Clinical trial results:
A Double-Blind, Placebo-Controlled Proof-of-Concept Study of a Selective p38 MAP Kinase Alpha Inhibitor, Neflamapimod, Administered for 24 Weeks in Subjects with Mild Alzheimer's Disease

Summary

EudraCT number	2017-004388-11
Trial protocol	GB DK NL CZ
Global end of trial date	17 July 2019

Results information

Result version number	v1 (current)
This version publication date	24 July 2020
First version publication date	24 July 2020
Summary attachment (see zip file)	EIP-VX17-745-304 Synopsis (EIP-VX17-745-304 Synopsis_Final_2020 Jan 27.pdf)

Trial information

Trial identification

Sponsor protocol code	EIP-VX17-745-304

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03402659
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	EIP Pharma
Sponsor organisation address	120 St James Ave, The Yard, Suite 6017, Boston, United States, 02116
Public contact	Project Management, Worldwide Clinical Trials Limited, +44 1159567711,
Scientific contact	Project Management, Worldwide Clinical Trials Limited, +44 1159567711,
Sponsor organisation name	EIP Pharma
Sponsor organisation address	120 St James Ave, The Yard, Suite 6017, Boston, United States, 02116
Public contact	Jennifer Conway, Clinical Development , EIP Pharma 120 St James Ave, The Yard, Suite 6017 Boston, MA 02116, jconway@eippharma.com
Scientific contact	John Alam, MD CEO and Founder, EIP Pharma 120 St James Ave, The Yard, Suite 6017 Boston, MA 02116, 617 744-4400, jalam@eippharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric	No

investigation plan (PIP)	
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	17 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 July 2019
Global end of trial reached?	Yes
Global end of trial date	17 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the effects of administration of neflamapimod (VX-745) for 24-weeks on immediate and delayed recall aspects of episodic memory, as assessed by the Hopkins Verbal Learning Test – Revised (HVLT-R) in patients with mild Alzheimer's disease (AD).

Protection of trial subjects:

No trial-related activities were performed until the subject had been consented and given an opportunity to ask questions and discuss the study with family/caregiver. Numbing agents were used, as necessary, for the lumbar puncture/CSF draw. Phone calls were implemented between visits that were 6 weeks apart to check in with the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 December 2017
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: 20
Country: Number of subjects enrolled	United Kingdom: 52
Country: Number of subjects enrolled	Czech Republic: 9
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	United States: 73
Worldwide total number of subjects	161
EEA total number of subjects	88

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)	23
From 65 to 84 years	136
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Recruitment Period: 22 December 2017 to 11 January 2019
Participating countries: United States, United Kingdom, Netherlands, Czech Republic, Denmark

Pre-assignment

Screening details:

477 subjects were screened, of which 13 were re-screened.
316 subjects were determined ineligible for the study. 119 subjects did not meet CSF criteria, 79 subjects did not meet MMSE criteria, 44 subjects were unable to provide consent, 40 subjects withdrew consent, 34 were for other exclusionary reasons.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

All subjects, caregivers, site staff, CRO staff (e.g. monitors, PMs, regulatory, data management) and sponsor staff were blinded to the treatment assignment until after database lock.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Arm

Arm description:

Arm of trial including the 83 subjects that were randomly assigned (1:1) to take placebo

Arm type	Placebo
Investigational medicinal product name	Matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received neflamapimod matching placebo capsules orally, BID with a meal or snack for 24 weeks. Doses were taken within 30 minutes following a meal or snack (i.e., breakfast and dinner) no less than 8 hours apart and at approximately the same times each day throughout the study.

Arm title	Neflamapimod Arm

Arm description:

Arm of trial including the 78 subjects that were randomly assigned (1:1) to take neflamapimod (active study drug).

Arm type	Active comparator
Investigational medicinal product name	neflamapimod
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received neflamapimod 40 mg capsules orally, BID with a meal or snack for 24 weeks. Doses were taken within 30 minutes following a meal or snack (i.e., breakfast and dinner) no less than 8 hours apart and at approximately the same times each day throughout the study.

Number of subjects in period 1	Placebo Arm	Neflamapimod Arm
Started	83	78
Completed	78	73
Not completed	5	5
Consent withdrawn by subject	3	3
Adverse event, non-fatal	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	161	161	
Age categorical			
161 subjects were enrolled between the ages of 56-85 years at Screening			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	23	23	
From 65-84 years	136	136	
85 years and over	2	2	
Age continuous			
161 subjects were enrolled between the ages of 56-85 years at Screening			
Units: years			
arithmetic mean	71.8		
standard deviation	± 6.84	-	
Gender categorical			
Units: Subjects			
Female	80	80	
Male	81	81	

End points

End points reporting groups

Reporting group title	Placebo Arm
Reporting group description:	
Arm of trial including the 83 subjects that were randomly assigned (1:1) to take placebo	
Reporting group title	Neflamapimod Arm
Reporting group description:	
Arm of trial including the 78 subjects that were randomly assigned (1:1) to take neflamapimod (active study drug).	

Primary: HVLT-R

End point title	HVLT-R
End point description:	
Combined change in z-scores of total recall and delayed recall on the HVLT-R (Hopkins Verbal Learning Test - Revised) in neflamapimod-treated subjects compared to placebo-recipients.	
End point type	Primary
End point timeframe:	
Baseline (Day 1) to End of Treatment (Week 24)	

End point values	Placebo Arm	Neflamapimod Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	71		
Units: Z-score	72	71		

Attachments (see zip file)	MMRM Change from Baseline (HVLT-R)/Table_14_02_03_03.rtf

Statistical analyses

Statistical analysis title	MMRM Analysis - HVLT-R
Statistical analysis description:	
The primary endpoint was analyzed using Mixed Model for Repeated Measures (MMRM) with fixed effects for treatment, background AD-specific therapy, CDR-Global Score of 0.5 versus 1.0, scheduled visit (nominal) and scheduled visit by treatment interaction, random effect for subject and baseline Z-score as a covariate. . Least-square means (LSM) and 2-sided 95% confidence intervals (CI) are provided for treatment group differences and estimated endpoint values by visit.	
Comparison groups	Neflamapimod Arm v Placebo Arm
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.564
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06098
upper limit	0.14777
Variability estimate	Standard error of the mean

Statistical analysis title	HVLT-R - PK/PD Analysis

Statistical analysis description:

In addition to the primary analysis, a pre-specified PK/PD analysis was conducted in which the change in the primary endpoint from baseline to Week 24 was assessed by plasma trough drug concentration (Ctrough) at Day 21 (i.e. at steady-state). Neflamapimood-treated subjects with Ctrough > 4 ng/mL tended to show less decline in the primary endpoint than either placebo-recipients or neflamapimod-treated subjects with Ctrough < 4 ng/mL.

Comparison groups	Placebo Arm v Neflamapimod Arm
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.06
Method	Mixed models analysis
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Notes:

[1] - The proportion of subjects with >1 SD decline in the primary endpoint in the placebo group was 15.4% (12 of 78) versus 0% (0 of 23) in neflamapimod subjects with Ctrough > 4 ng/mL (two-sided p-value=0.06 vs. placebo)

Secondary: WMS

End point title	WMS

End point description:

Change in WMS (Wechsler Memory Scale) immediate and delayed recall composites in neflamapimod-treated subjects compared to placebo-recipients.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to End of Treatment (Week 24)

End point values	Placebo Arm	Neflamapimod Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	71		
Units: composite score	77	71		

Attachments (see zip file)	MMRM Change from Baseline (WMS)/Table_14_02_02_03.rtf

Statistical analyses

Statistical analysis title	MMRM Analysis - WMS

Statistical analysis description:

WMS scores were analyzed using Mixed Model for Repeated Measures (MMRM) with fixed effects for treatment, background AD-specific therapy, CDR-Global Score of 0.5 versus 1.0, scheduled visit (nominal) and scheduled visit by treatment interaction, random effect for subject and baseline Z-score as a covariate. Least-square means (LSM) and 2-sided 95% confidence intervals (CI) are provided for treatment group differences and estimated endpoint values by visit.

Comparison groups	Placebo Arm v Neflamapimod Arm
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.823
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	4.8
Variability estimate	Standard error of the mean

Statistical analysis title	WMS - PK/PD Analysis

Statistical analysis description:

In pre-specified PK/PD analyses, in subjects on background AD therapy, neflamapimod subjects with Ctrough levels > 4 ng/mL demonstrated a significant improvement in WMS Immediate and Delayed Recall composite scores, relative to placebo
recipients at both week 12 (p=0.018) and at Week 24 (p=0.046).

Comparison groups	Neflamapimod Arm v Placebo Arm
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.046
Method	Mixed models analysis
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Secondary: CDR-SB

End point title	CDR-SB

End point description:

Change in CDR-SB (CDR Sum of Boxes) in neflamapimod-treated subjects compared to placebo-recipients.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to End of Treatment (Week 24)

End point values	Placebo Arm	Neflamapimod Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	74		
Units: score	78	74		

Attachments (see zip file)	MMRM Change from Baseline (CDR-SB)/Table_14_02_02_05.rtf

Statistical analyses

Statistical analysis title	MMRM Analysis - CDR-SB

Statistical analysis description:

CDR-SB scores were analyzed using Mixed Model for Repeated Measures (MMRM) with fixed effects for treatment, background AD-specific therapy, CDR-Global Score of 0.5 versus 1.0, scheduled visit (nominal) and scheduled visit by treatment interaction, random effect for subject and baseline Z-score as a covariate. Least-square means (LSM) and 2-sided 95% confidence intervals (CI) are provided for treatment group differences and estimated endpoint values by visit.

Comparison groups	Placebo Arm v Neflamapimod Arm
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.806
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.6
Variability estimate	Standard error of the mean

Secondary: MMSE

End point title	MMSE

End point description:

Change in MMSE (Mini-Mental State Exam) in neflamapimod-treated subjects compared to placebo-recipients.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Follow-up Visit (2 weeks after last dose)

End point values	Placebo Arm	Neflamapimod Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	70		
Units: score	79	70		

Attachments (see zip file)	ANCOVA Change from Baseline (MMSE)/Table_14_02_02_07.

Statistical analyses

Statistical analysis title	ANCOVA - MMSE

Statistical analysis description:

Changes MMSE scores were compared using an ANCOVA with treatment group, background AD-specific therapy, CDR-Global Score as main effects and the baseline assessment as the covariate. The results of the ANCOVA are summarized using the treatment groups' least square means, the difference between the treatment groups' least square means, the 95% confidence interval for the treatment group difference and the p-value.

Comparison groups	Placebo Arm v Neflamapimod Arm
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.489
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.5
Variability estimate	Standard error of the mean

Secondary: CSF Biomarkers

End point title	CSF Biomarkers

End point description:

Change in CSF biomarkers (total tau, p-tau181, Aβ1-40, Aβ1-42, neurogranin, neurofilament light chain) in neflamapimod-treated subjects compared to placebo-recipients.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to End of Treatment (Week 24)

End point values	Placebo Arm	Neflamapimod Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	62		
Units: value	68	62		

Attachments (see zip file)	ANCOVA Change from Baseline (t-tau) ANCOVA Change from Baseline (p-tau) ANCOVA Change from Baseline (AB1-40) ANCOVA Change from Baseline (AB1-42) ANCOVA Change from Baseline (neurogranin) ANCOVA Change from Baseline (NFL)/Table_14_02_02_08_07. ANCOVA Change from Baseline (p-tau/AB ratio)

Statistical analyses

Statistical analysis title	ANCOVA t-tau

Statistical analysis description:

Changes in Total Tau (t-tau) were compared using an ANCOVA with treatment group, background AD-specific therapy, CDR-Global Score as main effects and the baseline assessment as the covariate. The results of the ANCOVA are summarized using the treatment groups' least square means, the difference between the treatment groups' least square means, the 95% confidence interval for the treatment group difference and the p-value.

Comparison groups	Placebo Arm v Neflamapimod Arm
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.031
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-18.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.8
upper limit	-1.8
Variability estimate	Standard error of the mean

Statistical analysis title	ANCOVA p-tau181

Statistical analysis description:

Changes in Phospho-Tau (p-tau181) were compared using an ANCOVA with treatment group, background AD-specific therapy, CDR-Global Score as main effects and the baseline assessment as the covariate. The results of the ANCOVA are summarized using the treatment groups' least square means, the difference between the treatment groups' least square means, the 95% confidence interval for the treatment group difference and the p-value.

Comparison groups	Placebo Arm v Neflamapimod Arm

Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.012
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	-0.5
Variability estimate	Standard error of the mean

Statistical analysis title	ANCOVA AB1-40

Statistical analysis description:

Changes in Amyloid beta (AB1-40) were compared using an ANCOVA with treatment group, background AD-specific therapy, CDR-Global Score as main effects and the baseline assessment as the covariate. The results of the ANCOVA are summarized using the treatment groups' least square means, the difference between the treatment groups' least square means, the 95% confidence interval for the treatment group difference and the p-value.

Comparison groups	Placebo Arm v Neflamapimod Arm
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.709
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-117.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-738.9
upper limit	504.2
Variability estimate	Standard error of the mean

Statistical analysis title	ANCOVA AB1-42

Statistical analysis description:

Changes in Amyloid beta (AB1-42) were compared using an ANCOVA with treatment group, background AD-specific therapy, CDR-Global Score as main effects and the baseline assessment as the covariate. The results of the ANCOVA are summarized using the treatment groups' least square means, the difference between the treatment groups' least square means, the 95% confidence interval for the treatment group difference and the p-value.

Comparison groups	Placebo Arm v Neflamapimod Arm

Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.192
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52.7
upper limit	10.7
Variability estimate	Standard error of the mean

Statistical analysis title	ANCOVA Neurogranin

Statistical analysis description:

Changes in Neurogranin were compared using an ANCOVA with treatment group, background AD-specific therapy, CDR-Global Score as main effects and the baseline assessment as the covariate. The results of the ANCOVA are summarized using the treatment groups' least square means, the difference between the treatment groups' least square means, the 95% confidence interval for the treatment group difference and the p-value.

Comparison groups	Placebo Arm v Neflamapimod Arm
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.068
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-43.6
upper limit	1.6
Variability estimate	Standard error of the mean

Statistical analysis title	ANCOVA NFL

Statistical analysis description:

Changes in Neurofilament Light Chain (NFL) were compared using an ANCOVA with treatment group, background AD-specific therapy, CDR-Global Score as main effects and the baseline assessment as the covariate. The results of the ANCOVA are summarized using the treatment groups' least square means, the difference between the treatment groups' least square means, the 95% confidence interval for the treatment group difference and the p-value.

Comparison groups	Placebo Arm v Neflamapimod Arm

Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.156
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-110.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-262.7
upper limit	42.4
Variability estimate	Standard error of the mean

Statistical analysis title	ANCOVA p-tau/AB1-42

Statistical analysis description:

Changes in the ratio of Phospho-Tau/Amyloid Beta (p-tau181/AB1-42) were compared using an ANCOVA with treatment group, background AD-specific therapy, CDR-Global Score as main effects and the baseline assessment as the covariate. The results of the ANCOVA are summarized using the treatment groups' least square means, the difference between the treatment groups' least square means, the 95% confidence interval for the treatment group difference and the p-value.

Comparison groups	Placebo Arm v Neflamapimod Arm
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.59
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0
Variability estimate	Standard error of the mean

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs occurring from when the subject signed the ICF until the last study event were collected. Any AEs occurring before the start of treatment (i.e., before the first dose of the investigational product) were recorded in the medical history.

Adverse event reporting additional description:

Any sign, symptom, or disease present before starting the treatment period were only considered AEs if they worsen after starting the treatment period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Neflamapimod

Reporting group description:

This reporting group includes subjects who were randomized to the neflamapimod group. Adverse Events are only reported for incidence of 5% or higher.

Serious adverse events	Neflamapimod		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 78 (2.56%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Multiple Myeloma	Additional description: Multiple Myeloma occurred in one subject. It was not considered related to neflamapimod.		
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalemia	Additional description: One SAE of Hypokalemia was reported. It was considered not related to neflamapimod.		
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Neflamapimod		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 78 (23.08%)		
Injury, poisoning and procedural complications			
Fall	Additional description: The incidence of fall in the neflamapimod group was 6%. The incidence of fall in the placebo group was 4%		
subjects affected / exposed	5 / 78 (6.41%)		
occurrences (all)	5		
Nervous system disorders			
Headache	Additional description: The incidence of headache in the neflamapimod group was 6%. The incidence of headache in the placebo group was 4%.		
subjects affected / exposed	5 / 78 (6.41%)		
occurrences (all)	6		
Gastrointestinal disorders			
Diarrhea	Additional description: The incidence of diarrhea in the neflamapimod group was 5%. The incidence of diarrhea in the placebo group was 2%.		
subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	4		
Infections and infestations			
Upper respiratory tract infection	Additional description: The incidence of upper respiratory tract infection in the neflamapimod group was 5%. The incidence of upper respiratory tract infection in the placebo group was 8%.		
subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 September 2018	Amendment 2 was issued on 27 August, 2018. Changes made by the country-specific amendments were harmonized in this version. Notable changes made by Amendment 2 included: • It was clarified that the CDR-SB (rather than the CDR) would be employed. • With regard to CSF biomarkers, measurement of neurogranin was added. • Telephone contacts were to be conducted to determine subject status and assess compliance between Days 42 and 84 (Visits 5 and 6); Days 84 to 126 (Visits 6 and 7); and Days 126 and 168 (Visits 7 and 8). • The neflamapimod administration procedures relative to meals were clarified. In addition, editorial and administrative changes were made by Amendment 2.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported