



Clinical trial results:

A randomized, double-blind, placebo-controlled, cross-over, multi-center trial in healthy subjects to investigate the effects of lacosamide, pregabalin and tapentadol on biomarkers of pain processing observed by Peripheral Nerve Excitability Testing (NET)

Summary

EudraCT number	2019-000942-36
Trial protocol	BE DK IT
Global end of trial date	25 May 2022

Results information

Result version number	v1
This version publication date	16 July 2023
First version publication date	16 July 2023

Trial information

Trial identification

Sponsor protocol code	IMI2-PainCare-BioPain-RCT1
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus University
Sponsor organisation address	Palle Juul-Jensens Boulevard 165, J109, Aarhus, Denmark, 8200
Public contact	Danish Pain Research Center, Aarhus University, 45 93508575, dprc@clin.au.dk
Scientific contact	Danish Pain Research Center, Aarhus University, 45 93508575, dprc@clin.au.dk

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	09 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 February 2022
Global end of trial reached?	Yes
Global end of trial date	25 May 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

1. To test if the Strength Duration Time Constant (SDTC) changes (at planned first post-dose timing) of large sensory fibers differs in the lacosamide period as compared to the placebo period.
2. To test if the Strength Duration Time Constant (SDTC) changes (at planned first post-dose timing) of large motor fibers differs in the lacosamide period as compared to the placebo period.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the ICH Good Clinical Practice (GCP) guidelines. Local regulatory requirements were followed. Written informed consent was obtained from all subjects. The information interview was conducted in an office without disturbances and interruptions, and there was enough time to give information and discuss possible questions. The subjects were informed that their participation is voluntary, and that they can withdraw from the project at any time.

Background therapy:

-

Evidence for comparator:

-

Actual start date of recruitment	08 July 2020
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	Belgium: 12
Country: Number of subjects enrolled	Denmark: 20
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Italy: 3
Worldwide total number of subjects	43
EEA total number of subjects	43

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)	43
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was performed from July 8, 2020 to February 4, 2022 at 4 centers in Denmark, Belgium, Germany, and Italy. The trial had to be terminated early due operational impact of the Covid-19 pandemic during the past 2 years and as the overall timelines of the project did not allow any further extension of the trial

Pre-assignment

Screening details:

We screened 66 subjects, of which 25 were screened in Denmark, 16 in Belgium, 21 in Germany and 4 in Italy. In total, 43 subjects were enrolled/randomized.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Lacosamide

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Lacosamide
Investigational medicinal product code	N03AX18,
Other name	vimpat
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

composition: 2x 100 mg lacosamide tablets. Single dose.

Arm title	Pregabalin
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	pregabalin
Investigational medicinal product code	N03AX16
Other name	Lyrica
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

2 x 75 mg pregabalin capsules, single dose.

Arm title	Tapentadol
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Tapentadol
Investigational medicinal product code	N02AX06
Other name	Palexia
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2x 50 mg tapentadol immediate release tablet, single dose

Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

2 x hard gelatine capsules filled with mannitol and colloidal silicon dioxide (DAC - Deutscher Arzneimittel Codex). Single dose

Number of subjects in period 1	Lacosamide	Pregabalin	Tapentadol
Started	41	42	41
Completed	41	41	41
Not completed	0	1	0
Received a positive COVID-19 test	-	-	-
Protocol deviation	-	1	-

Number of subjects in period 1	Placebo
Started	42
Completed	41
Not completed	1
Received a positive COVID-19 test	1
Protocol deviation	-

Baseline characteristics

Reporting groups

Reporting group title	Overall study (overall period)
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Reporting group description: -

Reporting group values	Overall study (overall period)	Total	
Number of subjects	43	43	
Age categorical			
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)	43	43	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	25.4		
standard deviation	± 4.49	-	
Gender categorical			
Units: Subjects			
Female	21	21	
Male	22	22	

End points

End points reporting groups

Reporting group title	Lacosamide
Reporting group description: -	
Reporting group title	Pregabalin
Reporting group description: -	
Reporting group title	Tapentadol
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Co-primary: Changes of the Strength Duration Time Constant (SDTC) measured in large sensory fibers on the non-sensitized skin

End point title	Co-primary: Changes of the Strength Duration Time Constant (SDTC) measured in large sensory fibers on the non-sensitized skin
End point description: This co-primary objective is to test if the SDTC changes (at planned first post-dose timing) of large sensory fibers differs in the lacosamide period as compared to the placebo period.	
End point type	Primary
End point timeframe: The first measurement post dosing (i.e. around 1 hour after drug administration) relative to the pre-dose measurement (i.e. difference to period specific baseline)	

End point values	Lacosamide	Pregabalin	Tapentadol	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	37	36	38
Units: ms				
arithmetic mean (standard deviation)	-0.013 ($\pm$ 0.078)	0.045 ($\pm$ 0.079)	0.006 ($\pm$ 0.090)	0.036 ($\pm$ 0.089)

Statistical analyses

Statistical analysis title	Co-primary outcome (sensory) (primary objective)
Statistical analysis description: Changes of the Strength Duration Time Constant (SDTC) measured in large sensory fibers on the non-sensitized skin	
Comparison groups	Placebo v Lacosamide

Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.012
Method	Mixed models for repeated measures
Parameter estimate	Mean difference (final values)
Point estimate	-0.044
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.077
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.017

Notes:

[1] - As this is a cross-over study, the subject in the analysis is not 77 but 38

Statistical analysis title	Co-primary outcome (sensory) (secondary objective)
Statistical analysis description:	
Changes of the Strength Duration Time Constant (SDTC) measured in large sensory fibers on the non-sensitized skin	
Comparison groups	Pregabalin v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	= 0.32
Method	Mixed models for repeated measures
Parameter estimate	Mean difference (final values)
Point estimate	0.017
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.017
upper limit	0.051
Variability estimate	Standard error of the mean
Dispersion value	0.017

Notes:

[2] - As this is a cross-over study, the subject in the analysis is not 75 but 37

Statistical analysis title	Co-primary outcome (sensory) (secondary objective)
Statistical analysis description:	
Changes of the Strength Duration Time Constant (SDTC) measured in large sensory fibers on the non-sensitized skin	
Comparison groups	Tapentadol v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	= 0.27
Method	Mixed models for repeated measures
Parameter estimate	Mean difference (final values)
Point estimate	-0.019

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.054
upper limit	0.015
Variability estimate	Standard error of the mean
Dispersion value	0.017

Notes:

[3] - As this is a cross-over study, the subject in the analysis is not 74 but 36

Primary: Co-primary: Changes of the Strength Duration Time Constant (SDTC) measured in large motor fibers on the non-sensitized skin

End point title	Co-primary: Changes of the Strength Duration Time Constant (SDTC) measured in large motor fibers on the non-sensitized skin
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End point description:

End point type	Primary
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End point timeframe:

At the planned first PD time point post dosing relative to their pre-dose PD measurement (i.e. difference to period specific baseline).

End point values	Lacosamide	Pregabalin	Tapentadol	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	39	39	39
Units: ms				
arithmetic mean (standard deviation)	0.008 (± 0.067)	0.023 (± 0.092)	0.004 (± 0.12)	0.043 (± 0.076)

Statistical analyses

Statistical analysis title	Co-primary outcome (motor) (primary objective)
Comparison groups	Lacosamide v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority ^[4]
P-value	= 0.062
Method	Mixed models for repeated measures
Parameter estimate	Mean difference (final values)
Point estimate	-0.034
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	0.002
Variability estimate	Standard error of the mean
Dispersion value	0.018

Notes:

[4] - Since this is a cross-over study the subjects in this analysis is not 79 but 39.

Statistical analysis title	Co-primary outcome (motor) (secondary objective)
Comparison groups	Pregabalin v Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority ^[5]
P-value	= 0.27
Method	Mixed models for repeated measures
Parameter estimate	Mean difference (net)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.056
upper limit	0.016
Variability estimate	Standard error of the mean
Dispersion value	0.018

Notes:

[5] - As this is a cross-over study, the subject in the analysis is not 78 but 39

Statistical analysis title	Co-primary outcome (motor) (secondary objective)
Comparison groups	Tapentadol v Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority ^[6]
P-value	= 0.12
Method	Mixed models for repeated measures
Parameter estimate	Mean difference (final values)
Point estimate	-0.028
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.064
upper limit	0.008
Variability estimate	Standard error of the mean
Dispersion value	0.018

Notes:

[6] - As this is a cross-over study, the subject in the analysis is not 78 but 39

Secondary: Secondary: Changes of the Strength Duration Time Constant (SDTC) measured in small sensory fibers on the sensitized skin

End point title	Secondary: Changes of the Strength Duration Time Constant (SDTC) measured in small sensory fibers on the sensitized skin
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End point description:

End point type	Secondary
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End point timeframe:

At the planned first PD time point post dosing relative to their pre-dose PD measurement (i.e. difference

to period specific baseline).

End point values	Lacosamide	Pregabalin	Tapentadol	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	30	34
Units: ms				
arithmetic mean (standard deviation)	0.036 ($\pm$ 0.26)	-0.127 ($\pm$ 0.24)	-0.039 ($\pm$ 0.26)	-0.118 ($\pm$ 0.31)

Statistical analyses

Statistical analysis title	Secondary outcome (primary objective)
Comparison groups	Lacosamide v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority ^[7]
P-value	= 0.143
Method	Mixed models for repeated measures
Parameter estimate	Mean difference (final values)
Point estimate	0.092
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.032
upper limit	0.217
Variability estimate	Standard error of the mean
Dispersion value	0.063

Notes:

[7] - Since this a cross-over study, the subjects in this analysis is not 63 but 29

Statistical analysis title	Secondary outcome (secondary objective)
Comparison groups	Pregabalin v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority ^[8]
P-value	= 0.65
Method	Mixed models for repeated measures
Parameter estimate	Mean difference (net)
Point estimate	-0.028
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.094
Variability estimate	Standard error of the mean
Dispersion value	0.062

Notes:

[8] - As this is a cross-over study, the subject in the analysis is not 64 but 30

Statistical analysis title	Secondary outcome (secondary objective)
Comparison groups	Tapentadol v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority ^[9]
P-value	= 0.7
Method	Mixed models for repeated measures
Parameter estimate	Mean difference (net)
Point estimate	0.024
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.099
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.062

Notes:

[9] - As this is a cross-over study, the subject in the analysis is not 64 but 30

Secondary: Secondary: Changes of the Strength Duration Time Constant (SDTC) measured in small sensory fibers on the non-sensitized skin

End point title	Secondary: Changes of the Strength Duration Time Constant (SDTC) measured in small sensory fibers on the non-sensitized skin
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End point description:

End point type	Secondary
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End point timeframe:

The first measurement post dosing (i.e. around 1 hour after drug administration) relative to the pre-dose measurement (i.e. difference to period specific baseline)

End point values	Lacosamide	Pregabalin	Tapentadol	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	29	32	32
Units: ms				
arithmetic mean (standard deviation)	0.003 (± 0.27)	0.024 (± 0.24)	-0.004 (± 0.21)	-0.012 (± 0.27)

Statistical analyses

Statistical analysis title	Secondary outcome (primary objective)
Comparison groups	Lacosamide v Placebo

Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority ^[10]
P-value	= 0.68
Method	Mixed models for repeated measures
Parameter estimate	Mean difference (final values)
Point estimate	-0.019
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.073
Variability estimate	Standard error of the mean
Dispersion value	0.047

Notes:

[10] - Since this a cross-over study, the subjects in this analysis is not 65 but 33

Statistical analysis title	Secondary outcome (secondary objective)
Comparison groups	Pregabalin v Placebo
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority ^[11]
P-value	= 0.77
Method	Mixed models for repeated measures
Parameter estimate	Mean difference (final values)
Point estimate	0.014
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.109
Variability estimate	Standard error of the mean
Dispersion value	0.048

Notes:

[11] - As this is a cross-over study, the subject in the analysis is not 61 but 29

Statistical analysis title	Secondary outcome (secondary objective)
Comparison groups	Tapentadol v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority ^[12]
P-value	= 0.92
Method	Mixed models for repeated measures
Parameter estimate	Mean difference (final values)
Point estimate	0.005
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.088
upper limit	0.098

Variability estimate	Standard error of the mean
Dispersion value	0.047

Notes:

[12] - As this is a cross-over study, the subject in the analysis is not 64 but 32

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From study period 1 to 7-14 days after last study period

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25
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Reporting groups

Reporting group title	Lacosamide
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Reporting group description: -

Reporting group title	Pregabalin
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Reporting group description: -

Reporting group title	Tapentadol
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Lacosamide	Pregabalin	Tapentadol
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	0 / 41 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 42 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Lacosamide	Pregabalin	Tapentadol
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 41 (29.27%)	20 / 42 (47.62%)	30 / 41 (73.17%)
Nervous system disorders			

Dizziness			
subjects affected / exposed	3 / 41 (7.32%)	13 / 42 (30.95%)	22 / 41 (53.66%)
occurrences (all)	3	13	22
Cramp-fasciculation syndrome	Additional description: Jaw cramp and muscle cramp		
subjects affected / exposed	0 / 41 (0.00%)	2 / 42 (4.76%)	1 / 41 (2.44%)
occurrences (all)	0	2	1
Somnolence			
subjects affected / exposed	3 / 41 (7.32%)	8 / 42 (19.05%)	7 / 41 (17.07%)
occurrences (all)	3	8	7
Headache			
subjects affected / exposed	0 / 41 (0.00%)	2 / 42 (4.76%)	3 / 41 (7.32%)
occurrences (all)	0	2	3
Hyperacusis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Hypoaesthesia oral			
subjects affected / exposed	2 / 41 (4.88%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Balance disorder			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 41 (0.00%)	0 / 42 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Presyncope	Additional description: Lightheadedness		
subjects affected / exposed	1 / 41 (2.44%)	2 / 42 (4.76%)	2 / 41 (4.88%)
occurrences (all)	1	2	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 41 (7.32%)	7 / 42 (16.67%)	7 / 41 (17.07%)
occurrences (all)	3	7	7
Peripheral coldness			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Eye disorders			

Visual impairment subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	1 / 42 (2.38%) 1	0 / 41 (0.00%) 0
Asthenopia subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1	0 / 42 (0.00%) 0	1 / 41 (2.44%) 1
Gastrointestinal disorders			
Vomiting subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	0 / 42 (0.00%) 0	5 / 41 (12.20%) 5
Dry mouth subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3	3 / 42 (7.14%) 3	8 / 41 (19.51%) 8
Nausea subjects affected / exposed occurrences (all)	5 / 41 (12.20%) 5	2 / 42 (4.76%) 2	7 / 41 (17.07%) 7
Abdominal pain subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	1 / 42 (2.38%) 1	0 / 41 (0.00%) 0
Skin and subcutaneous tissue disorders			
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	0 / 42 (0.00%) 0	3 / 41 (7.32%) 3
Psychiatric disorders			
Disturbance in attention subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	1 / 42 (2.38%) 1	2 / 41 (4.88%) 2
Euphoric mood subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	2 / 42 (4.76%) 2	1 / 41 (2.44%) 1

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 42 (7.14%)		
Nervous system disorders			
Dizziness			

subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Cramp-fasciculation syndrome	Additional description: Jaw cramp and muscle cramp		
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hyperacusis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hypoaesthesia oral			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Balance disorder			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Presyncope	Additional description: Lightheadedness		
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Peripheral coldness			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Eye disorders			

Visual impairment subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Asthenopia subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Dry mouth subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Abdominal pain subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Psychiatric disorders Disturbance in attention subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Euphoric mood subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Intermittent interruptions due to COVID-19 lockdown

Notes: