Clinical trial results:
A Double-Blind, Placebo-Controlled 16-Week Study of the Cognitive Effects of the Oral P38 Alpha Kinase Inhibitor Neflamapimod in Dementia with Lewy Bodies (DLB)

Summary

EudraCT number	2019-001566-15
Trial protocol	NL
Global end of trial date	14 July 2020

Results information

Result version number	v1 (current)
This version publication date	16 July 2021
First version publication date	16 July 2021
Summary attachment (see zip file)	EIP19-NFD-501 CSR Synopsis (EIP19-NFD-501_CSR Synopsis_26Feb2021_FINAL.pdf)

Trial information

Trial identification

Sponsor protocol code	EIP19-NFD-501

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04001517
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Worldwide Clinical Trials Limited
Sponsor organisation address	Technology Drive, Beeston, Nottingham, United Kingdom, NG9 1LA
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 Avenue, Suite 6017, Boston, United States, 02116
Public contact	Dr. John Alam, EIP Pharma, 1 617-669-8426, johnjalam@gmail.com
Scientific contact	Dr. John Alam, EIP Pharma, 1 617-669-8426, johnjalam@gmail.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	30 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2020
Global end of trial reached?	Yes
Global end of trial date	14 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the effect of neflamapimod on cognitive function as assessed in a study-specific Neuropsychological Test Battery (NTB) comprised of:
•Cogstate Detection test (DET)
•Cogstate Identification test (IDN)
•Cogstate One Card Learning test (OCL)
•Cogstate One Back test (ONB)
•Letter Fluency Test
•Category Fluency Test (CFT)

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.

Background therapy:

All subjects were required to be receiving cholinesterase inhibitor therapy for at least 3 months and have been on a stable dose for at least 6 weeks at the time of randomization.

Evidence for comparator: -

Actual start date of recruitment	12 July 2019
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: 13
Country: Number of subjects enrolled	United States: 78
Worldwide total number of subjects	91
EEA total number of subjects	13

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)	11
From 65 to 84 years	77
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Active recruitment and screening began 12Jul2019. The first subject was screened on 29Aug2019 and the first subject was enrolled on 30Sep2019. The last subject was screened 14Feb2020 and the last subject was enrolled 06Mar2020. Participating countries were the United States and Netherlands.

Pre-assignment

Screening details:

125 subjects were screened. 33 were determined ineligible for the study therefore deemed screen failures: 12 due to not meeting MMSE inclusion criteria, 7 due to negative DaTscan, 4 withdrew consent, and 10 due to 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, investigators and site staff, CRO staff, and sponsor staff were blinded to treatment assignment until after database lock.

Arms

Are arms mutually exclusive?	Yes
Arm title	Neflamapimod TID

Arm description:

40 mg capsules administered orally TID with food for 16 weeks; subjects followed the TID regimen if Screening weight was ≥80 kg

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 3 neflamapimod 40 mg capsules per day (TID), given orally within 30 minutes following a meal or snack (i.e., morning, mid-day and evening meals). Doses were given at least 3 hours apart at approximately the same time each day for 16 weeks.

Arm title	Neflamapimod BID

Arm description:

40 mg capsules administered orally BID with food for 16 weeks; subjects followed the BID regimen if Screening weight was <80 kg

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 2 neflamapimod 40 mg capsules per day (BID), given orally within 30 minutes following a meal or snack (i.e., morning and evening meals). Doses were given at least 3 hours apart at approximately the same time each day for 16 weeks.

Arm title	Placebo

Arm description:

40 mg matching placebo capsules administered orally TID or BID with food for 16 weeks; subjects followed the TID regimen if Screening weight was ≥80 kg and the BID regimen if Screening weight was <80 kg

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:

For TID, subjects received 3 neflamapimod matching placebo capsules per day (TID), given orally within 30 minutes following a meal or snack (i.e., morning, mid-day and evening meals). For BID, subjects received 2 neflamapimod matching placebo capsules per day (BID), given orally within 30 minutes following a meal or snack (i.e., morning and evening meals). Doses were given at least 3 hours apart at approximately the same time each day for 16 weeks.

Number of subjects in period 1	Neflamapimod TID	Neflamapimod BID	Placebo
Started	20	26	45
Completed	20	20	41
Not completed	0	6	4
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	-	3	1
Physician decision	-	-	1
Adverse event, non-fatal	-	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Neflamapimod TID
Reporting group description:	
40 mg capsules administered orally TID with food for 16 weeks; subjects followed the TID regimen if Screening weight was ≥80 kg	
Reporting group title	Neflamapimod BID
Reporting group description:	
40 mg capsules administered orally BID with food for 16 weeks; subjects followed the BID regimen if Screening weight was <80 kg	
Reporting group title	Placebo
Reporting group description:	
40 mg matching placebo capsules administered orally TID or BID with food for 16 weeks; subjects followed the TID regimen if Screening weight was ≥80 kg and the BID regimen if Screening weight was <80 kg	

Reporting group values	Neflamapimod TID	Neflamapimod BID	Placebo
Number of subjects	20	26	45
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	2	7
From 65-84 years	18	23	36
85 years and over	0	1	2
Age continuous			
Units: years			
arithmetic mean	72.2	74.5	72.1
full range (min-max)	59 to 84	63 to 85	62 to 87
Gender categorical			
Units: Subjects			
Female	1	7	6
Male	19	19	39

Reporting group values	Total		
Number of subjects	91		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	11		
From 65-84 years	77		
85 years and over	3		
Age continuous			
Units: years			
arithmetic mean			
full range (min-max)	-		
Gender categorical			
Units: Subjects			
Female	14		
Male	77		

End points

End points reporting groups

Reporting group title	Neflamapimod TID
Reporting group description:	
40 mg capsules administered orally TID with food for 16 weeks; subjects followed the TID regimen if Screening weight was ≥80 kg	
Reporting group title	Neflamapimod BID
Reporting group description:	
40 mg capsules administered orally BID with food for 16 weeks; subjects followed the BID regimen if Screening weight was <80 kg	
Reporting group title	Placebo
Reporting group description:	
40 mg matching placebo capsules administered orally TID or BID with food for 16 weeks; subjects followed the TID regimen if Screening weight was ≥80 kg and the BID regimen if Screening weight was <80 kg	

Primary: NTB (Neuropsychological Test Battery)

End point title	NTB (Neuropsychological Test Battery)
End point description:	
Change from Baseline to Week 16 in the composite score of a study-specific Cogstate Neuropsychological Test Battery (NTB), including assessments of attention, executive function, and visuospatial function in neflamapimod treated-subjects as compared to the placebo-treated subjects, as analyzed using the Mixed Model Repeated Measures (MMRM) analysis method. The following six tests will be included in the composite: (1) Cogstate Detection test (DET), (2) Cogstate Identification test (IDN), (3) Cogstate One Card Learning test (OCL), (4) Cogstate One Back test (ONB), (5) Letter Fluency Test, (6) Category Fluency Test (CFT). Each score on the individual tests will be converted to a z-score, and then a total z-score will be calculated, in which each test is weighted equally. The change in total z-score in neflamapimod vs. placebo-recipients will be analyzed. As the analysis is based on z-scores, there is no minimum or maximum value.	
End point type	Primary
End point timeframe:	
16 weeks	

End point values	Neflamapimod TID	Neflamapimod BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	20	37	
Units: Z-Score by Time on Study				
arithmetic mean (standard error)				
Baseline	0.06 (± 0.17)	0.02 (± 0.15)	0.05 (± 0.11)	
Week 4	0.17 (± 0.14)	-0.08 (± 0.18)	-0.05 (± 0.13)	
Week 8	0.28 (± 0.16)	-0.12 (± 0.18)	0.05 (± 0.17)	
Week 16	0.21 (± 0.18)	-0.08 (± 0.21)	-0.03 (± 0.14)	

Statistical analyses

Statistical analysis title	Linear Mixed Effects (LME)

Statistical analysis description:

This was an exploratory trial and no explicit a priori hypothesis was established and contained in the protocol. As such, no formal power calculations were conducted. The primary objective of the study was to evaluate the effects of neflamapimod on cognition, and accordingly the primary endpoint was change in combined z-score of the six tests in the NTB, analyzed by Linear Mixed Effects (LME) model for repeated measures.

Comparison groups	Neflamapimod TID v Neflamapimod BID v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.049 [2]
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.175
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.001
upper limit	0.345

Notes:

[1] - Change from baseline analyzed by linear mixed effects model for repeated measures. Comparison of all NFMD vs. Placebo was not significant. p=0.015 (cohen's D effect size=0.52) for NFMD 40mg TID vs. combined other groups; p=0.049 (effect size=0.47) for NFMD 40mg TID vs. placebo.

[2] - Comparison of NFMD 40mg TID vs. placebo is reported. Comparison of all NFMD vs. Placebo was not significant. p=0.015 (cohen's D effect size=0.52) for NFMD 40mg TID vs. combined other groups .

Secondary: Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB)

End point title	Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB)

End point description:

Change in Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB) score based on semi-quantitative scoring of each domain (box) evaluating cognitive impairment in milder and more progressive forms of dementia, in neflamapimod-treated subjects compared to placebo-recipients. The domain (box) scores will be calculated for a Sum of Boxes score. Secondary efficacy endpoints will utilize the same analysis method and model as the primary endpoint.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Neflamapimod TID	Neflamapimod BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	20	37	
Units: Change from Baseline by Time on Study				
arithmetic mean (standard error)				
Week 8	0.11 (± 0.2)	0.19 (± 0.3)	0.76 (± 0.25)	
Week 16	0.34 (± 0.2)	0.34 (± 0.18)	0.86 (± 0.32)	

Statistical analyses

Statistical analysis title	Linear Mixed Effects (LME)

Statistical analysis description:

Due to Covid19 restrictions on clinical research CDR-SB evaluations were conducted remotely (i.e., via telephone or video conference, with the subject and informant at home rather than in person at the clinical site). However, within the study at home visits resulted in significantly better scores (~0.8 points lower, p=0.02). As the baseline visits were all conducted onsite, and at home CDR-SB visits has not been validated, the change analysis reported includes only data from onsite visits.

Comparison groups	Neflamapimod TID v Neflamapimod BID v Placebo
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.17 [3]
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	0.24

Notes:

[3] - p=0.028 for combined combined NFMD vs. placebo.

Secondary: Mini-Mental State Examination (MMSE)

End point title	Mini-Mental State Examination (MMSE)

End point description:

Change in Mini-Mental State Examination (MMSE) with respect to orientation, memory, concentration, language, and praxis (scores ranging from 0 to 30 with lower scores indicating greater cognitive impairment), in neflamapimod-treated subjects compared to placebo-recipients. Secondary efficacy endpoints will utilize the same analysis method and model as the primary endpoint.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Neflamapimod TID	Neflamapimod BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	21	41	
Units: Change from Baseline by Time on Study				
arithmetic mean (standard error)				
Week 8	0.11 (± 0.74)	0.08 (± 0.64)	-0.59 (± 0.38)	
Week 16	-0.85 (± 0.49)	-1.75 (± 0.67)	-0.53 (± 0.49)	

Statistical analyses

Statistical analysis title	Linear Mixed Effects (LME)
Comparison groups	Neflamapimod TID v Neflamapimod BID v Placebo

Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2 [4]
Method	Mixed models analysis

Notes:

[4] - There were no significant differences between treatment groups.

Secondary: Neuropsychiatric Inventory (NPI-10)

End point title	Neuropsychiatric Inventory (NPI-10)

End point description:

Change in Neuropsychiatric Inventory (NPI-10) domains, specifically depression (dysphoria), anxiety, hallucinations, and agitation/aggression, in neflamapimod-treated subjects compared to placebo-recipients. Responses indicating subject has a problem with a particular sub-domain lead to questions of the caregiver rating the frequency of the symptoms on a 4-point scale, severity on a 3-point scale, and the distress the symptoms cause them on a 5-point scale. Secondary efficacy endpoints will utilize the same analysis method and model as the primary endpoint.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Neflamapimod TID	Neflamapimod BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	20	37	
Units: Total Score by Time on Study				
arithmetic mean (standard error)				
Baseline	11.3 (± 2.8)	10.5 (± 1.9)	10.9 (± 1.5)	
Week 4	9.2 (± 2.2)	10 (± 2.2)	8.9 (± 1.5)	
Week 8	7.3 (± 1.9)	8.9 (± 1.8)	9.2 (± 1.6)	
Week 16	7.6 (± 2.0)	10.9 (± 2.4)	11.0 (± 1.9)	

Statistical analyses

Statistical analysis title	Linear Mixed Effects (LME)
Comparison groups	Neflamapimod TID v Neflamapimod BID v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.2 [5]
Method	Mixed models analysis

Notes:

[5] - There were no significant differences between the treatment groups for total NPI-10 score. For hallucinations there was a significant treatment effect (p=0.019,LME for repeated measures) for NFMD 40mg TID vs. placebo. p=0.05 for all NFMD vs. placebo.

Secondary: Timed Up and Go (TUG)

End point title	Timed Up and Go (TUG)

End point description:

Change in Timed Up and Go Test (TUG) to assess mobility (score of >15 seconds indicates subject has increased risk of falls) in neflamapimod-treated subjects compared to placebo-recipients. Secondary efficacy endpoints will utilize the same analysis method and model as the primary endpoint.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Neflamapimod TID	Neflamapimod BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	20	37	
Units: Change from Baseline by Time on Study				
arithmetic mean (standard error)				
Week 8	-0.2 (± 0.5)	1.0 (± 0.9)	0.4 (± 0.4)	
Week 16	-1.4 (± 1.0)	1.3 (± 0.7)	1.5 (± 0.9)	

Statistical analyses

Statistical analysis title	Linear Mixed Effects (LME)
Comparison groups	Neflamapimod TID v Neflamapimod BID v Placebo
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.28 [7]
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-2.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.84
upper limit	-0.28

Notes:

[6] - Change from baseline analyzed by linear mixed effects model for repeated measures. In the comparison of the combined NFMD groups vs. placebo, there was significant reduction in the time required to complete the TUG test (i.e. improvement) with neflamapimod treatment (p=0.04, difference of -1.36 sec, 95% CI -0.04 to -2.69). A significant difference favoring neflamapimod treatment was also noted for the comparison of NFMD TID vs. placebo (p=0.028, difference of –2.56 sec, 95% CI -0.28 to -4.84).

[7] - Comparison of NFMD 40mg TID vs. placebo is reported. For the comparison of the combined NFMD groups vs. placebo, p=0.044.

Secondary: International Shopping List Test (ISLT)

End point title	International Shopping List Test (ISLT)

End point description:

Change in International Shopping List Test (ISLT) immediate and delayed recall and recognition will be used to assess episodic memory in neflamapimod-treated subjects compared to placebo-recipients. Secondary efficacy endpoints will utilize the same analysis method as the primary endpoint.

End point type	Secondary
End point timeframe:	
16 weeks	

End point values	Neflamapimod TID	Neflamapimod BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	20	41	
Units: ISLT immediate recall score				
arithmetic mean (standard error)				
Change from Baseline to Week 4	0.29 (± 1.08)	-1.24 (± 0.61)	0.11 (± 0.54)	
Change from Baseline to Week 8	2.11 (± 1.66)	-0.75 (± 1.37)	0.41 (± 0.65)	
Change from Baseline to Week 16	0.30 (± 1.04)	0.11 (± 0.99)	-0.15 (± 0.46)	

Statistical analyses

Statistical analysis title	Linear Mixed Effects (LME)
Comparison groups	Neflamapimod TID v Neflamapimod BID v Placebo
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2 [8]
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.27
upper limit	1.91

Notes:

[8] - No significant treatment group differences were identified.

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.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Neflamapimod TID
Reporting group description: -	
Reporting group title	Neflamapimod BID
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Neflamapimod TID	Neflamapimod BID	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	3 / 26 (11.54%)	4 / 45 (8.89%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diagnosis of brain tumor			
subjects affected / exposed	0 / 20 (0.00%)	1 / 26 (3.85%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 20 (0.00%)	1 / 26 (3.85%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
New brain lesions of unclear etiology			
subjects affected / exposed	0 / 20 (0.00%)	1 / 26 (3.85%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Intraparenchymal hemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 26 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Blood and lymphatic system disorders			
Internal bleeding			
subjects affected / exposed	0 / 20 (0.00%)	0 / 26 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal disorders			
Hematochezia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 26 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma exacerbation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 26 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Neflamapimod TID	Neflamapimod BID	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 20 (40.00%)	8 / 26 (30.77%)	17 / 45 (37.78%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 20 (5.00%)	5 / 26 (19.23%)	4 / 45 (8.89%)
occurrences (all)	1	5	5
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 20 (15.00%)	1 / 26 (3.85%)	2 / 45 (4.44%)
occurrences (all)	3	1	3
Tremor			

subjects affected / exposed	0 / 20 (0.00%)	0 / 26 (0.00%)	3 / 45 (6.67%)
occurrences (all)	0	0	3
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	3 / 20 (15.00%)	0 / 26 (0.00%)	5 / 45 (11.11%)
occurrences (all)	3	0	5
Nausea			
subjects affected / exposed	1 / 20 (5.00%)	2 / 26 (7.69%)	3 / 45 (6.67%)
occurrences (all)	1	2	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported