| <p>Infections and infestations</p> <p>INFECTIONS - PATHOGEN UNSPECIFIED</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 9 (11.11%)</p> <p>19</p> | <p>1 / 7 (14.29%)</p> <p>9</p> | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--------------------------------------|
| 22 December 2015 | Amendment 2.0 dated 22 December 2015 |
| 15 March 2016 | Amendment 3.0 dated 15 March 2016 |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported