EU Clinical Trials Register

Clinical trial results:
Interventional, Open-label, Fixed-dose Multiple Administration Study to Evaluate Long-term Treatment With Eptinezumab in Patients With Chronic Cluster Headache

Summary

EudraCT number	2020-001968-28
Trial protocol	DE DK NL FI ES IT
Global end of trial date	29 June 2023

Results information

Result version number	v1 (current)
This version publication date	10 July 2024
First version publication date	10 July 2024

Trial information

Trial identification

Sponsor protocol code	19385A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05064397
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark, 2500
Public contact	Email contact via H. Lundbeck A/S, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@Lundbeck.com
Scientific contact	Email contact via H. Lundbeck A/S, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@Lundbeck.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	29 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main goal of this trial was to inform about long-term safety and tolerability of eptinezumab in participants with chronic cluster headache.

Protection of trial subjects:

This trial was conducted in compliance with Good Clinical Practice and in accordance with the ethical principles described in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 September 2021
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	Germany: 2
Country: Number of subjects enrolled	Denmark: 19
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Finland: 4
Country: Number of subjects enrolled	France: 51
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Italy: 26
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	131
EEA total number of subjects	125

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	127
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

131 participants were enrolled in 9 countries.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Eptinezumab

Arm description:

Participants received 4 intravenous (IV) infusions of 400 milligrams (mg) eptinezumab at Baseline (Day 0) and at the end of Weeks 12, 24, and 36.

Arm type	Experimental
Investigational medicinal product name	Eptinezumab
Investigational medicinal product code	
Other name	Vyepti
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eptinezumab was administered per schedule specified in the arm description.

Number of subjects in period 1	Eptinezumab
Started	131
Received at least 1 dose of study drug	131
Completed	108
Not completed	23
Consent withdrawn by subject	3
Adverse event, non-fatal	4
Other reasons	3
Lost to follow-up	1
Lack of efficacy	12

Baseline characteristics

Reporting groups

Reporting group title	Eptinezumab

Reporting group description:

Participants received 4 intravenous (IV) infusions of 400 milligrams (mg) eptinezumab at Baseline (Day 0) and at the end of Weeks 12, 24, and 36.

Reporting group values	Eptinezumab	Total	
Number of subjects	131	131	
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)	127	127	
From 65-84 years	4	4	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	45.2		
standard deviation	± 10.79	-	
Sex: Female, Male			
Units: participants			
Female	47	47	
Male	84	84	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	76	76	
More than one race	4	4	
Unknown or Not Reported	51	51	

End points

End points reporting groups

Reporting group title	Eptinezumab
Reporting group description:	

Participants received 4 intravenous (IV) infusions of 400 milligrams (mg) eptinezumab at Baseline (Day 0) and at the end of Weeks 12, 24, and 36.

Primary: Number of Participants With Treatment-emergent Adverse Events (AEs)

End point title	Number of Participants With Treatment-emergent Adverse Events (AEs)[1]
End point description:	

A treatment-emergent AE was defined as any on-treatment untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A summary of non-serious AEs and all serious AEs, regardless of causality is located in Reported AE section. Measured in the all-participants-treated set (APTS), which included all participants who received infusion with eptinezumab.

End point type	Primary
End point timeframe:	

From the day of first dose of study drug (Baseline [Week 0]) up to Week 56

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: Only summary statistics were planned for this endpoint.

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: participants	106			

Statistical analyses

No statistical analyses for this end point

Secondary: Conversion From Chronic Cluster Headache (cCH) to Episodic Cluster Headache (eCH): Number of Participants With No Cluster Headache (CH) Attacks for ≥3 Consecutive Months (≥12 consecutive weeks)

End point title	Conversion From Chronic Cluster Headache (cCH) to Episodic Cluster Headache (eCH): Number of Participants With No Cluster Headache (CH) Attacks for ≥3 Consecutive Months (≥12 consecutive weeks)
End point description:	

Participants counted as converting from cCH to eCH if they had no CH attacks for at least 3 months. The Full Analysis Set (FAS) included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary
End point timeframe:	

Week 1 to Week 48

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: participants	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Number of Times an Abortive Therapy (Oxygen and/or Triptans) Was Used

End point title	Change From Baseline in Weekly Number of Times an Abortive Therapy (Oxygen and/or Triptans) Was Used

End point description:

Abortive therapy was defined as oxygen and/or triptans, where it counted as 2 times if oxygen and triptans were used for the same attack. The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 1, 2, 3, 4, 13, 14, 15, 16, 25, 26, 27, 28, 37, 38, 39, 40

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	127			
Units: Abortive therapy use per week				
least squares mean (standard error)				
Week 1	-3.63 (± 0.53)			
Week 2	-4.24 (± 0.70)			
Week 3	-4.90 (± 0.76)			
Week 4	-4.99 (± 0.94)			
Week 13	-7.22 (± 0.84)			
Week 14	-6.83 (± 0.85)			
Week 15	-6.06 (± 0.84)			
Week 16	-6.42 (± 0.96)			
Week 25	-6.18 (± 0.99)			
Week 26	-6.56 (± 0.86)			
Week 27	-7.56 (± 0.82)			
Week 28	-7.12 (± 0.83)			
Week 37	-6.55 (± 0.98)			
Week 38	-6.97 (± 0.84)			
Week 39	-6.71 (± 1.04)			
Week 40	-7.09 (± 0.84)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Number of Times An Abortive Therapy (Oxygen) Was Used

End point title	Change From Baseline in Weekly Number of Times An Abortive Therapy (Oxygen) Was Used
End point description:	
The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.	
End point type	Secondary
End point timeframe:	
Baseline (Week 0), Weeks 1, 2, 3, 4, 13, 14, 15, 16, 25, 26, 27, 28, 37, 38, 39, 40	

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	127			
Units: Oxygen use per week				
least squares mean (standard error)				
Week 1	-1.72 (± 0.33)			
Week 2	-2.43 (± 0.40)			
Week 3	-3.17 (± 0.48)			
Week 4	-3.23 (± 0.59)			
Week 13	-3.97 (± 0.57)			
Week 14	-3.93 (± 0.56)			
Week 15	-3.09 (± 0.53)			
Week 16	-3.78 (± 0.61)			
Week 25	-3.56 (± 0.67)			
Week 26	-3.75 (± 0.58)			
Week 27	-4.06 (± 0.52)			
Week 28	-4.02 (± 0.54)			
Week 37	-3.60 (± 0.64)			
Week 38	-3.74 (± 0.52)			
Week 39	-3.99 (± 0.66)			
Week 40	-3.82 (± 0.55)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Number of Times An Abortive Therapy (Triptans) Were Used

End point title	Change From Baseline in Weekly Number of Times An Abortive Therapy (Triptans) Were Used
End point description:	
The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.	
End point type	Secondary
End point timeframe:	
Baseline (Week 0), Weeks 1, 2, 3, 4, 13, 14, 15, 16, 25, 26, 27, 28, 37, 38, 39, 40	

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	127			
Units: Triptans use per week				
least squares mean (standard error)				
Week 1	-1.75 (± 0.33)			
Week 2	-1.73 (± 0.42)			
Week 3	-1.74 (± 0.44)			
Week 4	-1.90 (± 0.45)			
Week 13	-2.94 (± 0.46)			
Week 14	-2.78 (± 0.50)			
Week 15	-2.81 (± 0.49)			
Week 16	-2.50 (± 0.51)			
Week 25	-2.05 (± 0.52)			
Week 26	-2.48 (± 0.48)			
Week 27	-3.06 (± 0.45)			
Week 28	-2.86 (± 0.46)			
Week 37	-2.55 (± 0.50)			
Week 38	-2.54 (± 0.49)			
Week 39	-2.52 (± 0.58)			
Week 40	-2.95 (± 0.54)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Average Number of Weekly Attacks

End point title	Change From Baseline in the Average Number of Weekly Attacks
End point description:	
The participant completed a CH eDiary, daily, and record for each day/week whether he/she had any CH attacks. The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.	
End point type	Secondary
End point timeframe:	
Baseline (Week 0), Weeks 1, 2, 3, 4, 13, 14, 15, 16, 25, 26, 27, 28, 37, 38, 39, 40	

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	127			
Units: Attacks per week				
least squares mean (standard error)				
Week 1	-3.00 (± 0.54)			
Week 2	-3.92 (± 0.79)			
Week 3	-4.51 (± 0.93)			
Week 4	-4.98 (± 1.18)			
Week 13	-6.18 (± 1.20)			
Week 14	-6.31 (± 1.15)			
Week 15	-5.81 (± 1.08)			
Week 16	-6.63 (± 1.24)			
Week 25	-5.56 (± 1.26)			
Week 26	-5.95 (± 1.27)			
Week 27	-7.09 (± 1.22)			
Week 28	-6.51 (± 1.31)			
Week 37	-6.25 (± 1.27)			
Week 38	-6.57 (± 1.14)			
Week 39	-5.99 (± 1.23)			
Week 40	-6.39 (± 1.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Number of Weekly Attacks (Weeks 1-4)

End point title	Change from Baseline in the Number of Weekly Attacks (Weeks 1-4)
End point description:	
The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.	
End point type	Secondary
End point timeframe:	
Baseline (Week 0), Weeks 1-4	

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	127			
Units: Attacks per week				
least squares mean (standard error)	-4.11 (± 0.79)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Number of Weekly Attacks (Weeks 1-2)

End point title	Change from Baseline in the Number of Weekly Attacks (Weeks 1-2)
End point description:	
The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.	
End point type	Secondary
End point timeframe:	
Baseline (Week 0), Weeks 1-2	

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	127			
Units: Attacks per week				
least squares mean (standard error)	-3.46 (± 0.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Number of Monthly Attacks

End point title	Change from Baseline in the Number of Monthly Attacks
End point description:	
The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.	
End point type	Secondary
End point timeframe:	
Baseline (Week 0), Months 1-12	

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	129			
Units: Attacks per month				
least squares mean (standard error)	-22.65 (± 4.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Average Attack Related Daily Pain (including days with no attacks), as Assessed Using the 5-point Self-rating Pain Severity Scale

End point title	Change from Baseline in the Average Attack Related Daily Pain (including days with no attacks), as Assessed Using the 5-point Self-rating Pain Severity Scale

End point description:

The severity of pain for each attack was rated on an ordinal scale that ranged from 0 to 4 with higher scores indicating more headache pain (headache pain ratings: 0 = none/barely any pain; 1 = mild; 2 = moderate; 3 = severe; 4 = excruciating). The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 1, 2, 3, 4, 13, 14, 15, 16, 25, 26, 27, 28, 37, 38, 39, 40

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	127			
Units: score on a scale				
least squares mean (standard error)				
Week 1	-0.47 (± 0.06)			
Week 2	-0.51 (± 0.07)			
Week 3	-0.58 (± 0.07)			
Week 4	-0.59 (± 0.08)			
Week 13	-0.78 (± 0.09)			
Week 14	-0.75 (± 0.09)			
Week 15	-0.82 (± 0.08)			
Week 16	-0.90 (± 0.09)			
Week 25	-0.80 (± 0.09)			
Week 26	-0.79 (± 0.09)			
Week 27	-0.88 (± 0.09)			
Week 28	-0.84 (± 0.09)			
Week 37	-0.77 (± 0.09)			
Week 38	-0.79 (± 0.10)			
Week 39	-0.70 (± 0.10)			
Week 40	-0.79 (± 0.10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Response: Number of Participants With ≥30% Reduction From Baseline in Number of Weekly Attacks

End point title	Response: Number of Participants With ≥30% Reduction From Baseline in Number of Weekly Attacks

End point description:

The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 1, 2, 3, 4, 13, 14, 15, 16, 25, 26, 27, 28, 37, 38, 39, 40

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	127			
Units: participants				
Week 1	49			
Week 2	52			
Week 3	55			
Week 4	55			
Week 13	54			
Week 14	63			
Week 15	58			
Week 16	62			
Week 25	60			
Week 26	60			
Week 27	62			
Week 28	48			
Week 37	57			
Week 38	51			
Week 39	43			
Week 40	44			

Statistical analyses

No statistical analyses for this end point

Secondary: Response: Number of Participants With ≥50% Reduction From Baseline in Number of Weekly Attacks

End point title	Response: Number of Participants With ≥50% Reduction From Baseline in Number of Weekly Attacks
End point description:	
The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.	
End point type	Secondary
End point timeframe:	
Baseline (Week 0), Weeks 1, 2, 3, 4, 13, 14, 15, 16, 25, 26, 27, 28, 37, 38, 39, 40	

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	127			
Units: participants				
Week 1	30			
Week 2	36			
Week 3	42			
Week 4	40			
Week 13	35			
Week 14	45			
Week 15	43			
Week 16	48			
Week 25	43			
Week 26	45			
Week 27	45			
Week 28	39			
Week 37	40			
Week 38	41			
Week 39	34			
Week 40	38			

Statistical analyses

No statistical analyses for this end point

Secondary: Response: Number of Participants With ≥75% Reduction From Baseline in Number of Weekly Attacks

End point title	Response: Number of Participants With ≥75% Reduction From Baseline in Number of Weekly Attacks
End point description:	
The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.	
End point type	Secondary
End point timeframe:	
Baseline (Week 0), Weeks 1, 2, 3, 4, 13, 14, 15, 16, 25, 26, 27, 28, 37, 38, 39, 40	

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	127			
Units: participants				
Week 1	11			
Week 2	13			
Week 3	21			
Week 4	20			
Week 13	23			
Week 14	25			
Week 15	23			
Week 16	29			
Week 25	29			
Week 26	24			
Week 27	28			
Week 28	24			
Week 37	27			
Week 38	28			
Week 39	21			
Week 40	25			

Statistical analyses

No statistical analyses for this end point

Secondary: cCH Remission: Number of Participants With No Cluster Headache Attacks For ≥1 Month (>=4 Consecutive Weeks)

End point title	cCH Remission: Number of Participants With No Cluster Headache Attacks For ≥1 Month (>=4 Consecutive Weeks)

End point description:

Participants counted as being in remission if they had no cluster headache attacks for at least 1 month. The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Week 1 to Week 48

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: participants	19			

Statistical analyses

No statistical analyses for this end point

Secondary: cCH Remission: Number of Participants With No Cluster Headache Attacks For ≥1 Month (>=4 Consecutive Weeks between the First and Second Infusion)

End point title	cCH Remission: Number of Participants With No Cluster Headache Attacks For ≥1 Month (>=4 Consecutive Weeks between the First and Second Infusion)

End point description:

The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Week 1 to Week 12

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	129			
Units: participants	8			

Statistical analyses

No statistical analyses for this end point

Secondary: cCH Remission: Number of Participants With No Cluster Headache Attacks For ≥1 Month (>=4 Consecutive Weeks between the Second and Third Infusion)

End point title	cCH Remission: Number of Participants With No Cluster Headache Attacks For ≥1 Month (>=4 Consecutive Weeks between the Second and Third Infusion)

End point description:

The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Week 13 to Week 24

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: participants	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression of Change (PGIC) Score

End point title	Patient Global Impression of Change (PGIC) Score

End point description:

The PGIC is a patient-reported measure of improvement in pain sensation and quality of life scored on a scale from 1 (very much improved) to 7 (very much worse). Lower scores indicate better health status. The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: score on a scale				
least squares mean (standard error)				
Week 4	2.74 (± 0.12)			
Week 8	2.69 (± 0.13)			
Week 12	2.69 (± 0.13)			
Week 16	2.58 (± 0.13)			
Week 20	2.72 (± 0.14)			
Week 24	2.58 (± 0.13)			
Week 28	2.54 (± 0.13)			
Week 32	2.64 (± 0.13)			
Week 36	2.58 (± 0.12)			
Week 40	2.73 (± 0.14)			
Week 44	2.67 (± 0.13)			
Week 48	2.65 (± 0.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: cCH Remission: Number of Participants With No Cluster Headache Attacks For ≥1 Month (>=4 Consecutive Weeks Between the Third and Fourth

Infusion)

End point title	cCH Remission: Number of Participants With No Cluster Headache Attacks For ≥1 Month (>=4 Consecutive Weeks Between the Third and Fourth Infusion)

End point description:

The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Week 25 to Week 36

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	111			
Units: participants	9			

Statistical analyses

No statistical analyses for this end point

Secondary: cCH Remission: Number of Participants With No Cluster Headache Attacks For ≥1 Month (>=4 Consecutive Weeks Within the First 12 Weeks After the Fourth Infusion)

End point title	cCH Remission: Number of Participants With No Cluster Headache Attacks For ≥1 Month (>=4 Consecutive Weeks Within the First 12 Weeks After the Fourth Infusion)

End point description:

The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Week 37 to Week 48

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	104			
Units: participants	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Received a Transitional Therapy During the Treatment Period

End point title	Number of Participants who Received a Transitional Therapy During the Treatment Period
End point description:	
Transitional treatments were defined as greater occipital nerve (GON) block or oral steroids. The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.	
End point type	Secondary
End point timeframe:	
Week 1 to Week 48	

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: participants	17			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Sleep Impact Scale (SIS) Domain Scores Over the Time

End point title	Change From Baseline in Sleep Impact Scale (SIS) Domain Scores Over the Time
End point description:	
The SIS is a patient-reported clinical outcome assessment used to assess quality of life resulting from sleep disturbance. The SIS questionnaire includes 35 items belonging to 7 domains to assess sleep impact on: daily activities (5 items); emotional well-being (4 items); emotional impact (4 items); energy/fatigue (5 items); social well-being (6 items); mental fatigue (3 items); and satisfaction with sleep (8 items). Each item, for 6 out of the 7 domains, is rated on a 5-point scale ranging from 1 (always or all of the time) to 5 (never or none of the time), whereas satisfaction with sleep is rated on a 5-point scale ranging from 1 (very satisfied) to 5 (very dissatisfied). Each domain yields a score ranging from 0 to 100; items within each domain are summed and transformed using a formula. A higher score indicates better quality of life (reverse scoring for the satisfaction with sleep domain).	
End point type	Secondary
End point timeframe:	
Baseline (Week 0), Weeks 4, 12, 16, 24, 28, 36, 40, 48	

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	109			
Units: score on a scale				
arithmetic mean (standard deviation)				
Daily Activities - Week 4	14.98 (± 2.05)			
Daily Activities - Week 12	15.26 (± 2.36)			

Daily Activities - Week 16	16.36 (± 2.48)				
Daily Activities - Week 24	15.54 (± 2.33)				
Daily Activities - Week 28	16.17 (± 2.42)				
Daily Activities - Week 36	14.51 (± 2.39)				
Daily Activities - Week 40	17.83 (± 2.15)				
Daily Activities - Week 48	13.29 (± 2.34)				
Emotional Well-being - Week 4	17.63 (± 2.19)				
Emotional Well-being - Week 12	16.28 (± 2.32)				
Emotional Well-being - Week 16	15.72 (± 2.37)				
Emotional Well-being - Week 24	14.04 (± 2.47)				
Emotional Well-being - Week 28	17.98 (± 2.51)				
Emotional Well-being - Week 36	15.75 (± 2.34)				
Emotional Well-being - Week 40	15.40 (± 2.35)				
Emotional Well-being - Week 48	14.61 (± 2.53)				
Emotional Impact - Week 4	17.41 (± 2.42)				
Emotional Impact - Week 12	17.00 (± 2.48)				
Emotional Impact - Week 16	18.34 (± 2.59)				
Emotional Impact - Week 24	17.01 (± 2.42)				
Emotional Impact - Week 28	20.78 (± 2.53)				
Emotional Impact - Week 36	16.53 (± 2.53)				
Emotional Impact - Week 40	17.21 (± 2.57)				
Emotional Impact - Week 48	15.61 (± 2.58)				
Energy/Fatigue - Week 4	16.00 (± 2.35)				
Energy/Fatigue - Week 12	16.67 (± 2.50)				
Energy/Fatigue - Week 16	16.87 (± 2.63)				
Energy/Fatigue - Week 24	16.59 (± 2.71)				
Energy/Fatigue - Week 28	19.67 (± 2.73)				
Energy/Fatigue - Week 36	15.93 (± 2.62)				
Energy/Fatigue - Week 40	19.16 (± 2.53)				
Energy/Fatigue - Week 48	17.65 (± 2.62)				
Social Well-being - Week 4	14.73 (± 2.06)				
Social Well-being - Week 12	15.28 (± 2.31)				
Social Well-being - Week 16	14.68 (± 2.55)				
Social Well-being - Week 24	14.59 (± 2.46)				
Social Well-being - Week 28	17.30 (± 2.64)				
Social Well-being - Week 36	13.27 (± 2.43)				
Social Well-being - Week 40	15.59 (± 2.42)				
Social Well-being - Week 48	14.13 (± 2.59)				
Mental Fatigue - Week 4	13.00 (± 2.23)				
Mental Fatigue - Week 12	15.00 (± 2.34)				
Mental Fatigue - Week 16	15.15 (± 2.27)				
Mental Fatigue - Week 24	13.57 (± 2.39)				
Mental Fatigue - Week 28	14.86 (± 2.36)				
Mental Fatigue - Week 36	13.64 (± 2.49)				
Mental Fatigue - Week 40	13.98 (± 2.39)				
Mental Fatigue - Week 48	13.55 (± 2.42)				
Satisfaction With Sleep - Week 4	-13.86 (± 2.25)				
Satisfaction With Sleep - Week 12	-13.47 (± 2.29)				
Satisfaction With Sleep - Week 16	-14.50 (± 2.40)				

Satisfaction With Sleep - Week 24	-12.30 (± 2.20)			
Satisfaction With Sleep - Week 28	-16.67 (± 2.39)			
Satisfaction With Sleep - Week 36	-13.95 (± 2.43)			
Satisfaction With Sleep - Week 40	-14.99 (± 2.60)			
Satisfaction With Sleep - Week 48	-14.19 (± 2.59)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EuroQol 5-Dimension 5-Level (EQ-5D-5L) Score at Weeks 4, 16, 28, 40 and 48

End point title	Change From Baseline in EuroQol 5-Dimension 5-Level (EQ-5D-5L) Score at Weeks 4, 16, 28, 40 and 48

End point description:

The EQ-5D-5L is a patient-reported assessment designed to measure the participant's well-being. It consists of 5 descriptive items (mobility, self-care, usual activities, pain/discomfort, and depression/anxiety). Each descriptive item is rated on a 5-point index ranging from 1 (no problems) to 5 (extreme problems). The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks. The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 4, 16, 28, 40, 48

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: score on a scale				
arithmetic mean (standard deviation)				
Mobility - Week 4	0.1 (± 0.89)			
Self Care - Week 4	0.0 (± 0.47)			
Usual Activities - Week 4	-0.2 (± 1.13)			
Pain/Discomfort - Week 4	-0.1 (± 1.28)			
Anxiety/Depression - Week 4	-0.1 (± 0.70)			
Mobility - Week 16	0.1 (± 1.02)			
Self Care - Week 16	0.0 (± 0.69)			
Usual Activities - Week 16	-0.2 (± 1.07)			
Pain/Discomfort - Week 16	-0.2 (± 1.48)			
Anxiety/Depression - Week 16	-0.1 (± 0.98)			
Mobility - Week 28	0.1 (± 0.92)			
Self Care - Week 28	0.1 (± 0.65)			
Usual Activities - Week 28	-0.1 (± 1.14)			
Pain/Discomfort - Week 28	-0.1 (± 1.26)			

Anxiety/Depression - Week 28	-0.1 (± 0.98)			
Mobility - Week 40	0.0 (± 0.96)			
Self Care - Week 40	0.0 (± 0.49)			
Usual Activities - Week 40	-0.4 (± 1.04)			
Pain/Discomfort - Week 40	-0.3 (± 1.42)			
Anxiety/Depression - Week 40	-0.1 (± 0.97)			
Mobility - Week 48	-0.0 (± 0.90)			
Self Care - Week 48	0.0 (± 0.53)			
Usual Activities - Week 48	-0.2 (± 1.17)			
Pain/Discomfort - Week 48	-0.1 (± 1.24)			
Anxiety/Depression - Week 48	-0.0 (± 1.04)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Work Productivity Activity Impairment: General Health Second Version (WPAI:GH2.0) Sub-Scores (Absenteeism, Presenteeism, Work Productivity Loss, Activity Impairment) at Weeks 4, 16, 28, 40 and 48

End point title	Change From Baseline in the Work Productivity Activity Impairment: General Health Second Version (WPAI:GH2.0) Sub-Scores (Absenteeism, Presenteeism, Work Productivity Loss, Activity Impairment) at Weeks 4, 16, 28, 40 and 48

End point description:

The WPAI:GH2.0 is a patient self-rated clinical outcome assessment designed to provide a quantitative measure of the work productivity and activity impairment due to a health condition. The WPAI:GH2.0 assesses activities over the preceding 7 days and consists of 6 items: 1 item assesses employment (yes/no); 3 items assess the number of hours worked, the number of hours missed from work due to the participant's condition, or due to other reasons; and 2 visual numerical scales assess how much the participant's condition affects his/her productivity at work and his/her ability to complete normal daily activities. Scores were calculated as impairment percentages (0-100%), with higher numbers indicating greater impairment and less productivity, i.e, worse outcomes. The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 4, 16, 28, 40, 48

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	95			
Units: score on a scale				
arithmetic mean (standard deviation)				
Absenteeism - Week 4	-12.03 (± 2.82)			
Absenteeism - Week 16	-8.19 (± 2.98)			
Absenteeism - Week 28	-12.73 (± 1.70)			
Absenteeism - Week 40	-12.05 (± 2.29)			

Absenteeism - Week 48	-5.30 (± 2.99)
Presenteeism - Week 4	-14.29 (± 3.23)
Presenteeism - Week 16	-14.54 (± 3.74)
Presenteeism - Week 28	-11.86 (± 3.78)
Presenteeism - Week 40	-9.88 (± 3.58)
Presenteeism - Week 48	-12.70 (± 3.53)
Work productivity loss - Week 4	-17.28 (± 3.34)
Work productivity loss - Week 16	-16.53 (± 3.98)
Work productivity loss - Week 28	-14.60 (± 3.96)
Work productivity loss - Week 40	-12.50 (± 3.78)
Work productivity loss - Week 48	-12.16 (± 3.77)
Activity impairment - Week 4	-15.99 (± 2.56)
Activity impairment - Week 16	-15.64 (± 2.84)
Activity impairment - Week 28	-17.37 (± 2.74)
Activity impairment - Week 40	-18.73 (± 2.79)
Activity impairment - Week 48	-14.35 (± 2.95)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the EQ-5D-5L Visual Analog Scale (VAS) Score at Weeks 4, 16, 28, 40 and 48

End point title	Change from Baseline in the EQ-5D-5L Visual Analog Scale (VAS) Score at Weeks 4, 16, 28, 40 and 48

End point description:

The EQ-5D-5L VAS is a participant-reported assessment designed to measure the participant's well-being and ranges from 0 (worst imaginable health state) to 100 (best imaginable health state). The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 4, 16, 28, 40, 48

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: score on a scale				
least squares mean (standard error)				
Week 4	9.03 (± 2.07)			
Week 16	9.26 (± 2.30)			
Week 28	6.99 (± 2.39)			
Week 40	8.61 (± 2.11)			
Week 48	6.90 (± 2.31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization - Number of visits to a family doctor/general practitioner

End point title	Health Care Resource Utilization - Number of visits to a family doctor/general practitioner

End point description:

Number of participants who visited a family doctor/general practitioner has been reported. The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 4, 16, 28, 40, 48

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: participants				
Week 0 - 0 visits	81			
Week 0 - 1 visit	18			
Week 0 - 2 visits	10			
Week 0 - 3 visits	1			
Week 0 - 4 visits	2			
Week 4 - 0 visits	82			
Week 4 - 1 visit	17			
Week 4 - 2 visits	5			
Week 4 - 3 visits	1			
Week 16 - 0 visits	80			
Week 16 - 1 visit	15			
Week 16 - 2 visits	2			
Week 16 - 3 visits	2			
Week 16 - 4 visits	1			
Week 16 - 5 visits	1			
Week 28 - 0 visits	76			

Week 28 - 1 visit	14				
Week 28 - 2 visits	6				
Week 28 - 3 visits	4				
Week 40 - 0 visits	67				
Week 40 - 1 visit	13				
Week 40 - 2 visits	8				
Week 40 - 3 visits	1				
Week 40 - 6 visits	2				
Week 48 - 0 visits	78				
Week 48 - 1 visit	9				
Week 48 - 2 visits	5				
Week 48 - 3 visits	1				
Week 48 - 6 visits	1				

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization - Number of visits to a specialist

End point title	Health Care Resource Utilization - Number of visits to a specialist

End point description:

Number of participants who visited a specialist has been reported. The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 4, 16, 28, 40, 48

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: participants				
Week 0 - 0 visits	51			
Week 0 - 1 visit	40			
Week 0 - 2 visits	18			
Week 0 - 3 visits	2			
Week 0 - 6 visits	1			
Week 4 - 0 visits	74			
Week 4 - 1 visit	28			
Week 4 - 2 visits	1			
Week 4 - 3 visits	1			
Week 4 - 4 visits	1			
Week 16 - 0 visits	64			
Week 16 - 1 visit	23			
Week 16 - 2 visits	9			
Week 16 - 3 visits	2			

Week 16 - 4 visits	1				
Week 16 - 5 visits	1				
Week 16 - 7 visits	1				
Week 28 - 0 visits	68				
Week 28 - 1 visit	25				
Week 28 - 2 visits	4				
Week 28 - 4 visits	2				
Week 28 - 5 visits	1				
Week 40 - 0 visits	62				
Week 40 - 1 visit	22				
Week 40 - 2 visits	4				
Week 40 - 3 visits	1				
Week 40 - 4 visits	1				
Week 40 - 6 visits	1				
Week 48 - 0 visits	72				
Week 48 - 1 visit	17				
Week 48 - 2 visits	3				
Week 48 - 3 visits	1				
Week 48 - 6 visits	1				

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization - Number of emergency department visits due to cluster headache

End point title	Health Care Resource Utilization - Number of emergency department visits due to cluster headache

End point description:

Number of participants who visited an emergency department due to CH has been reported. The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 4, 16, 28, 40, 48

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: participants				
Week 0 - 0 visits	108			
Week 0 - 1 visit	1			
Week 0 - 2 visits	1			
Week 0 - 4 visits	2			
Week 4 - 0 visits	102			
Week 4 - 1 visit	2			
Week 4 - 4 visits	1			

Week 16 - 0 visits	97			
Week 16 - 1 visit	2			
Week 16 - 2 visits	1			
Week 16 - 4 visits	1			
Week 28 - 0 visits	96			
Week 28 - 1 visit	2			
Week 28 - 2 visits	1			
Week 28 - 4 visits	1			
Week 40 - 0 visits	88			
Week 40 - 1 visit	1			
Week 40 - 2 visits	2			
Week 48 - 0 visits	91			
Week 48 - 1 visit	1			
Week 48 - 2 visits	1			
Week 48 - 3 visits	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization - Number of hospital admissions due to cluster headache

End point title	Health Care Resource Utilization - Number of hospital admissions due to cluster headache

End point description:

Number of participants admitted to the hospital due to CH has been reported. The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 4, 16, 28, 40, 48

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: participants				
Week 0 - 0 admissions	110			
Week 0 - 1 admission	2			
Week 4 - 0 admissions	103			
Week 4 - 1 admission	2			
Week 16 - 0 admissions	98			
Week 16 - 1 admission	2			
Week 16 - 5 admissions	1			
Week 28 - 0 admissions	97			
Week 28 - 1 admission	3			
Week 40 - 0 admissions	89			
Week 40 - 1 admission	1			

Week 40 - 5 admissions	1			
Week 48 - 0 admissions	92			
Week 48 - 1 admission	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization - Total number of overnight hospital stays due to cluster headache

End point title	Health Care Resource Utilization - Total number of overnight hospital stays due to cluster headache

End point description:

Number of participants who had overnight hospital stays due to CH has been reported. The FAS included all participants in the APTS who had a valid assessment of the baseline number of weekly attacks and a post-baseline assessment of the number of weekly attacks.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 4, 16, 28, 40, 48

End point values	Eptinezumab			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: participants				
Week 0 - 0 visits	109			
Week 0 - 1 visit	2			
Week 0 - 2 visits	1			
Week 4 - 0 visits	105			
Week 16 - 0 visits	98			
Week 16 - 1 visit	1			
Week 16 - 7 visits	1			
Week 16 - 10 visits	1			
Week 28 - 0 visits	99			
Week 28 - 1 visit	1			
Week 40 - 0 visits	90			
Week 40 - 1 visit	1			
Week 48 - 0 visits	92			
Week 48 - 1 visit	1			
Week 48 - 5 visits	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
From the day of first dose of study drug (Baseline [Week 0]) up to Week 56	
Adverse event reporting additional description:	
The APTS included all participants who received infusion with eptinezumab	
Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Eptinezumab

Reporting group description:

Participants received 4 IV infusions of 400 mg eptinezumab at Baseline (Day 0) and at the end of Weeks 12, 24, and 36.

Serious adverse events	Eptinezumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 131 (8.40%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Weight decreased			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Jaw fracture			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Cluster headache			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Impaired gastric emptying			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			

Thyroiditis acute			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Eptinezumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	96 / 131 (73.28%)		
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	3		
Hypertension			
subjects affected / exposed	4 / 131 (3.05%)		
occurrences (all)	4		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	22 / 131 (16.79%)		
occurrences (all)	30		
Influenza like illness			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	4		
Oedema peripheral			
subjects affected / exposed	5 / 131 (3.82%)		
occurrences (all)	7		
Asthenia			
subjects affected / exposed	6 / 131 (4.58%)		
occurrences (all)	11		

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 131 (3.05%)		
occurrences (all)	4		
Dyspnoea			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	3		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	8 / 131 (6.11%)		
occurrences (all)	9		
Nightmare			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	3		
Sleep disorder			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	3		
Suicidal ideation			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	3		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	4		
Blood triglycerides increased			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	3		
Weight increased			
subjects affected / exposed	8 / 131 (6.11%)		
occurrences (all)	8		
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	3		
Fall			

subjects affected / exposed	4 / 131 (3.05%)		
occurrences (all)	5		
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	5		
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 131 (5.34%)		
occurrences (all)	7		
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	4 / 131 (3.05%)		
occurrences (all)	4		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	8 / 131 (6.11%)		
occurrences (all)	8		
Constipation			
subjects affected / exposed	6 / 131 (4.58%)		
occurrences (all)	9		
Abdominal pain upper			
subjects affected / exposed	4 / 131 (3.05%)		
occurrences (all)	6		
Vomiting			
subjects affected / exposed	7 / 131 (5.34%)		
occurrences (all)	7		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	9 / 131 (6.87%)		
occurrences (all)	9		
Alopecia			
subjects affected / exposed	4 / 131 (3.05%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	9 / 131 (6.87%)		
occurrences (all)	9		
Neck pain			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	5		
Infections and infestations			
Influenza			
subjects affected / exposed	10 / 131 (7.63%)		
occurrences (all)	10		
Bronchitis			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	3		
COVID-19			
subjects affected / exposed	29 / 131 (22.14%)		
occurrences (all)	31		
Gastroenteritis			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	3		
Sinusitis			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	3		
Rhinitis			
subjects affected / exposed	6 / 131 (4.58%)		
occurrences (all)	6		
Pneumonia			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	4		
Pharyngitis			
subjects affected / exposed	5 / 131 (3.82%)		
occurrences (all)	5		
Nasopharyngitis			

subjects affected / exposed	24 / 131 (18.32%)		
occurrences (all)	33		
Urinary tract infection			
subjects affected / exposed	4 / 131 (3.05%)		
occurrences (all)	5		
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	6 / 131 (4.58%)		
occurrences (all)	6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 November 2021	Updated inclusion criteria and allowable concomitant medications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported