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

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

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