Clinical trial results:
Interventional, Randomized, Double-blind, Parallel-group, Placebo-controlled Study With an Extension Period to Evaluate the Efficacy and Safety of Eptinezumab for the Prevention of Migraine in Patients With Unsuccessful Prior Preventive Treatments

Summary

EudraCT number	2019-004497-25
Trial protocol	DE CZ DK FI BE PL GB SK HU SE BG IT
Global end of trial date	15 September 2022

Results information

Result version number	v1 (current)
This version publication date	21 February 2024
First version publication date	21 February 2024

Trial information

Trial identification

Sponsor protocol code	18898A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04418765
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark, 2500
Public contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@lundbeck.com
Scientific contact	LundbeckClinicalTrials@lundbeck.com, 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	15 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the efficacy of eptinezumab for the prevention of migraine in participants with unsuccessful prior preventive treatments.

Protection of trial subjects:

This study 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	01 June 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 17
Country: Number of subjects enrolled	Bulgaria: 33
Country: Number of subjects enrolled	Czechia: 218
Country: Number of subjects enrolled	Germany: 21
Country: Number of subjects enrolled	Denmark: 12
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	Finland: 13
Country: Number of subjects enrolled	France: 22
Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	Georgia: 176
Country: Number of subjects enrolled	Hungary: 19
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Poland: 256
Country: Number of subjects enrolled	Russian Federation: 13
Country: Number of subjects enrolled	Slovakia: 34
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	892
EEA total number of subjects	677

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)	867
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study included 2 periods: Placebo-controlled Period – 24-week double-blind treatment period with placebo or eptinezumab and Extension Period – 48-week dose-blinded period with eptinezumab after completion of the Placebo-controlled Period.

Pre-assignment

Screening details:

Participants assigned to placebo in the Placebo-controlled Period were randomized 1:1 to treatment with either eptinezumab 100 milligrams (mg) or eptinezumab 300 mg. Participants assigned to eptinezumab 100 mg or 300 mg in the Placebo-controlled Period continued their treatment.

Period 1

Period 1 title	Placebo-controlled Period (24 Weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo matched to eptinezumab by intravenous (IV) infusion on Baseline (Day 0) and on Week 12 in the double-blind treatment period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo was administered per schedule specified in the arm description.

Arm title	Eptinezumab 100 mg

Arm description:

Participants received eptinezumab 100 mg by IV infusion on Baseline (Day 0); and thereafter, every 12 weeks up to Week 60 (2 doses in the double-blind treatment period and 4 doses in the dose-blinded extension period).

Arm type	Experimental
Investigational medicinal product name	Eptinezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eptinezumab was administered per schedule specified in the arm description.

Arm title	Eptinezumab 300 mg

Arm description:

Participants received eptinezumab 300 mg by IV infusion on Baseline (Day 0); and thereafter, every 12 weeks up to Week 60 (2 doses in the double-blind treatment period and 4 doses in the dose-blinded extension period).

Arm type	Experimental

Investigational medicinal product name	Eptinezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for 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	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg
Started	299	299	294
Received at least 1 dose of study drug	298	299	294
Completed	293	288	284
Not completed	6	11	10
Consent withdrawn by subject	1	5	2
Adverse event, non-fatal	1	1	6
Randomized but not treated	1	-	-
Other than specified	2	-	1
Lost to follow-up	-	1	-
Lack of efficacy	1	3	-
Protocol deviation	-	1	1

Period 2

Period 2 title	Extension Period (48 Weeks)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Eptinezumab 100 mg

Arm description:

Participants received eptinezumab 100 mg by IV infusion on Baseline (Day 0); and thereafter, every 12 weeks up to Week 60 (2 doses in the double-blind treatment period and 4 doses in the dose-blinded extension period).

Arm type	Experimental
Investigational medicinal product name	Eptinezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eptinezumab was administered per schedule specified in the arm description.

Arm title	Eptinezumab 300 mg

Arm description:

Participants received eptinezumab 300 mg by IV infusion on Baseline (Day 0); and thereafter, every 12 weeks up to Week 60 (2 doses in the double-blind treatment period and 4 doses in the dose-blinded extension period).

Arm type	Experimental
Investigational medicinal product name	Eptinezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for 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 2	Eptinezumab 100 mg	Eptinezumab 300 mg
Started	433	432
Received at least 1 dose of study drug	433	432
Completed	392	390
Not completed	41	42
Consent withdrawn by subject	21	14
Adverse event, non-fatal	2	9
Non-compliance with study drug	-	2
Other than specified	5	2
Lack of efficacy	13	13
Protocol deviation	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to eptinezumab by intravenous (IV) infusion on Baseline (Day 0) and on Week 12 in the double-blind treatment period.	
Reporting group title	Eptinezumab 100 mg
Reporting group description:	
Participants received eptinezumab 100 mg by IV infusion on Baseline (Day 0); and thereafter, every 12 weeks up to Week 60 (2 doses in the double-blind treatment period and 4 doses in the dose-blinded extension period).	
Reporting group title	Eptinezumab 300 mg
Reporting group description:	
Participants received eptinezumab 300 mg by IV infusion on Baseline (Day 0); and thereafter, every 12 weeks up to Week 60 (2 doses in the double-blind treatment period and 4 doses in the dose-blinded extension period).	

Reporting group values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg
Number of subjects	299	299	294
Age categorical Units: Subjects			
Age Continuous			
Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 293 (Eptinezumab 300 mg).			
Units: years			
arithmetic mean	43.8	44.6	43.1
standard deviation	± 10.83	± 10.76	± 10.2
Sex: Female, Male Units: participants			
Female	264	277	261
Male	35	22	33
Monthly Migraine Days (MMDs)			
A migraine day was defined as any day the participant reported a headache that met criterion A, B, C, or D as defined in the outcome measure 1. Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 293 (Eptinezumab 300 mg).			
Units: days/month			
arithmetic mean	13.9	13.8	13.7
standard deviation	± 5.72	± 5.58	± 5.44
Monthly Headache Days (MHDs)			
A headache day was defined as a day with a headache that lasted ≥30 minutes or met the definition of a migraine day (as defined in criterion A, B, C, or D in outcome measure 1). Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 293 (Eptinezumab 300 mg).			
Units: days/month			
arithmetic mean	14.5	14.5	14.4
standard deviation	± 5.79	± 5.63	± 5.45
Headache Impact Test (HIT-6) Score			
The HIT-6 contains 6 questions, each item was rated from never to always with the following response scores: never = 6, rarely = 8, sometimes = 10, very often = 11, and always = 13. The total score for the HIT-6 was the sum of each response score ranging from 36 to 78. The life impact derived from the total score was described as followed: severe (≥60), substantial (56-59), some (50-55), little to none (≤49). Here N = 288 (placebo), 281 (Eptinezumab 100 mg), and 287 (Eptinezumab 300 mg).			

Units: units on a scale			
arithmetic mean	66.2	66.6	66.5
standard deviation	± 4.38	± 4.7	± 4.41
Percentage of Migraine Attacks With Severe Pain Intensity			
A migraine attack was defined as a headache that occurred on a single day or lasted >1 day and that met the criteria for a migraine day (as defined in criterion A, B, C, or D in outcome measure 1). Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 293 (Eptinezumab 300 mg).			
Units: percentage of migraine attacks			
arithmetic mean	40.4	47.1	43.9
standard deviation	± 29.74	± 29.82	± 28.4
Percentage of Headache Episodes With Severe Pain Intensity			
A headache episode was defined as a headache lasted ≥30 minutes or that met the criteria for a migraine (as defined in criterion A, B, C, or D in outcome measure 1). Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 293 (Eptinezumab 300 mg).			
Units: percentage of headache episodes			
arithmetic mean	38.5	44.2	41
standard deviation	± 29.29	± 28.56	± 27.01
Acute Migraine Medication Days			
Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 292 (Eptinezumab 300 mg).			
Units: days			
arithmetic mean	11.2	11.2	11
standard deviation	± 5.93	± 5.47	± 5.29
MMDs With Use of Acute Medication			
Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 293 (Eptinezumab 300 mg).			
Units: days/month			
arithmetic mean	12.5	12.7	12.4
standard deviation	± 5.62	± 5.48	± 5.38
Migraine-Specific Quality of Life (MSQ) Subscores - MSQ role function-restrictive			
The MSQ is a participant-reported outcome designed to assess the quality of life in participants with migraine. It consists of 14 items covering 3 domains: role function restrictive (7 items); role function preventive (4 items); and emotional function (3 items). Each item was scored on a 6-point scale ranging from 1 (none of the time) to 6 (all of the time). Raw domain scores were summed and transformed to a 0- to 100-point scale. Higher scores indicated better quality of life. Here N = 288 (placebo), 276 (Eptinezumab 100 mg), and 287 (Eptinezumab 300 mg).			
Units: units on a scale			
arithmetic mean	35.1	35.7	35.7
standard deviation	± 17.14	± 17.33	± 16.68
Migraine-Specific Quality of Life (MSQ) Subscores - MSQ role function-preventive			
The MSQ is a participant-reported outcome designed to assess the quality of life in participants with migraine. It consists of 14 items covering 3 domains: role function restrictive (7 items); role function preventive (4 items); and emotional function (3 items). Each item was scored on a 6-point scale ranging from 1 (none of the time) to 6 (all of the time). Raw domain scores were summed and transformed to a 0- to 100-point scale. Higher scores indicated better quality of life. Here N = 288 (placebo), 276 (Eptinezumab 100 mg), and 287 (Eptinezumab 300 mg).			
Units: units on a scale			
arithmetic mean	50.5	50.2	51
standard deviation	± 22.14	± 21.39	± 21.47
Migraine-Specific Quality of Life (MSQ) Subscores - MSQ emotional function			
The MSQ is a participant-reported outcome designed to assess the quality of life in participants with migraine. It consists of 14 items covering 3 domains: role function restrictive (7 items); role function preventive (4 items); and emotional function (3 items). Each item was scored on a 6-point scale ranging from 1 (none of the time) to 6 (all of the time). Raw domain scores were summed and transformed to a			

0- to 100-point scale. Higher scores indicated better quality of life. Here N = 288 (placebo), 276 (Eptinezumab 100 mg), and 287 (Eptinezumab 300 mg).			
Units: units on a scale			
arithmetic mean	48.4	50.3	48.6
standard deviation	± 26.63	± 24.7	± 23.8
Health-Related Quality of Life (EQ-5D-5L) Visual Analog Scale (VAS) Score			
The EQ-5D-5L is a participant-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) and a VAS of the overall health state. Each descriptive item was rated on a 5-point index ranging from 1 (no problems) to 5 (extreme problems). The VAS ranged from 0 (worst imaginable health state) to 100 (best imaginable health state). Here N = 287 (placebo), 276 (Eptinezumab 100 mg), and 285 (Eptinezumab 300 mg).			
Units: units on a scale			
arithmetic mean	74	75.9	74.5
standard deviation	± 20.36	± 19.01	± 20.72
WPAI Questionnaire Subscore (Absenteeism)			
It contains 6 items that measure: 1) employment status, 2) hours missed from work due to specific health problem, 3) hours missed from work for other reasons, 4) hours actually worked, 5) degree health affected productivity while working, and 6) degree health affected productivity in regular unpaid activities. 4 scores calculated from responses to 6 items: absenteeism, presenteeism, work productivity loss, activity impairment. Scores were calculated as impairment percentages (0-100). Higher Scores = greater impairment. N = 218 (placebo), 196 (Eptinezumab 100 mg), and 209 (Eptinezumab 300 mg).			
Units: units on a scale			
arithmetic mean	12.8	11.4	12
standard deviation	± 20.7	± 19.4	± 19.31
WPAI Questionnaire Subscores (Presenteeism)			
It contains 6 items that measure: 1) employment status, 2) hours missed from work due to specific health problem, 3) hours missed from work for other reasons, 4) hours actually worked, 5) degree health affected productivity while working, and 6) degree health affected productivity in regular unpaid activities. 4 scores calculated from responses to 6 items: absenteeism, presenteeism, work productivity loss, activity impairment. Scores were calculated as impairment percentages (0-100). Higher Scores = greater impairment. N = 212 (placebo), 191 (Eptinezumab 100 mg), and 206 (Eptinezumab 300 mg).			
Units: units on a scale			
arithmetic mean	51.7	50.8	53.3
standard deviation	± 24.22	± 25.61	± 24.01
WPAI Questionnaire Subscores (Work Productivity Loss)			
It contains 6 items that measure: 1) employment status, 2) hours missed from work due to specific health problem, 3) hours missed from work for other reasons, 4) hours actually worked, 5) degree health affected productivity while working, and 6) degree health affected productivity in regular unpaid activities. 4 scores calculated from responses to 6 items: absenteeism, presenteeism, work productivity loss, activity impairment. Scores were calculated as impairment percentages (0-100). Higher Scores = greater impairment. N = 212 (placebo), 191 (Eptinezumab 100 mg), and 206 (Eptinezumab 300 mg).			
Units: units on a scale			
arithmetic mean	55.6	53.7	57
standard deviation	± 24.7	± 26.17	± 24.1
WPAI Questionnaire Subscores (Activity Impairment)			
It contains 6 items that measure: 1) employment status, 2) hours missed from work due to specific health problem, 3) hours missed from work for other reasons, 4) hours actually worked, 5) degree health affected productivity while working, and 6) degree health affected productivity in regular unpaid activities. 4 scores calculated from responses to 6 items: absenteeism, presenteeism, work productivity loss, activity impairment. Scores were calculated as impairment percentages (0-100). Higher Scores = greater impairment. N = 286 (placebo), 274 (Eptinezumab 100 mg), and 285 (Eptinezumab 300 mg).			
Units: units on a scale			
arithmetic mean	58.7	58.5	59.1
standard deviation	± 23.52	± 23.47	± 23.37

Reporting group values	Total		
Number of subjects	892		
Age categorical Units: Subjects			

Age Continuous			
Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 293 (Eptinezumab 300 mg).			
Units: years arithmetic mean standard deviation	- -		
Sex: Female, Male Units: participants			
Female Male	802 90		
Monthly Migraine Days (MMDs)			
A migraine day was defined as any day the participant reported a headache that met criterion A, B, C, or D as defined in the outcome measure 1. Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 293 (Eptinezumab 300 mg).			
Units: days/month arithmetic mean standard deviation	- -		
Monthly Headache Days (MHDs)			
A headache day was defined as a day with a headache that lasted ≥30 minutes or met the definition of a migraine day (as defined in criterion A, B, C, or D in outcome measure 1). Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 293 (Eptinezumab 300 mg).			
Units: days/month arithmetic mean standard deviation	- -		
Headache Impact Test (HIT-6) Score			
The HIT-6 contains 6 questions, each item was rated from never to always with the following response scores: never = 6, rarely = 8, sometimes = 10, very often = 11, and always = 13. The total score for the HIT-6 was the sum of each response score ranging from 36 to 78. The life impact derived from the total score was described as followed: severe (≥60), substantial (56-59), some (50-55), little to none (≤49). Here N = 288 (placebo), 281 (Eptinezumab 100 mg), and 287 (Eptinezumab 300 mg).			
Units: units on a scale arithmetic mean standard deviation	- -		
Percentage of Migraine Attacks With Severe Pain Intensity			
A migraine attack was defined as a headache that occurred on a single day or lasted >1 day and that met the criteria for a migraine day (as defined in criterion A, B, C, or D in outcome measure 1). Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 293 (Eptinezumab 300 mg).			
Units: percentage of migraine attacks arithmetic mean standard deviation	- -		
Percentage of Headache Episodes With Severe Pain Intensity			
A headache episode was defined as a headache lasted ≥30 minutes or that met the criteria for a migraine (as defined in criterion A, B, C, or D in outcome measure 1). Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 293 (Eptinezumab 300 mg).			
Units: percentage of headache episodes arithmetic mean standard deviation	- -		
Acute Migraine Medication Days			
Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 292 (Eptinezumab 300 mg).			

Units: days arithmetic mean standard deviation	-		
MMDs With Use of Acute Medication			
Here N = 298 (placebo), 299 (Eptinezumab 100 mg), and 293 (Eptinezumab 300 mg).			
Units: days/month arithmetic mean standard deviation	-		
Migraine-Specific Quality of Life (MSQ) Subscores - MSQ role function-restrictive			
The MSQ is a participant-reported outcome designed to assess the quality of life in participants with migraine. It consists of 14 items covering 3 domains: role function restrictive (7 items); role function preventive (4 items); and emotional function (3 items). Each item was scored on a 6-point scale ranging from 1 (none of the time) to 6 (all of the time). Raw domain scores were summed and transformed to a 0- to 100-point scale. Higher scores indicated better quality of life. Here N = 288 (placebo), 276 (Eptinezumab 100 mg), and 287 (Eptinezumab 300 mg).			
Units: units on a scale arithmetic mean standard deviation	-		
Migraine-Specific Quality of Life (MSQ) Subscores - MSQ role function-preventive			
The MSQ is a participant-reported outcome designed to assess the quality of life in participants with migraine. It consists of 14 items covering 3 domains: role function restrictive (7 items); role function preventive (4 items); and emotional function (3 items). Each item was scored on a 6-point scale ranging from 1 (none of the time) to 6 (all of the time). Raw domain scores were summed and transformed to a 0- to 100-point scale. Higher scores indicated better quality of life. Here N = 288 (placebo), 276 (Eptinezumab 100 mg), and 287 (Eptinezumab 300 mg).			
Units: units on a scale arithmetic mean standard deviation	-		
Migraine-Specific Quality of Life (MSQ) Subscores - MSQ emotional function			
The MSQ is a participant-reported outcome designed to assess the quality of life in participants with migraine. It consists of 14 items covering 3 domains: role function restrictive (7 items); role function preventive (4 items); and emotional function (3 items). Each item was scored on a 6-point scale ranging from 1 (none of the time) to 6 (all of the time). Raw domain scores were summed and transformed to a 0- to 100-point scale. Higher scores indicated better quality of life. Here N = 288 (placebo), 276 (Eptinezumab 100 mg), and 287 (Eptinezumab 300 mg).			
Units: units on a scale arithmetic mean standard deviation	-		
Health-Related Quality of Life (EQ-5D-5L) Visual Analog Scale (VAS) Score			
The EQ-5D-5L is a participant-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) and a VAS of the overall health state. Each descriptive item was rated on a 5-point index ranging from 1 (no problems) to 5 (extreme problems). The VAS ranged from 0 (worst imaginable health state) to 100 (best imaginable health state). Here N = 287 (placebo), 276 (Eptinezumab 100 mg), and 285 (Eptinezumab 300 mg).			
Units: units on a scale arithmetic mean standard deviation	-		
WPAI Questionnaire Subscore (Absenteeism)			
It contains 6 items that measure: 1) employment status, 2) hours missed from work due to specific health problem, 3) hours missed from work for other reasons, 4) hours actually worked, 5) degree health affected productivity while working, and 6) degree health affected productivity in regular unpaid activities. 4 scores calculated from responses to 6 items: absenteeism, presenteeism, work productivity loss, activity impairment. Scores were calculated as impairment percentages (0-100). Higher Scores =			

greater impairment. N = 218 (placebo), 196 (Eptinezumab 100 mg), and 209 (Eptinezumab 300 mg).			
Units: units on a scale arithmetic mean standard deviation	- 		
WPAI Questionnaire Subscores (Presenteeism)			
It contains 6 items that measure: 1) employment status, 2) hours missed from work due to specific health problem, 3) hours missed from work for other reasons, 4) hours actually worked, 5) degree health affected productivity while working, and 6) degree health affected productivity in regular unpaid activities. 4 scores calculated from responses to 6 items: absenteeism, presenteeism, work productivity loss, activity impairment. Scores were calculated as impairment percentages (0-100). Higher Scores = greater impairment. N = 212 (placebo), 191 (Eptinezumab 100 mg), and 206 (Eptinezumab 300 mg).			
Units: units on a scale arithmetic mean standard deviation	- 		
WPAI Questionnaire Subscores (Work Productivity Loss)			
It contains 6 items that measure: 1) employment status, 2) hours missed from work due to specific health problem, 3) hours missed from work for other reasons, 4) hours actually worked, 5) degree health affected productivity while working, and 6) degree health affected productivity in regular unpaid activities. 4 scores calculated from responses to 6 items: absenteeism, presenteeism, work productivity loss, activity impairment. Scores were calculated as impairment percentages (0-100). Higher Scores = greater impairment. N = 212 (placebo), 191 (Eptinezumab 100 mg), and 206 (Eptinezumab 300 mg).			
Units: units on a scale arithmetic mean standard deviation	- 		
WPAI Questionnaire Subscores (Activity Impairment)			
It contains 6 items that measure: 1) employment status, 2) hours missed from work due to specific health problem, 3) hours missed from work for other reasons, 4) hours actually worked, 5) degree health affected productivity while working, and 6) degree health affected productivity in regular unpaid activities. 4 scores calculated from responses to 6 items: absenteeism, presenteeism, work productivity loss, activity impairment. Scores were calculated as impairment percentages (0-100). Higher Scores = greater impairment. N = 286 (placebo), 274 (Eptinezumab 100 mg), and 285 (Eptinezumab 300 mg).			
Units: units on a scale arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to eptinezumab by intravenous (IV) infusion on Baseline (Day 0) and on Week 12 in the double-blind treatment period.	
Reporting group title	Eptinezumab 100 mg
Reporting group description:	
Participants received eptinezumab 100 mg by IV infusion on Baseline (Day 0); and thereafter, every 12 weeks up to Week 60 (2 doses in the double-blind treatment period and 4 doses in the dose-blinded extension period).	
Reporting group title	Eptinezumab 300 mg
Reporting group description:	
Participants received eptinezumab 300 mg by IV infusion on Baseline (Day 0); and thereafter, every 12 weeks up to Week 60 (2 doses in the double-blind treatment period and 4 doses in the dose-blinded extension period).	
Reporting group title	Eptinezumab 100 mg
Reporting group description:	
Participants received eptinezumab 100 mg by IV infusion on Baseline (Day 0); and thereafter, every 12 weeks up to Week 60 (2 doses in the double-blind treatment period and 4 doses in the dose-blinded extension period).	
Reporting group title	Eptinezumab 300 mg
Reporting group description:	
Participants received eptinezumab 300 mg by IV infusion on Baseline (Day 0); and thereafter, every 12 weeks up to Week 60 (2 doses in the double-blind treatment period and 4 doses in the dose-blinded extension period).	
Subject analysis set title	Placebo to Eptinezumab 100 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received placebo in the double-blind placebo-controlled period, received eptinezumab 100 mg in the dose-blinded extension period.	
Subject analysis set title	Placebo to Eptinezumab 300 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received placebo in the double-blind placebo-controlled period, received eptinezumab 300 mg in the dose-blinded extension period.	
Subject analysis set title	Eptinezumab 100 mg to Eptinezumab 100 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received eptinezumab 100 mg in the double-blind placebo-controlled period, continued to receive the same dose of eptinezumab in the dose-blinded extension period.	
Subject analysis set title	Eptinezumab 300 mg to Eptinezumab 300 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received eptinezumab 300 mg in the double-blind placebo-controlled period, continued to receive the same dose of eptinezumab in the dose-blinded extension period.	

Primary: Change From Baseline in the Number of Monthly Migraine Days (MMDs) Averaged Over Weeks 1 to 12

End point title	Change From Baseline in the Number of Monthly Migraine Days (MMDs) Averaged Over Weeks 1 to 12

End point description:

A migraine day defined as any day participant reported a headache that met criterion A, B, C, or D: A (all of following): lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality;

moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity; and accompanied by ≥1 of following: nausea; vomiting; photophobia and phonophobia. B: lasted ≥30 minutes and participant had an aura with headache. C: lasted ≥30 minutes and met ≥2 of following criteria: lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality; moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity, and was accompanied by ≥1 of following: nausea; vomiting; photophobia and phonophobia. D: participant took medication to treat headache because he/she believed as having a migraine. FAS: all randomized participants who had a valid baseline and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1-12.

End point type	Primary

End point timeframe:

Baseline, Weeks 1 - 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	298	299	293	
Units: days/month				
arithmetic mean (standard error)	-2.1 (± 0.38)	-4.8 (± 0.37)	-5.3 (± 0.37)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Analysis was performed using an REML-based MMRM with month (Weeks 1-4, Weeks 5-8, Weeks 9-12, Weeks 13-16, Weeks 17-20, Weeks 21-24), country, stratification factor (monthly MHDs at baseline: ≤14/>14) and treatment as factors, baseline score as a continuous covariate, treatment-by-month interaction, baseline score-by-month interaction, and stratum-by-month interaction. A testing strategy (sequence of tests) was applied to ensure protection of the type 1 error.

Comparison groups	Placebo v Eptinezumab 100 mg
Number of subjects included in analysis	597
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.0001 [2]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	-2
Variability estimate	Standard error of the mean
Dispersion value	0.36

Notes:

[1] - Testing sequence: 1. Change in MMDs (Weeks 1-12) 300 mg vs placebo; 2. 50% responders for MMDs (Weeks 1-12) 300 mg vs placebo; 3. Change in MMDs (Weeks 1-12) 100 mg vs placebo; 4. 50% responders for MMDs (Weeks 1-12) 100 mg vs placebo; 5a. Change in MMDs (Weeks 13-24), 5b. 75% responders for MMDs (Weeks 1-12), 5c. Change in HIT-6 (Week 12) 300 mg vs placebo; 6a. Change in MMDs (Weeks 13-24), 6b. 75% responders for MMDs (Weeks 1-12), 6c. Change in HIT-6 (Week 12) 100 mg vs placebo.

[2] - Testing continued only, if the previous comparison was statistically significant. Threshold for significance: p-value <α, where α = 0.05. Here it is test no. 3 of testing order.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed using a restricted maximum likelihood (REML)-based mixed model for repeated measurements (MMRM) with month (Weeks 1-4, 5-8, 9-12, 13-16, 17-20, 21-24), country, stratification factor (monthly MHDs at baseline: ≤14/>14) and treatment as factors, baseline score as a continuous covariate, treatment-by-month interaction, baseline score-by-month interaction, and stratum-by-month interaction. A testing strategy was applied to ensure protection of the type 1 error.

Comparison groups	Placebo v Eptinezumab 300 mg
Number of subjects included in analysis	591
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	< 0.0001 [4]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	-2.5
Variability estimate	Standard error of the mean
Dispersion value	0.36

Notes:

[3] - Testing sequence: 1. Change in MMDs (Weeks 1-12) 300 mg vs placebo; 2. 50% responders for MMDs (Weeks 1-12) 300 mg vs placebo; 3. Change in MMDs (Weeks 1-12) 100 mg vs placebo; 4. 50% responders for MMDs (Weeks 1-12) 100 mg vs placebo; 5a. Change in MMDs (Weeks 13-24), 5b. 75% responders for MMDs (Weeks 1-12), 5c. Change in HIT-6 (Week 12) 300 mg vs placebo; 6a. Change in MMDs (Weeks 13-24), 6b. 75% responders for MMDs (Weeks 1-12), 6c. Change in HIT-6 (Week 12) 100 mg vs placebo.

[4] - Testing continued only, if the previous comparison was statistically significant. Threshold for significance: p-value <α, where α = 0.05. Here it is test no. 1 of testing order.

Secondary: Percentage of Participants With ≥50% Reduction From Baseline in MMDs Averaged Over Weeks 1 to 12

End point title	Percentage of Participants With ≥50% Reduction From Baseline in MMDs Averaged Over Weeks 1 to 12

End point description:

A migraine day defined as any day participant reported a headache that met criterion A, B, C, or D: A (all of following): lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality; moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity; and accompanied by ≥1 of following: nausea; vomiting; photophobia and phonophobia. B: lasted ≥30 minutes and participant had an aura with headache. C: lasted ≥30 minutes and met ≥2 of following criteria: lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality; moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity, and was accompanied by ≥1 of following: nausea; vomiting; photophobia and phonophobia. D: participant took medication to treat headache because he/she believed as having a migraine. FAS: all randomized participants who had a valid baseline and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1-12.

End point type	Secondary

End point timeframe:

Baseline to Weeks 1 - 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	298	299	293	
Units: percentage of participants				
number (not applicable)	13.1	42.1	49.5	

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Analysis was performed using logistic regression model including baseline MMDs as a continuous covariate, and treatment and stratification factor (MHD at baseline: ≤14/>14) as factors. A testing strategy (sequence of tests) was applied to ensure protection of the type 1 error.

Comparison groups	Placebo v Eptinezumab 100 mg
Number of subjects included in analysis	597
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	< 0.0001 [6]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.29
upper limit	7.47

Notes:

[5] - Testing sequence: 1. Change in MMDs (Weeks 1-12) 300 mg vs placebo; 2. 50% responders for MMDs (Weeks 1-12) 300 mg vs placebo; 3. Change in MMDs (Weeks 1-12) 100 mg vs placebo; 4. 50% responders for MMDs (Weeks 1-12) 100 mg vs placebo; 5a. Change in MMDs (Weeks 13-24), 5b. 75% responders for MMDs (Weeks 1-12), 5c. Change in HIT-6 (Week 12) 300 mg vs placebo; 6a. Change in MMDs (Weeks 13-24), 6b. 75% responders for MMDs (Weeks 1-12), 6c. Change in HIT-6 (Week 12) 100 mg vs placebo.

[6] - Testing continued only, if the previous comparison was statistically significant. Threshold for significance: p-value <α, where α = 0.05. Here it is test no. 4 of testing order.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed using logistic regression model including baseline MMDs as a continuous covariate, and treatment and stratification factor (MHD at baseline: ≤14/>14) as factors. A testing strategy (sequence of tests) was applied to ensure protection of the type 1 error.

Comparison groups	Placebo v Eptinezumab 300 mg
Number of subjects included in analysis	591
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	< 0.0001 [8]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.58

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.41
upper limit	10.01

Notes:

[7] - Testing sequence: 1. Change in MMDs (Weeks 1-12) 300 mg vs placebo; 2. 50% responders for MMDs (Weeks 1-12) 300 mg vs placebo; 3. Change in MMDs (Weeks 1-12) 100 mg vs placebo; 4. 50% responders for MMDs (Weeks 1-12) 100 mg vs placebo; 5a. Change in MMDs (Weeks 13-24), 5b. 75% responders for MMDs (Weeks 1-12), 5c. Change in HIT-6 (Week 12) 300 mg vs placebo; 6a. Change in MMDs (Weeks 13-24), 6b. 75% responders for MMDs (Weeks 1-12), 6c. Change in HIT-6 (Week 12) 100 mg vs placebo.

[8] - Testing continued only, if the previous comparison was statistically significant. Threshold for significance: p-value <α, where α = 0.05. Here it is test no. 2 of testing order.

Secondary: Change From Baseline in the Number of MMDs Averaged Over Weeks 13 to 24

End point title	Change From Baseline in the Number of MMDs Averaged Over Weeks 13 to 24

End point description:

A migraine day defined as any day participant reported headache that met criterion A, B, C, or D: A (all of following): lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality; moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity; with ≥1 of following: nausea; vomiting; photophobia and phonophobia. B: lasted ≥30 minutes and participant had an aura with headache. C: lasted ≥30 minutes and met ≥2 of following: lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality; moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity, with ≥1 of following: nausea; vomiting; photophobia and phonophobia. D: participant took medication to treat headache because he/she believed as having migraine. FAS: all randomized participants who had a valid baseline and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1-12. N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13 - 24

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	295	287	286	
Units: days/month				
arithmetic mean (standard error)	-2.4 (± 0.39)	-5.4 (± 0.39)	-6.1 (± 0.39)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Analysis was performed using an REML-based MMRM with month (Weeks 1-4, Weeks 5-8, Weeks 9-12, Weeks 13-16, Weeks 17-20, Weeks 21-24), country, stratification factor (monthly MHDs at baseline: ≤14/>14) and treatment as factors, baseline score as a continuous covariate, treatment-by-month interaction, baseline score-by-month interaction, and stratum-by-month interaction. A testing strategy (sequence of tests) was applied to ensure protection of the type 1 error.

Comparison groups	Placebo v Eptinezumab 100 mg

Number of subjects included in analysis	582
Analysis specification	Pre-specified
Analysis type	other[9]
P-value	< 0.0001 [10]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	-2.2
Variability estimate	Standard error of the mean
Dispersion value	0.39

Notes:

[9] - Testing sequence: 1. Change in MMDs (Weeks 1-12) 300 mg vs placebo; 2. 50% responders for MMDs (Weeks 1-12) 300 mg vs placebo; 3. Change in MMDs (Weeks 1-12) 100 mg vs placebo; 4. 50% responders for MMDs (Weeks 1-12) 100 mg vs placebo; 5a. Change in MMDs (Weeks 13-24), 5b. 75% responders for MMDs (Weeks 1-12), 5c. Change in HIT-6 (Week 12) 300 mg vs placebo; 6a. Change in MMDs (Weeks 13-24), 6b. 75% responders for MMDs (Weeks 1-12), 6c. Change in HIT-6 (Week 12) 100 mg vs placebo.

[10] - Threshold for significance: The consecutive order of the smallest (p1), the second smallest (p2), and the largest p-value (p3) had to be $<\alpha/3$, $<\alpha/2$, and $<\alpha$, where $\alpha = 0.05$. Here it is test no. 6a of testing order.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed using an REML-based MMRM with month (Weeks 1-4, Weeks 5-8, Weeks 9-12, Weeks 13-16, Weeks 17-20, Weeks 21-24), country, stratification factor (monthly MHDs at baseline: ≤14/>14) and treatment as factors, baseline score as a continuous covariate, treatment-by-month interaction, baseline score-by-month interaction, and stratum-by-month interaction. A testing strategy (sequence of tests) was applied to ensure protection of the type 1 error.

Comparison groups	Placebo v Eptinezumab 300 mg
Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	< 0.0001 [12]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	-3
Variability estimate	Standard error of the mean
Dispersion value	0.39

Notes:

[11] - Testing sequence: 1. Change in MMDs (Weeks 1-12) 300 mg vs placebo; 2. 50% responders for MMDs (Weeks 1-12) 300 mg vs placebo; 3. Change in MMDs (Weeks 1-12) 100 mg vs placebo; 4. 50% responders for MMDs (Weeks 1-12) 100 mg vs placebo; 5a. Change in MMDs (Weeks 13-24), 5b. 75% responders for MMDs (Weeks 1-12), 5c. Change in HIT-6 (Week 12) 300 mg vs placebo; 6a. Change in MMDs (Weeks 13-24), 6b. 75% responders for MMDs (Weeks 1-12), 6c. Change in HIT-6 (Week 12) 100 mg vs placebo.

[12] - Threshold for significance: p-value $<\alpha$, where $\alpha = 0.05$. Here it is test no. 5a of testing order.

Secondary: Percentage of Participants With ≥75% Reduction From Baseline in

MMDs Averaged Over Weeks 1 to 12

End point title	Percentage of Participants With ≥75% Reduction From Baseline in MMDs Averaged Over Weeks 1 to 12

End point description:

A migraine day defined as any day participant reported a headache that met criterion A, B, C, or D: A (all of following): lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality; moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity; and accompanied by ≥1 of following: nausea; vomiting; photophobia and phonophobia. B: lasted ≥30 minutes and participant had an aura with headache. C: lasted ≥30 minutes and met ≥2 of following criteria: lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality; moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity, and was accompanied by ≥1 of following: nausea; vomiting; photophobia and phonophobia. D: participant took medication to treat headache because he/she believed as having a migraine. FAS: all randomized participants who had a valid baseline and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1-12.

End point type	Secondary

End point timeframe:

Baseline to Weeks 1 - 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	298	299	293	
Units: percentage of participants				
number (not applicable)	2.0	15.7	18.8	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed using logistic regression model including baseline MMDs as a continuous covariate, and treatment and stratification factor (MHD at baseline: ≤14/>14) as factors. A testing strategy (sequence of tests) was applied to ensure protection of the type 1 error. Testing continued only, if the previous comparison was statistically significant.

Comparison groups	Placebo v Eptinezumab 300 mg
Number of subjects included in analysis	591
Analysis specification	Pre-specified
Analysis type	other[13]
P-value	< 0.0001 [14]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	11.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.22
upper limit	30.15

Notes:

[13] - Testing sequence: 1. Change in MMDs (Weeks 1-12) 300 mg vs placebo; 2. 50% responders for MMDs (Weeks 1-12) 300 mg vs placebo; 3. Change in MMDs (Weeks 1-12) 100 mg vs placebo; 4. 50% responders for MMDs (Weeks 1-12) 100 mg vs placebo; 5a. Change in MMDs (Weeks 13-24), 5b. 75% responders for MMDs (Weeks 1-12), 5c. Change in HIT-6 (Week 12) 300 mg vs placebo; 6a. Change in

MMDs (Weeks 13-24), 6b. 75% responders for MMDs (Weeks 1-12), 6c. Change in HIT-6 (Week 12) 100 mg vs placebo.
[14] - Threshold for significance: The consecutive order of the smallest (p1), the second smallest (p2), and the largest p-value (p3) had to be <α/3, <α/2, and <α, where α = 0.05. Here it is test no. 5b of testing order.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Analysis was performed using logistic regression model including baseline MMDs as a continuous covariate, and treatment and stratification factor (MHD at baseline: ≤14/>14) as factors. A testing strategy (sequence of tests) was applied to ensure protection of the type 1 error. Testing continued only, if the previous comparison was statistically significant.

Comparison groups	Placebo v Eptinezumab 100 mg
Number of subjects included in analysis	597
Analysis specification	Pre-specified
Analysis type	other[15]
P-value	< 0.0001 [16]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	9.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.16
upper limit	24.35

Notes:

[15] - Testing sequence: 1. Change in MMDs (Weeks 1-12) 300 mg vs placebo; 2. 50% responders for MMDs (Weeks 1-12) 300 mg vs placebo; 3. Change in MMDs (Weeks 1-12) 100 mg vs placebo; 4. 50% responders for MMDs (Weeks 1-12) 100 mg vs placebo; 5a. Change in MMDs (Weeks 13-24), 5b. 75% responders for MMDs (Weeks 1-12), 5c. Change in HIT-6 (Week 12) 300 mg vs placebo; 6a. Change in MMDs (Weeks 13-24), 6b. 75% responders for MMDs (Weeks 1-12), 6c. Change in HIT-6 (Week 12) 100 mg vs placebo.
[16] - Threshold for significance: The consecutive order of the smallest (p1), the second smallest (p2), and the largest p-value (p3) had to be <α/3, <α/2, and <α, where α = 0.05. Here it is test no. 6b of testing order.

Secondary: Change From Baseline in the Headache Impact Test (HIT-6) Score at Week 12

End point title	Change From Baseline in the Headache Impact Test (HIT-6) Score at Week 12

End point description:

The HIT-6 (version 1.0) is a Likert-type, self-reporting questionnaire designed to assess the impact of an occurring headache and its effect on the ability to function normally in daily life. The HIT-6 contains 6 questions, each item was rated from never to always with the following response scores: never = 6, rarely = 8, sometimes = 10, very often = 11, and always = 13. The total score for the HIT-6 was the sum of each response score ranging from 36 to 78. The life impact derived from the total score was described as followed: severe (≥60), substantial (56-59), some (50-55), little to none (≤49). FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	288	277	283	
Units: units on a scale				
arithmetic mean (standard error)	-3.1 (± 0.61)	-6.9 (± 0.61)	-8.5 (± 0.60)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Analysis was performed using MMRM with the following fixed effects: visit, country, stratification factor (MHDs at baseline: ≤14/>14) and treatment as factors, baseline HIT-6 Total Score as a continuous covariate, baseline score-by-visit interaction, treatment-by-visit interaction, and stratum-by-visit interaction. A testing strategy (sequence of tests) was applied to ensure protection of the type 1 error. Testing continued only, if the previous comparison was statistically significant.

Comparison groups	Placebo v Eptinezumab 100 mg
Number of subjects included in analysis	565
Analysis specification	Pre-specified
Analysis type	other[17]
P-value	< 0.0001 [18]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	-2.5
Variability estimate	Standard error of the mean
Dispersion value	0.63

Notes:

[17] - Testing sequence: 1. Change in MMDs (Weeks 1-12) 300 mg vs placebo; 2. 50% responders for MMDs (Weeks 1-12) 300 mg vs placebo; 3. Change in MMDs (Weeks 1-12) 100 mg vs placebo; 4. 50% responders for MMDs (Weeks 1-12) 100 mg vs placebo; 5a. Change in MMDs (Weeks 13-24), 5b. 75% responders for MMDs (Weeks 1-12), 5c. Change in HIT-6 (Week 12) 300 mg vs placebo; 6a. Change in MMDs (Weeks 13-24), 6b. 75% responders for MMDs (Weeks 1-12), 6c. Change in HIT-6 (Week 12) 100 mg vs placebo.

[18] - Threshold for significance: The consecutive order of the smallest (p1), the second smallest (p2), and the largest p-value (p3) had to be $<\alpha/3$, $<\alpha/2$, and $<\alpha$, where $\alpha = 0.05$. Here it is test no. 6c of testing order.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed using MMRM with the following fixed effects: visit, country, stratification factor (MHDs at baseline: ≤14/>14) and treatment as factors, baseline HIT-6 Total Score as a continuous covariate, baseline score-by-visit interaction, treatment-by-visit interaction, and stratum-by-visit interaction. A testing strategy (sequence of tests) was applied to ensure protection of the type 1 error. Testing continued only, if the previous comparison was statistically significant.

Comparison groups	Placebo v Eptinezumab 300 mg

Number of subjects included in analysis	571
Analysis specification	Pre-specified
Analysis type	other[19]
P-value	< 0.0001 [20]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	-4.2
Variability estimate	Standard error of the mean
Dispersion value	0.63

Notes:

[19] - Testing sequence: 1. Change in MMDs (Weeks 1-12) 300 mg vs placebo; 2. 50% responders for MMDs (Weeks 1-12) 300 mg vs placebo; 3. Change in MMDs (Weeks 1-12) 100 mg vs placebo; 4. 50% responders for MMDs (Weeks 1-12) 100 mg vs placebo; 5a. Change in MMDs (Weeks 13-24), 5b. 75% responders for MMDs (Weeks 1-12), 5c. Change in HIT-6 (Week 12) 300 mg vs placebo; 6a. Change in MMDs (Weeks 13-24), 6b. 75% responders for MMDs (Weeks 1-12), 6c. Change in HIT-6 (Week 12) 100 mg vs placebo.

[20] - Threshold for significance: The consecutive order of the smallest (p1), the second smallest (p2), and the largest p-value (p3) had to be $<\alpha/3$, $<\alpha/2$, and $<\alpha$, where $\alpha = 0.05$. Here it is test no. 5c of testing order.

Secondary: Percentage of Participants With ≥50% Reduction From Baseline in MMDs Averaged Over Weeks 13 to 24

End point title	Percentage of Participants With ≥50% Reduction From Baseline in MMDs Averaged Over Weeks 13 to 24

End point description:

A migraine day defined as any day participant reported headache that met criterion A, B, C, or D: A (all of following): lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality; moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity; with ≥1 of following: nausea; vomiting; photophobia and phonophobia. B: lasted ≥30 minutes and participant had an aura with headache. C: lasted ≥30 minutes and met ≥2 of following: lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality; moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity, with ≥1 of following: nausea; vomiting; photophobia and phonophobia. D: participant took medication to treat headache because he/she believed as having migraine. FAS: all randomized participants who had a valid baseline and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1-12. N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline to Weeks 13 - 24

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	295	287	286	
Units: percentage of participants				
number (not applicable)	23.7	52.3	59.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With 100% Reduction From Baseline in MMDs Averaged Over Weeks 1 to 12

End point title	Percentage of Participants With 100% Reduction From Baseline in MMDs Averaged Over Weeks 1 to 12

End point description:

A migraine day defined as any day participant reported a headache that met criterion A, B, C, or D: A (all of following): lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality; moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity; and accompanied by ≥1 of following: nausea; vomiting; photophobia and phonophobia. B: lasted ≥30 minutes and participant had an aura with headache. C: lasted ≥30 minutes and met ≥2 of following criteria: lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality; moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity, and was accompanied by ≥1 of following: nausea; vomiting; photophobia and phonophobia. D: participant took medication to treat headache because he/she believed as having a migraine. FAS: all randomized participants who had a valid baseline and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1-12.

End point type	Secondary

End point timeframe:

Baseline to Weeks 1 - 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	298	299	293	
Units: percentage of participants				
number (not applicable)	1.1	5.9	7.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With ≥75% Reduction From Baseline in MMDs Averaged Over Weeks 13 to 24

End point title	Percentage of Participants With ≥75% Reduction From Baseline in MMDs Averaged Over Weeks 13 to 24

End point description:

A migraine day defined as any day participant reported headache that met criterion A, B, C, or D: A (all of following): lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality; moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity; with ≥1 of following: nausea; vomiting; photophobia and phonophobia. B: lasted ≥30 minutes and participant had an aura with headache. C: lasted ≥30 minutes and met ≥2 of following: lasted ≥4 hours, had ≥2 of following: unilateral location; pulsating quality; moderate/severe pain intensity; aggravation by, or causing avoidance of, routine physical activity, with ≥1 of following: nausea; vomiting; photophobia and phonophobia. D: participant took medication to treat headache because he/she believed as having migraine. FAS: all randomized participants who had a valid baseline and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1-12. N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline to Weeks 13 - 24

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	295	287	293	
Units: percentage of participants				
number (not applicable)	6.8	21.3	27.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With ≥50% Reduction From Baseline in Monthly Headache Days (MHDs) Averaged Over Weeks 1 to 12

End point title	Percentage of Participants With ≥50% Reduction From Baseline in Monthly Headache Days (MHDs) Averaged Over Weeks 1 to 12

End point description:

A headache day was defined as a day with a headache that lasted ≥30 minutes or met the definition of a migraine day (as defined in criterion A, B, C, or D above in outcome measure 1). FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12.

End point type	Secondary

End point timeframe:

Baseline to Weeks 1 - 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	298	299	293	
Units: percentage of participants				
number (not applicable)	12.8	39.5	45.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With ≥75% Reduction From Baseline in Monthly Headache Days (MHDs) Averaged Over Weeks 1 to 12

End point title	Percentage of Participants With ≥75% Reduction From Baseline in Monthly Headache Days (MHDs) Averaged Over Weeks 1 to 12

End point description:

A headache day was defined as a day with a headache that lasted ≥30 minutes or met the definition of

a migraine day (as defined in criterion A, B, C, or D above in outcome measure 1). FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12.

End point type	Secondary

End point timeframe:

Baseline to Weeks 1 - 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	298	299	293	
Units: percentage of participants				
number (not applicable)	2.3	15.1	16.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With 100% Reduction From Baseline in Monthly Headache Days (MHDs) Averaged Over Weeks 1 to 12

End point title	Percentage of Participants With 100% Reduction From Baseline in Monthly Headache Days (MHDs) Averaged Over Weeks 1 to 12

End point description:

A headache day was defined as a day with a headache that lasted ≥30 minutes or met the definition of a migraine day (as defined in criterion A, B, C, or D above in outcome measure 1). FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12.

End point type	Secondary

End point timeframe:

Baseline to Weeks 1 - 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	298	299	293	
Units: percentage of participants				
number (not applicable)	1.1	4.1	5.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Percentage of Migraine Attacks With

Severe Pain Intensity Averaged Over Weeks 1 to 12

End point title	Change From Baseline in the Percentage of Migraine Attacks With Severe Pain Intensity Averaged Over Weeks 1 to 12

End point description:

A migraine attack was defined as a headache that occurred on a single day or lasted >1 day and that met the criteria for a migraine day (as defined in criterion A, B, C, or D above in outcome measure 1). FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1 - 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	298	299	293	
Units: percentage of migraine attacks				
arithmetic mean (standard error)	-10.2 (± 1.91)	-17.9 (± 1.87)	-21.3 (± 1.87)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Number of MHDs Averaged Over Weeks 1 to 12

End point title	Change From Baseline in the Number of MHDs Averaged Over Weeks 1 to 12

End point description:

A headache day was defined as a day with a headache that lasted ≥30 minutes or met the definition of a migraine day (as defined in criterion A, B, C, or D above in outcome measure 1). FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1 - 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	298	299	293	
Units: days/month				
arithmetic mean (standard error)	-2.1 (± 0.38)	-4.6 (± 0.37)	-5.1 (± 0.37)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Number of MMDs With Use of Acute Medication Averaged Over Weeks 1 to 12

End point title	Change From Baseline in the Number of MMDs With Use of Acute Medication Averaged Over Weeks 1 to 12

End point description:

Number of MMDs with acute medication usage was derived using the answer to "Did you take any medications to treat this headache?" in the headache diary. The question was asked when a participant was ending a headache. Thus, a migraine day with acute medication usage was defined as a migraine day with the extra condition that this question was answered as "Yes". FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1 - 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	298	299	293	
Units: days/month				
arithmetic mean (standard error)	-2.0 (± 0.36)	-4.6 (± 0.36)	-5.2 (± 0.36)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Percentage of Headache Episodes With Severe Pain Intensity Averaged Over Weeks 1 to 12

End point title	Change From Baseline in the Percentage of Headache Episodes With Severe Pain Intensity Averaged Over Weeks 1 to 12

End point description:

A headache episode was defined as a headache lasted ≥30 minutes or that met the criteria for a migraine (as defined in criterion A, B, C, or D above in outcome measure 1). FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1 - 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	298	299	293	
Units: percentage of headache episodes				
arithmetic mean (standard error)	-8.8 (± 1.85)	-16.2 (± 1.81)	-19.5 (± 1.81)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Number of Monthly Days With Use of Acute Migraine Medication Averaged Over Weeks 13 to 24

End point title	Change From Baseline in the Number of Monthly Days With Use of Acute Migraine Medication Averaged Over Weeks 13 to 24

End point description:

In the evening eDiary, participants were asked each day to fill out whether they used any of the following medications during that day: Ergotamine, triptan, analgesic, opioid, or combination analgesic. A day where the participant answered that they took any of those in the evening eDiary was considered a day with use of acute migraine medication. FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13- 24

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	294	287	285	
Units: days/month				
arithmetic mean (standard error)	-1.7 (± 0.36)	-4.6 (± 0.36)	-5.2 (± 0.36)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Number of Monthly Days With Use of Acute Migraine Medication Averaged Over Weeks 1 to 12

End point title	Change From Baseline in the Number of Monthly Days With Use of Acute Migraine Medication Averaged Over Weeks 1 to 12

End point description:

In the evening eDiary, participants were asked each day to fill out whether they used any of the following medications during that day: Ergotamine, triptan, analgesic, opioid, or combination analgesic. A day where the participant answered that they took any of those in the evening eDiary was considered a day with use of acute migraine medication. FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1 - 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	298	298	290	
Units: days/month				
arithmetic mean (standard error)	-1.6 (± 0.34)	-4.1 (± 0.33)	-4.6 (± 0.34)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Number of MMDs With Use of Acute Medication Averaged Over Weeks 13 to 24

End point title	Change From Baseline in the Number of MMDs With Use of Acute Medication Averaged Over Weeks 13 to 24

End point description:

Number of MMDs with acute medication usage was derived using the answer to "Did you take any medications to treat this headache?" in the headache diary. The question was asked when a participant was ending a headache. Thus, a migraine day with acute medication usage was defined as a migraine day with the extra condition that this question was answered as "Yes". FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13 - 24

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	295	287	286	
Units: days/month				
arithmetic mean (standard error)	-2.1 (± 0.39)	-4.9 (± 0.39)	-5.8 (± 0.38)	

Statistical analyses

No statistical analyses for this end point

Secondary: PGIC Score at Week 24

End point title	PGIC Score at Week 24

End point description:

The PGIC is a single, participant-reported item reflecting the participant's impression of change in his/her disease status since the start of the study (that is, in relation to activity limitations, symptoms, emotions, and overall quality of life). Participants rated their impression of change in disease status on a 7-point scale (1 = very much improved; 2 = much improved; 3 = minimally improved; 4 = no change; 5 = minimally worse; 6 = much worse; 7 = very much worse) where a higher score indicated worsening. Score ranges from 1 (Very Much Improved) to 7 (Very Much Worse). Lower scores indicate better health status. FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	286	280	281	
Units: units on a scale				
arithmetic mean (standard error)	3.5 (± 0.09)	2.5 (± 0.09)	2.4 (± 0.09)	

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression of Change (PGIC) Score at Week 12

End point title	Patient Global Impression of Change (PGIC) Score at Week 12

End point description:

The PGIC is a single, participant-reported item reflecting the participant's impression of change in his/her disease status since the start of the study (that is, in relation to activity limitations, symptoms, emotions, and overall quality of life). Participants rated their impression of change in disease status on a 7-point scale (1 = very much improved; 2 = much improved; 3 = minimally improved; 4 = no change; 5 = minimally worse; 6 = much worse; 7 = very much worse) where a higher score indicated worsening. Score ranges from 1 (Very Much Improved) to 7 (Very Much Worse). Lower scores indicate better health status. FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	297	292	289	
Units: units on a scale				
arithmetic mean (standard error)	3.6 (± 0.09)	2.6 (± 0.09)	2.5 (± 0.09)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Migraine on the Day After First Dosing

End point title	Percentage of Participants With Migraine on the Day After First Dosing

End point description:

FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12.

End point type	Secondary

End point timeframe:

Day 1

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	298	299	293	
Units: percentage of participants				
number (not applicable)	43.7	27.2	24.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the HIT-6 Score at Week 24

End point title	Change From Baseline in the HIT-6 Score at Week 24

End point description:

The HIT-6 (version 1.0) is a Likert-type, self-reporting questionnaire designed to assess the impact of an occurring headache and its effect on the ability to function normally in daily life. The HIT-6 contains 6 questions, each item was rated from never to always with the following response scores: never = 6, rarely = 8, sometimes = 10, very often = 11, and always = 13. The total score for the HIT-6 was the sum of each response score ranging from 36 to 78. The life impact derived from the total score was described as followed: severe (≥60), substantial (56-59), some (50-55), little to none (≤49). FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	278	266	276	
Units: units on a scale				
arithmetic mean (standard error)	-3.9 (± 0.63)	-8.9 (± 0.63)	-9.9 (± 0.62)	

Statistical analyses

No statistical analyses for this end point

Secondary: Most Bothersome Symptom (MBS) Score at Week 12

End point title	Most Bothersome Symptom (MBS) Score at Week 12

End point description:

Participants were asked about their most bothersome symptom associated with their migraines during the Baseline Visit. Participants were asked to rate the improvement in this symptom from baseline on a 7-point scale (1 = very much improved; 2 = much improved; 3 = minimally improved; 4 = no change; 5 = minimally worse; 6 = much worse; 7 = very much worse) where a high score indicated worsening. Score ranges from 1 (Very Much Improved) to 7 (Very Much Worse). Lower scores indicate better health status. The MBS areas included: nausea, vomiting, sensitivity to light, sensitivity to sound, mental cloudiness, fatigue, pain with activity, mood changes, and other symptoms. FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	293	289	287	
Units: units on a scale				
arithmetic mean (standard error)	3.7 (± 0.09)	2.8 (± 0.09)	2.7 (± 0.09)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Number of MMDs in Participants With Medication Overuse Headache (MOH) Averaged Over Weeks 1 to 12

End point title	Change From Baseline in the Number of MMDs in Participants With Medication Overuse Headache (MOH) Averaged Over Weeks 1 to 12

End point description:

FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1 - 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	38	35	
Units: days/month				
arithmetic mean (standard error)	-2.3 (± 1.12)	-5.6 (± 1.07)	-7.3 (± 1.18)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Migraine-Specific Quality of Life (MSQ) Subscores (Role Function-Restrictive, Role Function-Preventive, Emotional Function) at Week 12

End point title	Change From Baseline in the Migraine-Specific Quality of Life (MSQ) Subscores (Role Function-Restrictive, Role Function-Preventive, Emotional Function) at Week 12

End point description:

The MSQ is a participant-reported outcome designed to assess the quality of life in participants with migraine. It consists of 14 items covering 3 domains: role function restrictive (7 items); role function preventive (4 items); and emotional function (3 items). Each item was scored on a 6-point scale ranging from 1 (none of the time) to 6 (all of the time). Raw domain scores were summed and transformed to a 0- to 100-point scale. Higher scores indicated better quality of life. FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	288	271	283	
Units: units on a scale				
arithmetic mean (standard error)				
MSQ Role Function-Restrictive	13.7 (± 1.75)	25.0 (± 1.75)	28.7 (± 1.72)	
MSQ Role Function-Preventive	11.6 (± 1.63)	22.7 (± 1.64)	25.0 (± 1.61)	
MSQ Emotional Function	9.6 (± 1.83)	20.6 (± 1.84)	23.1 (± 1.80)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Health-Related Quality of Life (EQ-5D-5L) Visual Analog Scale (VAS) Score at Week 12

End point title	Change From Baseline in the Health-Related Quality of Life (EQ-5D-5L) Visual Analog Scale (VAS) Score at Week 12

End point description:

The EQ-5D-5L is a participant-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) and a VAS of the overall health state. Each descriptive item was rated on a 5-point index ranging from 1 (no problems) to 5 (extreme problems). The VAS ranged from 0 (worst imaginable health state) to 100 (best imaginable health state). FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	287	271	281	
Units: units on a scale				
arithmetic mean (standard error)	-3.1 (± 1.39)	2.0 (± 1.40)	4.4 (± 1.38)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the MSQ Subscores (Role Function-Restrictive, Role Function-Preventive, Emotional Function) at Week 24

End point title	Change From Baseline in the MSQ Subscores (Role Function-Restrictive, Role Function-Preventive, Emotional Function) at Week 24

End point description:

The MSQ is a participant-reported outcome designed to assess the quality of life in participants with migraine. It consists of 14 items covering 3 domains: role function restrictive (7 items); role function preventive (4 items); and emotional function (3 items). Each item was scored on a 6-point scale ranging from 1 (none of the time) to 6 (all of the time). Raw domain scores were summed and transformed to a 0- to 100-point scale. Higher scores indicated better quality of life. FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	278	259	275	
Units: units on a scale				
arithmetic mean (standard error)				
MSQ Role Function-Restrictive	15.0 (± 1.76)	30.1 (± 1.78)	30.0 (± 1.73)	
MSQ Role Function-Preventive	13.1 (± 1.63)	25.7 (± 1.65)	26.3 (± 1.61)	
MSQ Emotional Function	9.9 (± 1.84)	24.1 (± 1.86)	24.1 (± 1.81)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Health-Related Quality of Life (EQ-5D-5L) VAS Score at Week 24

End point title	Change From Baseline in the Health-Related Quality of Life (EQ-5D-5L) VAS Score at Week 24

End point description:

The EQ-5D-5L is a participant-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) and a VAS of the overall health state. Each descriptive item was rated on a 5-point index ranging from 1 (no problems) to 5 (extreme problems). The VAS ranged from 0 (worst imaginable health state) to 100 (best imaginable health state). FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	276	258	273	
Units: units on a scale				
arithmetic mean (standard error)	-2.8 (± 1.38)	2.0 (± 1.40)	5.2 (± 1.37)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Work Productivity and Activity Impairment (WPAI) Questionnaire Subscores (Absenteeism, Presenteeism, Work Productivity Loss, Activity Impairment) at Week 12

End point title	Change From Baseline in the Work Productivity and Activity Impairment (WPAI) Questionnaire Subscores (Absenteeism, Presenteeism, Work Productivity Loss, Activity Impairment) at Week 12

End point description:

WPAI Questionnaire contains 6 items that measure: 1) employment status, 2) hours missed from work due to the specific health problem, 3) hours missed from work for other reasons, 4) hours actually worked, 5) degree health affected productivity while working, and 6) degree health affected productivity in regular unpaid activities. Four scores were calculated from the responses to these 6 items: absenteeism, presenteeism, work productivity loss, and activity impairment. Scores were calculated as impairment percentages (0-100%), with higher numbers indicating greater impairment and less productivity, i.e, worse outcomes. FAS: all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N= participants evaluable for this endpoint. n = participants evaluable for specified categories.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	286	268	280	
Units: units on a scale				
arithmetic mean (standard error)				
Absenteeism (n= 196,174,183)	-0.1 (± 1.49)	-5.8 (± 1.53)	-3.8 (± 1.50)	
Presenteeism (n= 188,169,179)	-9.9 (± 2.42)	-19.0 (± 2.46)	-23.3 (± 2.40)	
Work productivity loss (n= 188,169,179)	-9.7 (± 2.56)	-19.5 (± 2.61)	-24.0 (± 2.54)	
Activity impairment (n= 286,268,280)	-11.2 (± 2.07)	-21.3 (± 2.07)	-23.8 (± 2.05)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the WPAI Questionnaire Subscores (Absenteeism, Presenteeism, Work Productivity Loss, Activity Impairment) at Week 24

End point title	Change From Baseline in the WPAI Questionnaire Subscores (Absenteeism, Presenteeism, Work Productivity Loss, Activity Impairment) at Week 24

End point description:

WPAI Questionnaire contains 6 items that measure: 1) employment status, 2) hours missed from work due to the specific health problem, 3) hours missed from work for other reasons, 4) hours actually worked, 5) degree health affected productivity while working, and 6) degree health affected productivity in regular unpaid activities. Four scores were calculated from the responses to these 6 items: absenteeism, presenteeism, work productivity loss, and activity impairment. Scores were calculated as impairment percentages (0-100%), with higher numbers indicating greater impairment and less productivity, i.e, worse outcomes. FAS: all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N= participants evaluable for this endpoint. n = participants evaluable for specified categories.

End point type	Secondary
End point timeframe: Baseline, Week 24	

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	275	256	273	
Units: units on a scale				
arithmetic mean (standard error)				
Absenteeism (n= 180,151,168)	-0.7 (± 1.46)	-5.2 (± 1.53)	-5.4 (± 1.47)	
Presenteeism (n= 173,145,166)	-7.5 (± 2.49)	-22.2 (± 2.59)	-19.3 (± 2.46)	
Work productivity loss (n= 173,145,166)	-7.2 (± 2.62)	-22.6 (± 2.73)	-20.2 (± 2.60)	
Activity impairment (n= 275,256,273)	-10.1 (± 2.07)	-24.7 (± 2.09)	-22.6 (± 2.04)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With ≥5-Point Reduction From Baseline to Week 12 in HIT-6 Score

End point title	Percentage of Participants With ≥5-Point Reduction From Baseline to Week 12 in HIT-6 Score

End point description:

The HIT-6 (version 1.0) is a Likert-type, self-reporting questionnaire designed to assess the impact of an occurring headache and its effect on the ability to function normally in daily life. The HIT-6 contains 6 questions, each item was rated from never to always with the following response scores: never = 6, rarely = 8, sometimes = 10, very often = 11, and always = 13. The total score for the HIT-6 was the sum of each response score ranging from 36 to 78. The life impact derived from the total score was described as followed: severe (≥60), substantial (56-59), some (50-55), little to none (≤49). FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N = participants evaluable for this endpoint.

End point type	Secondary
End point timeframe: Baseline to Week 12	

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	288	280	284	
Units: percentage of participants				
number (not applicable)	39.9	62.1	62.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With ≥5-Point Reduction From Baseline to Week 24 in HIT-6 Score

End point title	Percentage of Participants With ≥5-Point Reduction From Baseline to Week 24 in HIT-6 Score

End point description:

The HIT-6 (version 1.0) is a Likert-type, self-reporting questionnaire designed to assess the impact of an occurring headache and its effect on the ability to function normally in daily life. The HIT-6 contains 6 questions, each item was rated from never to always with the following response scores: never = 6, rarely = 8, sometimes = 10, very often = 11, and always = 13. The total score for the HIT-6 was the sum of each response score ranging from 36 to 78. The life impact derived from the total score was described as followed: severe (≥60), substantial (56-59), some (50-55), little to none (≤49). FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	288	280	285	
Units: percentage of participants				
number (not applicable)	46.2	72.1	71.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization (HCRU): Visits to a Family Doctor/General Practitioner

End point title	Health Care Resource Utilization (HCRU): Visits to a Family Doctor/General Practitioner

End point description:

Number of participants who visited to a family doctor/general practitioner has been reported. FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	297	291	289	
Units: participants				
0 Visit	244	259	256	
1 Visit	35	22	22	
2 Visits	6	5	6	
3 Visits	7	2	3	
4 Visits	1	1	1	
5 Visits	1	2	1	
6 Visits	2	0	0	
8 Visits	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: HCRU: Visits to a Specialist

End point title	HCRU: Visits to a Specialist

End point description:

Number of participants who visited to a specialist has been reported. FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	297	291	289	
Units: participants				
0 Visit	249	256	257	
1 Visit	33	31	24	
2 Visits	2	2	4	
3 Visits	7	2	4	
5 Visits	1	0	0	
6 Visits	4	0	0	
8 Visits	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: HCRU: Number of Emergency Department Visits Due to Your Migraine

End point title	HCRU: Number of Emergency Department Visits Due to Your Migraine

End point description:

Number of participants who visited to emergency department due to your migraine has been reported. FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	297	291	289	
Units: participants				
0 Visit	289	289	285	
1 Visit	6	1	3	
2 Visits	0	1	1	
3 Visits	1	0	0	
8 Visits	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: HCRU: Number of Hospital Admissions Due to Migraine

End point title	HCRU: Number of Hospital Admissions Due to Migraine

End point description:

Number of participants who admitted in the hospital due to migraine has been reported. FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	297	291	289	
Units: participants				
0 Visit	295	289	287	
1 Visit	1	1	2	
2 Visits	0	1	0	
4 Visits	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: HCRU: Total Number of Overnight Hospital Stays Due to Migraine

End point title	HCRU: Total Number of Overnight Hospital Stays Due to Migraine

End point description:

Number of participants who had total number of overnight hospital stays due to migraine has been reported. FAS included all randomized participants who had a valid baseline assessment and at least 1 valid post-baseline 4-week assessment of MMDs in Weeks 1 to 12. Here, N = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	297	291	289	
Units: participants				
0 Visit	295	290	289	
1 Visit	1	0	0	
3 Visits	1	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Number of MMDs Averaged Over Weeks 25 to 36, 37 to 48, 49 to 60, and 61 to 72

End point title	Change From Baseline in the Number of MMDs Averaged Over Weeks 25 to 36, 37 to 48, 49 to 60, and 61 to 72

End point description:

A migraine day was defined in endpoint #1. Full-analysis-long-term set (FAS_LT) included all randomized participants who received at least 1 infusion of study drug, had a visit in the Extension Period, and who had a valid baseline assessment and a valid assessment of monthly migraine days in the Extension Period. Here, 'N' = participants evaluable for this endpoint. 'n' = participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 25 - 36, 37 - 48, 49 - 60, and 61 - 72

End point values	Placebo to Eptinezumab 100 mg	Placebo to Eptinezumab 300 mg	Eptinezumab 100 mg to Eptinezumab 100 mg	Eptinezumab 300 mg to Eptinezumab 300 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	144	146	282	282
Units: days/month				
arithmetic mean (standard error)				
Change at Weeks 25-36 (n=144,146,282,282)	-4.7 (± 0.49)	-6.1 (± 0.49)	-5.8 (± 0.39)	-5.9 (± 0.39)
Change at Weeks 37-48 (n=140,146,282,273)	-5.0 (± 0.50)	-6.0 (± 0.50)	-5.8 (± 0.40)	-6.0 (± 0.40)
Change at Weeks 49-60 (n=134,140,270,265)	-5.6 (± 0.51)	-6.6 (± 0.51)	-5.8 (± 0.41)	-6.0 (± 0.41)
Change at Weeks 61-72 (n=126,136,252,246)	-5.9 (± 0.51)	-6.8 (± 0.51)	-6.6 (± 0.41)	-6.5 (± 0.41)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With ≥50% Reduction From Baseline in MMDs Averaged Over Weeks 25 to 36, 37 to 48, 49 to 60, and 61 to 72

End point title	Percentage of Participants With ≥50% Reduction From Baseline in MMDs Averaged Over Weeks 25 to 36, 37 to 48, 49 to 60, and 61 to 72

End point description:

A migraine day was defined in endpoint #1. FAS_LT included all randomized participants who received at least 1 infusion of study drug, had a visit in the Extension Period, and who had a valid baseline assessment and a valid assessment of monthly migraine days in the Extension Period. Here, 'N' = participants evaluable for this endpoint. 'n' = participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline to Weeks 25 - 36, 37 - 48, 49 - 60, and 61 - 72

End point values	Placebo to Eptinezumab 100 mg	Placebo to Eptinezumab 300 mg	Eptinezumab 100 mg to Eptinezumab 100 mg	Eptinezumab 300 mg to Eptinezumab 300 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	144	146	282	282
Units: percentage of participants				
number (not applicable)				
Weeks 25-36 (n=144,146,282,282)	48.6	63.0	59.6	61.0
Weeks 37-48 (n=140,146,282,273)	49.3	60.3	60.6	61.9
Weeks 49-60 (n=134,140,270,265)	59.7	68.6	62.6	62.3
Weeks 61-72 (n=126,136,252,246)	63.5	69.9	68.3	65.9

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With ≥75% Reduction From Baseline in MMDs Averaged Over Weeks 25 to 36, 37 to 48, 49 to 60, and 61 to 72

End point title	Percentage of Participants With ≥75% Reduction From Baseline in MMDs Averaged Over Weeks 25 to 36, 37 to 48, 49 to 60, and 61 to 72

End point description:

A migraine day was defined in endpoint #1. FAS_LT included all randomized participants who received at least 1 infusion of study drug, had a visit in the Extension Period, and who had a valid baseline assessment and a valid assessment of monthly migraine days in the Extension Period. Here, 'N' = participants evaluable for this endpoint. 'n' = participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline to Weeks 25 - 36, 37 - 48, 49 - 60, and 61 - 72

End point values	Placebo to Eptinezumab 100 mg	Placebo to Eptinezumab 300 mg	Eptinezumab 100 mg to Eptinezumab 100 mg	Eptinezumab 300 mg to Eptinezumab 300 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	144	146	282	282
Units: percentage of participants				
number (not applicable)				
Weeks 25-36 (n=144,146,282,282)	19.4	28.1	25.9	31.2
Weeks 37-48 (n=140,146,282,273)	27.9	30.8	31.6	32.6
Weeks 49-60 (n=134,140,270,265)	32.1	33.6	29.3	38.9
Weeks 61-72 (n=126,136,252,246)	36.5	39.0	37.7	44.7

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HIT-6 Score at Weeks 36, 48, 60, and 72

End point title	Change From Baseline in HIT-6 Score at Weeks 36, 48, 60, and 72

End point description:

The HIT-6 (version 1.0) is a Likert-type, self-reporting questionnaire designed to assess the impact of an occurring headache and its effect on the ability to function normally in daily life. The HIT-6 contains 6 questions, each item was rated from never to always with the following response scores: never = 6, rarely = 8, sometimes = 10, very often = 11, and always = 13. The total score for the HIT-6 was the sum of each response score ranging from 36 to 78. The life impact derived from the total score was

described as followed: severe (≥60), substantial (56-59), some (50-55), little to none (≤49). FAS_LT included all randomized participants who received at least 1 infusion of study drug, had a visit in the Extension Period, and who had a valid baseline assessment and a valid assessment of monthly migraine days in the Extension Period. Here, 'N' = participants evaluable for this endpoint. 'n' = participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 36, 48, 60, and 72

End point values	Placebo to Eptinezumab 100 mg	Placebo to Eptinezumab 300 mg	Eptinezumab 100 mg to Eptinezumab 100 mg	Eptinezumab 300 mg to Eptinezumab 300 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	138	139	265	272
Units: units on a scale				
arithmetic mean (standard error)				
Change at Week 36 (n=138,137,265,272)	-10.01 (± 0.69)	-12.15 (± 0.73)	-10.99 (± 0.57)	-12.0 (± 0.56)
Change at Week 48 (n=134,139,260,260)	-10.71 (± 0.77)	-12.71 (± 0.75)	-12.55 (± 0.59)	-12.68 (± 0.60)
Change at Week 60 (n=128,136,249,258)	-12.54 (± 0.80)	-13.21 (± 0.71)	-12.57 (± 0.56)	-13.15 (± 0.59)
Change at Week 72 (n=124,131,239,237)	-12.68 (± 0.87)	-15.02 (± 0.78)	-13.28 (± 0.63)	-14.13 (± 0.63)

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 72

Adverse event reporting additional description:

All-patients-treated set (APTS) included all randomized participants who received at least 1 infusion of the study drug.
All-patients-treated-long-term set (APTS_LT) included all randomized participants who received at least 1 infusion of the study drug and had a visit in the Extension Period.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Placebo-controlled Period: Placebo

Reporting group description:

Participants received placebo matched to eptinezumab by IV infusion on Baseline (Day 0) and on Week 12.

Reporting group title	Placebo-controlled Period: Eptinezumab 300 mg

Reporting group description:

Participants received eptinezumab 100 mg by IV infusion on Baseline (Day 0) and on Week 12.

Reporting group title	Placebo-controlled Period: Eptinezumab 100 mg

Reporting group description:

Participants received eptinezumab 100 mg by IV infusion on Baseline (Day 0) and on Week 12.

Reporting group title	Extension Period: Eptinezumab 300 mg to Eptinezumab 300 mg

Reporting group description:

Participants who received eptinezumab 300 mg in the double-blind placebo-controlled period, continued to receive the same dose of eptinezumab in the dose-blinded extension period.

Reporting group title	Extension Period: Placebo to Eptinezumab 100 mg

Reporting group description:

Participants who received placebo in the double-blind placebo-controlled period, received eptinezumab 100 mg in the dose-blinded extension period.

Reporting group title	Extension Period: Placebo to Eptinezumab 300 mg

Reporting group description:

Participants who received placebo in the double-blind placebo-controlled period, received eptinezumab 300 mg in the dose-blinded extension period.

Reporting group title	Extension Period: Eptinezumab 100 mg to Eptinezumab 100 mg

Reporting group description:

Participants who received eptinezumab 100 mg in the double-blind placebo-controlled period, continued to receive the same dose of eptinezumab in the dose-blinded extension period.

Serious adverse events	Placebo-controlled Period: Placebo	Placebo-controlled Period: Eptinezumab 300 mg	Placebo-controlled Period: Eptinezumab 100 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 298 (1.01%)	7 / 294 (2.38%)	6 / 299 (2.01%)
number of deaths (all causes)	0	0	0
number of deaths resulting from			

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 298 (0.00%)	1 / 294 (0.34%)	0 / 299 (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
Colorectal adenocarcinoma			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer in situ			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal papilloma of breast			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal carcinoma			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal neoplasm			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 298 (0.00%)	2 / 294 (0.68%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			

subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal turbinate hypertrophy			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 298 (0.34%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	1 / 298 (0.34%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	1 / 298 (0.34%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	1 / 298 (0.34%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 298 (0.00%)	1 / 294 (0.34%)	0 / 299 (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
Psychogenic seizure			
subjects affected / exposed	0 / 298 (0.00%)	1 / 294 (0.34%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	1 / 298 (0.34%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical radiculopathy			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial aneurysm			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculopathy			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Conductive deafness			

subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye pain			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin and subcutaneous tissue disorders			
Lichen planus			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Bladder prolapse			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 298 (0.00%)	1 / 294 (0.34%)	0 / 299 (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
Periarthritis			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diastasis recti abdominis			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 298 (0.00%)	2 / 294 (0.68%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis intestinal perforated			

subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal disease			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Extension Period: Eptinezumab 300 mg to Eptinezumab 300 mg	Extension Period: Placebo to Eptinezumab 100 mg	Extension Period: Placebo to Eptinezumab 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 284 (3.17%)	2 / 145 (1.38%)	7 / 148 (4.73%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			

subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal adenocarcinoma			
subjects affected / exposed	0 / 284 (0.00%)	1 / 145 (0.69%)	0 / 148 (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
Breast cancer in situ			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal papilloma of breast			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal carcinoma			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal neoplasm			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Epistaxis			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal turbinate hypertrophy			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychogenic seizure			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical radiculopathy			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial aneurysm			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculopathy			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Conductive deafness			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Retinal detachment			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye pain			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 284 (0.35%)	1 / 145 (0.69%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Lichen planus			

subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Bladder prolapse			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periarthritis			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diastasis recti abdominis			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis intestinal perforated			

subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal disease			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Extension Period: Eptinezumab 100 mg to Eptinezumab 100 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 288 (3.13%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			

subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colorectal adenocarcinoma			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer in situ			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intraductal papilloma of breast			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophageal carcinoma			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Laryngeal neoplasm			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Epistaxis			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nasal turbinate hypertrophy			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hand fracture			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Concussion			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychogenic seizure			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Migraine			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cervical radiculopathy			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intracranial aneurysm			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radiculopathy			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Conductive deafness			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			

Retinal detachment			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye pain			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Lichen planus			

subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Bladder prolapse			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Periarthritis			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diastasis recti abdominis			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis intestinal perforated			

subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic sinusitis			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Peritonitis			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pilonidal disease			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Placebo-controlled Period: Placebo	Placebo-controlled Period: Eptinezumab 300 mg	Placebo-controlled Period: Eptinezumab 100 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 298 (28.52%)	90 / 294 (30.61%)	95 / 299 (31.77%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 298 (1.01%)	4 / 294 (1.36%)	4 / 299 (1.34%)
occurrences (all)	3	4	4

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 298 (1.34%)	6 / 294 (2.04%)	2 / 299 (0.67%)
occurrences (all)	4	6	2
Pyrexia			
subjects affected / exposed	4 / 298 (1.34%)	4 / 294 (1.36%)	0 / 299 (0.00%)
occurrences (all)	5	4	0
Asthenia			
subjects affected / exposed	2 / 298 (0.67%)	3 / 294 (1.02%)	3 / 299 (1.00%)
occurrences (all)	2	3	3
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	2 / 298 (0.67%)	3 / 294 (1.02%)	0 / 299 (0.00%)
occurrences (all)	3	4	0
Social circumstances			
Menopause			
subjects affected / exposed	1 / 298 (0.34%)	0 / 294 (0.00%)	1 / 299 (0.33%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	1 / 298 (0.34%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences (all)	1	0	0
Menopausal symptoms			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	1 / 299 (0.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 298 (0.00%)	3 / 294 (1.02%)	2 / 299 (0.67%)
occurrences (all)	0	3	2
Cough			
subjects affected / exposed	2 / 298 (0.67%)	0 / 294 (0.00%)	2 / 299 (0.67%)
occurrences (all)	2	0	3
Nasal congestion			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	1 / 299 (0.33%)
occurrences (all)	0	0	1
Psychiatric disorders			

Insomnia			
subjects affected / exposed	0 / 298 (0.00%)	3 / 294 (1.02%)	2 / 299 (0.67%)
occurrences (all)	0	3	2
Depressive symptom			
subjects affected / exposed	3 / 298 (1.01%)	1 / 294 (0.34%)	0 / 299 (0.00%)
occurrences (all)	3	1	0
Anxiety			
subjects affected / exposed	2 / 298 (0.67%)	1 / 294 (0.34%)	1 / 299 (0.33%)
occurrences (all)	2	1	1
Depression			
subjects affected / exposed	1 / 298 (0.34%)	0 / 294 (0.00%)	1 / 299 (0.33%)
occurrences (all)	1	0	1
Investigations			
Weight decreased			
subjects affected / exposed	0 / 298 (0.00%)	2 / 294 (0.68%)	0 / 299 (0.00%)
occurrences (all)	0	2	0
Blood pressure increased			
subjects affected / exposed	3 / 298 (1.01%)	0 / 294 (0.00%)	2 / 299 (0.67%)
occurrences (all)	4	0	2
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 298 (0.67%)	1 / 294 (0.34%)	3 / 299 (1.00%)
occurrences (all)	2	1	3
Weight increased			
subjects affected / exposed	2 / 298 (0.67%)	1 / 294 (0.34%)	1 / 299 (0.33%)
occurrences (all)	2	1	1
Blood cholesterol increased			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Post vaccination syndrome			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	4 / 299 (1.34%)
occurrences (all)	0	0	4
Procedural pain			
subjects affected / exposed	1 / 298 (0.34%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			

subjects affected / exposed	1 / 298 (0.34%)	0 / 294 (0.00%)	2 / 299 (0.67%)
occurrences (all)	1	0	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 298 (1.68%)	5 / 294 (1.70%)	2 / 299 (0.67%)
occurrences (all)	5	5	2
Migraine			
subjects affected / exposed	3 / 298 (1.01%)	3 / 294 (1.02%)	1 / 299 (0.33%)
occurrences (all)	3	5	1
Sciatica			
subjects affected / exposed	1 / 298 (0.34%)	3 / 294 (1.02%)	1 / 299 (0.33%)
occurrences (all)	1	3	1
Somnolence			
subjects affected / exposed	4 / 298 (1.34%)	0 / 294 (0.00%)	1 / 299 (0.33%)
occurrences (all)	4	0	2
Headache			
subjects affected / exposed	3 / 298 (1.01%)	3 / 294 (1.02%)	3 / 299 (1.00%)
occurrences (all)	4	3	4
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 298 (0.34%)	0 / 294 (0.00%)	1 / 299 (0.33%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 298 (1.68%)	5 / 294 (1.70%)	0 / 299 (0.00%)
occurrences (all)	5	5	0
Constipation			
subjects affected / exposed	3 / 298 (1.01%)	1 / 294 (0.34%)	3 / 299 (1.00%)
occurrences (all)	3	2	3
Abdominal pain upper			
subjects affected / exposed	2 / 298 (0.67%)	4 / 294 (1.36%)	5 / 299 (1.67%)
occurrences (all)	3	5	5
Abdominal pain			
subjects affected / exposed	2 / 298 (0.67%)	2 / 294 (0.68%)	4 / 299 (1.34%)
occurrences (all)	2	2	4
Nausea			

subjects affected / exposed	4 / 298 (1.34%)	5 / 294 (1.70%)	4 / 299 (1.34%)
occurrences (all)	5	5	4
Haemorrhoids			
subjects affected / exposed	2 / 298 (0.67%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences (all)	3	0	0
Dyspepsia			
subjects affected / exposed	0 / 298 (0.00%)	1 / 294 (0.34%)	1 / 299 (0.33%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	4 / 299 (1.34%)
occurrences (all)	0	0	4
Pruritus			
subjects affected / exposed	0 / 298 (0.00%)	2 / 294 (0.68%)	2 / 299 (0.67%)
occurrences (all)	0	2	2
Rash			
subjects affected / exposed	1 / 298 (0.34%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 298 (0.00%)	4 / 294 (1.36%)	6 / 299 (2.01%)
occurrences (all)	0	5	7
Back pain			
subjects affected / exposed	4 / 298 (1.34%)	3 / 294 (1.02%)	6 / 299 (2.01%)
occurrences (all)	4	3	6
Neck pain			
subjects affected / exposed	1 / 298 (0.34%)	3 / 294 (1.02%)	1 / 299 (0.33%)
occurrences (all)	1	3	1
Pain in extremity			
subjects affected / exposed	3 / 298 (1.01%)	1 / 294 (0.34%)	3 / 299 (1.00%)
occurrences (all)	3	1	3
Myalgia			
subjects affected / exposed	0 / 298 (0.00%)	1 / 294 (0.34%)	2 / 299 (0.67%)
occurrences (all)	0	1	2
Osteoarthritis			

subjects affected / exposed	0 / 298 (0.00%)	2 / 294 (0.68%)	0 / 299 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 298 (1.01%)	9 / 294 (3.06%)	5 / 299 (1.67%)
occurrences (all)	3	11	7
COVID-19			
subjects affected / exposed	16 / 298 (5.37%)	15 / 294 (5.10%)	19 / 299 (6.35%)
occurrences (all)	16	15	19
Urinary tract infection			
subjects affected / exposed	5 / 298 (1.68%)	5 / 294 (1.70%)	1 / 299 (0.33%)
occurrences (all)	6	5	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 298 (0.34%)	2 / 294 (0.68%)	4 / 299 (1.34%)
occurrences (all)	1	2	4
Sinusitis			
subjects affected / exposed	3 / 298 (1.01%)	1 / 294 (0.34%)	0 / 299 (0.00%)
occurrences (all)	3	1	0
Gastroenteritis			
subjects affected / exposed	3 / 298 (1.01%)	2 / 294 (0.68%)	0 / 299 (0.00%)
occurrences (all)	3	2	0
Bronchitis			
subjects affected / exposed	1 / 298 (0.34%)	3 / 294 (1.02%)	0 / 299 (0.00%)
occurrences (all)	1	3	0
Pharyngitis			
subjects affected / exposed	1 / 298 (0.34%)	1 / 294 (0.34%)	1 / 299 (0.33%)
occurrences (all)	1	1	1
Oral herpes			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	1 / 299 (0.33%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	1 / 298 (0.34%)	0 / 294 (0.00%)	0 / 299 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	0 / 298 (0.00%)	1 / 294 (0.34%)	1 / 299 (0.33%)
occurrences (all)	0	1	1

Cystitis			
subjects affected / exposed	1 / 298 (0.34%)	2 / 294 (0.68%)	0 / 299 (0.00%)
occurrences (all)	1	2	0
Rhinitis			
subjects affected / exposed	0 / 298 (0.00%)	1 / 294 (0.34%)	0 / 299 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	0 / 298 (0.00%)	2 / 294 (0.68%)	0 / 299 (0.00%)
occurrences (all)	0	2	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	1 / 299 (0.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	0 / 298 (0.00%)	0 / 294 (0.00%)	3 / 299 (1.00%)
occurrences (all)	0	0	3
Vitamin B12 deficiency			
subjects affected / exposed	0 / 298 (0.00%)	1 / 294 (0.34%)	0 / 299 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 298 (0.34%)	1 / 294 (0.34%)	2 / 299 (0.67%)
occurrences (all)	1	1	2
Dyslipidaemia			
subjects affected / exposed	2 / 298 (0.67%)	2 / 294 (0.68%)	1 / 299 (0.33%)
occurrences (all)	2	2	1

Non-serious adverse events	Extension Period: Eptinezumab 300 mg to Eptinezumab 300 mg	Extension Period: Placebo to Eptinezumab 100 mg	Extension Period: Placebo to Eptinezumab 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	118 / 284 (41.55%)	57 / 145 (39.31%)	62 / 148 (41.89%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 284 (0.70%)	3 / 145 (2.07%)	0 / 148 (0.00%)
occurrences (all)	2	4	0
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	2 / 284 (0.70%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences (all)	3	0	1
Pyrexia			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	1 / 284 (0.35%)	1 / 145 (0.69%)	0 / 148 (0.00%)
occurrences (all)	1	1	0
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	2 / 284 (0.70%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences (all)	3	0	1
Social circumstances			
Menopause			
subjects affected / exposed	0 / 284 (0.00%)	1 / 145 (0.69%)	3 / 148 (2.03%)
occurrences (all)	0	1	3
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences (all)	1	0	1
Menopausal symptoms			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	2 / 148 (1.35%)
occurrences (all)	1	0	2
Nasal congestion			
subjects affected / exposed	3 / 284 (1.06%)	1 / 145 (0.69%)	0 / 148 (0.00%)
occurrences (all)	4	1	0
Psychiatric disorders			

Insomnia			
subjects affected / exposed	2 / 284 (0.70%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences (all)	3	0	1
Depressive symptom			
subjects affected / exposed	0 / 284 (0.00%)	1 / 145 (0.69%)	0 / 148 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	2 / 284 (0.70%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences (all)	2	0	1
Depression			
subjects affected / exposed	0 / 284 (0.00%)	2 / 145 (1.38%)	0 / 148 (0.00%)
occurrences (all)	0	2	0
Investigations			
Weight decreased			
subjects affected / exposed	2 / 284 (0.70%)	0 / 145 (0.00%)	2 / 148 (1.35%)
occurrences (all)	2	0	2
Blood pressure increased			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences (all)	1	0	1
Weight increased			
subjects affected / exposed	2 / 284 (0.70%)	2 / 145 (1.38%)	2 / 148 (1.35%)
occurrences (all)	2	2	2
Blood cholesterol increased			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	2 / 148 (1.35%)
occurrences (all)	1	0	2
Injury, poisoning and procedural complications			
Post vaccination syndrome			
subjects affected / exposed	5 / 284 (1.76%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences (all)	6	0	1
Procedural pain			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	2 / 148 (1.35%)
occurrences (all)	0	0	3
Ligament sprain			

subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 284 (1.41%)	1 / 145 (0.69%)	1 / 148 (0.68%)
occurrences (all)	5	1	1
Migraine			
subjects affected / exposed	2 / 284 (0.70%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences (all)	4	0	1
Sciatica			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	1 / 284 (0.35%)	2 / 145 (1.38%)	2 / 148 (1.35%)
occurrences (all)	1	3	3
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 284 (0.00%)	1 / 145 (0.69%)	0 / 148 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 284 (0.70%)	0 / 145 (0.00%)	2 / 148 (1.35%)
occurrences (all)	2	0	2
Constipation			
subjects affected / exposed	2 / 284 (0.70%)	1 / 145 (0.69%)	1 / 148 (0.68%)
occurrences (all)	2	1	2
Abdominal pain upper			
subjects affected / exposed	3 / 284 (1.06%)	1 / 145 (0.69%)	3 / 148 (2.03%)
occurrences (all)	4	1	4
Abdominal pain			
subjects affected / exposed	2 / 284 (0.70%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences (all)	2	0	1
Nausea			

subjects affected / exposed	3 / 284 (1.06%)	1 / 145 (0.69%)	5 / 148 (3.38%)
occurrences (all)	3	2	5
Haemorrhoids			
subjects affected / exposed	2 / 284 (0.70%)	2 / 145 (1.38%)	1 / 148 (0.68%)
occurrences (all)	2	2	1
Dyspepsia			
subjects affected / exposed	5 / 284 (1.76%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences (all)	6	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 284 (0.00%)	1 / 145 (0.69%)	1 / 148 (0.68%)
occurrences (all)	0	1	1
Pruritus			
subjects affected / exposed	6 / 284 (2.11%)	1 / 145 (0.69%)	0 / 148 (0.00%)
occurrences (all)	6	1	0
Rash			
subjects affected / exposed	3 / 284 (1.06%)	1 / 145 (0.69%)	0 / 148 (0.00%)
occurrences (all)	3	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 284 (2.11%)	1 / 145 (0.69%)	2 / 148 (1.35%)
occurrences (all)	6	1	3
Back pain			
subjects affected / exposed	2 / 284 (0.70%)	1 / 145 (0.69%)	2 / 148 (1.35%)
occurrences (all)	2	1	2
Neck pain			
subjects affected / exposed	0 / 284 (0.00%)	1 / 145 (0.69%)	0 / 148 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	3 / 284 (1.06%)	0 / 145 (0.00%)	1 / 148 (0.68%)
occurrences (all)	3	0	1
Myalgia			
subjects affected / exposed	1 / 284 (0.35%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences (all)	1	0	0
Osteoarthritis			

subjects affected / exposed	2 / 284 (0.70%)	2 / 145 (1.38%)	1 / 148 (0.68%)
occurrences (all)	2	2	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	27 / 284 (9.51%)	7 / 145 (4.83%)	13 / 148 (8.78%)
occurrences (all)	38	8	15
COVID-19			
subjects affected / exposed	63 / 284 (22.18%)	25 / 145 (17.24%)	31 / 148 (20.95%)
occurrences (all)	63	26	33
Urinary tract infection			
subjects affected / exposed	4 / 284 (1.41%)	3 / 145 (2.07%)	4 / 148 (2.70%)
occurrences (all)	5	4	4
Upper respiratory tract infection			
subjects affected / exposed	8 / 284 (2.82%)	4 / 145 (2.76%)	6 / 148 (4.05%)
occurrences (all)	8	4	8
Sinusitis			
subjects affected / exposed	5 / 284 (1.76%)	2 / 145 (1.38%)	2 / 148 (1.35%)
occurrences (all)	5	2	2
Gastroenteritis			
subjects affected / exposed	5 / 284 (1.76%)	1 / 145 (0.69%)	1 / 148 (0.68%)
occurrences (all)	6	1	1
Bronchitis			
subjects affected / exposed	3 / 284 (1.06%)	1 / 145 (0.69%)	3 / 148 (2.03%)
occurrences (all)	3	1	3
Pharyngitis			
subjects affected / exposed	4 / 284 (1.41%)	0 / 145 (0.00%)	3 / 148 (2.03%)
occurrences (all)	5	0	3
Oral herpes			
subjects affected / exposed	0 / 284 (0.00%)	2 / 145 (1.38%)	1 / 148 (0.68%)
occurrences (all)	0	2	1
Influenza			
subjects affected / exposed	1 / 284 (0.35%)	2 / 145 (1.38%)	1 / 148 (0.68%)
occurrences (all)	1	2	1
Herpes zoster			
subjects affected / exposed	0 / 284 (0.00%)	1 / 145 (0.69%)	0 / 148 (0.00%)
occurrences (all)	0	1	0

Cystitis			
subjects affected / exposed	3 / 284 (1.06%)	0 / 145 (0.00%)	5 / 148 (3.38%)
occurrences (all)	3	0	5
Rhinitis			
subjects affected / exposed	3 / 284 (1.06%)	1 / 145 (0.69%)	0 / 148 (0.00%)
occurrences (all)	3	1	0
Tonsillitis			
subjects affected / exposed	4 / 284 (1.41%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences (all)	5	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 284 (1.41%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences (all)	5	0	0
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	2 / 284 (0.70%)	1 / 145 (0.69%)	2 / 148 (1.35%)
occurrences (all)	2	1	2
Vitamin B12 deficiency			
subjects affected / exposed	0 / 284 (0.00%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	2 / 284 (0.70%)	2 / 145 (1.38%)	1 / 148 (0.68%)
occurrences (all)	2	2	1
Dyslipidaemia			
subjects affected / exposed	2 / 284 (0.70%)	0 / 145 (0.00%)	0 / 148 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Extension Period: Eptinezumab 100 mg to Eptinezumab 100 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	133 / 288 (46.18%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 288 (1.04%)		
occurrences (all)	4		
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all)	5 / 288 (1.74%) 5 0 / 288 (0.00%) 0 1 / 288 (0.35%) 3		
Immune system disorders Immunisation reaction subjects affected / exposed occurrences (all)	2 / 288 (0.69%) 2		
Social circumstances Menopause subjects affected / exposed occurrences (all)	1 / 288 (0.35%) 1		
Reproductive system and breast disorders Menstruation irregular subjects affected / exposed occurrences (all) Menopausal symptoms subjects affected / exposed occurrences (all)	3 / 288 (1.04%) 3 3 / 288 (1.04%) 3		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all)	3 / 288 (1.04%) 3 2 / 288 (0.69%) 5 2 / 288 (0.69%) 2		
Psychiatric disorders			

Insomnia subjects affected / exposed occurrences (all)	4 / 288 (1.39%) 4		
Depressive symptom subjects affected / exposed occurrences (all)	1 / 288 (0.35%) 1		
Anxiety subjects affected / exposed occurrences (all)	3 / 288 (1.04%) 3		
Depression subjects affected / exposed occurrences (all)	2 / 288 (0.69%) 2		
Investigations Weight decreased subjects affected / exposed occurrences (all)	1 / 288 (0.35%) 1		
Blood pressure increased subjects affected / exposed occurrences (all)	1 / 288 (0.35%) 1		
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	3 / 288 (1.04%) 3		
Weight increased subjects affected / exposed occurrences (all)	3 / 288 (1.04%) 3		
Blood cholesterol increased subjects affected / exposed occurrences (all)	0 / 288 (0.00%) 0		
Injury, poisoning and procedural complications Post vaccination syndrome subjects affected / exposed occurrences (all)	0 / 288 (0.00%) 0		
Procedural pain subjects affected / exposed occurrences (all)	0 / 288 (0.00%) 0		
Ligament sprain			

subjects affected / exposed	3 / 288 (1.04%)		
occurrences (all)	3		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 288 (0.69%)		
occurrences (all)	3		
Migraine			
subjects affected / exposed	7 / 288 (2.43%)		
occurrences (all)	7		
Sciatica			
subjects affected / exposed	2 / 288 (0.69%)		
occurrences (all)	2		
Somnolence			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	3 / 288 (1.04%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 288 (1.04%)		
occurrences (all)	3		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	3 / 288 (1.04%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	4 / 288 (1.39%)		
occurrences (all)	5		
Abdominal pain			
subjects affected / exposed	3 / 288 (1.04%)		
occurrences (all)	3		
Nausea			

subjects affected / exposed	2 / 288 (0.69%)		
occurrences (all)	2		
Haemorrhoids			
subjects affected / exposed	2 / 288 (0.69%)		
occurrences (all)	2		
Dyspepsia			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	2 / 288 (0.69%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	0 / 288 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 288 (2.08%)		
occurrences (all)	6		
Back pain			
subjects affected / exposed	8 / 288 (2.78%)		
occurrences (all)	8		
Neck pain			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	2 / 288 (0.69%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	3 / 288 (1.04%)		
occurrences (all)	3		
Osteoarthritis			

subjects affected / exposed	4 / 288 (1.39%)		
occurrences (all)	4		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	19 / 288 (6.60%)		
occurrences (all)	25		
COVID-19			
subjects affected / exposed	63 / 288 (21.88%)		
occurrences (all)	69		
Urinary tract infection			
subjects affected / exposed	3 / 288 (1.04%)		
occurrences (all)	4		
Upper respiratory tract infection			
subjects affected / exposed	13 / 288 (4.51%)		
occurrences (all)	14		
Sinusitis			
subjects affected / exposed	4 / 288 (1.39%)		
occurrences (all)	4		
Gastroenteritis			
subjects affected / exposed	2 / 288 (0.69%)		
occurrences (all)	2		
Bronchitis			
subjects affected / exposed	4 / 288 (1.39%)		
occurrences (all)	4		
Pharyngitis			
subjects affected / exposed	3 / 288 (1.04%)		
occurrences (all)	3		
Oral herpes			
subjects affected / exposed	1 / 288 (0.35%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	4 / 288 (1.39%)		
occurrences (all)	4		
Herpes zoster			
subjects affected / exposed	3 / 288 (1.04%)		
occurrences (all)	3		

Cystitis subjects affected / exposed occurrences (all)	1 / 288 (0.35%) 1		
Rhinitis subjects affected / exposed occurrences (all)	1 / 288 (0.35%) 1		
Tonsillitis subjects affected / exposed occurrences (all)	2 / 288 (0.69%) 2		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 288 (0.00%) 0		
Metabolism and nutrition disorders Hyperlipidaemia subjects affected / exposed occurrences (all)	0 / 288 (0.00%) 0		
Vitamin B12 deficiency subjects affected / exposed occurrences (all)	3 / 288 (1.04%) 3		
Hypercholesterolaemia subjects affected / exposed occurrences (all)	4 / 288 (1.39%) 4		
Dyslipidaemia subjects affected / exposed occurrences (all)	3 / 288 (1.04%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 January 2021	It included following changes: - Added section describing how to manage reactions to investigational medicinal product; - Added withdrawal criteria for participants who have: • anaphylactic reactions or other severe and/or serious hypersensitivity reactions; • significant risk of suicide according to Columbia Suicide Severity Rating Scale (C-SSRS). - Made changes to the statistical methodology: • Primary analysis: MMRM replaced analysis of covariance (ANCOVA); • Key secondary responder endpoint analyses: logistic regression replaced the Cochran–Mantel–Haenszel (CMH) test; • Analysis of MMDs (Weeks 13-24): MMRM replaced ANCOVA • Added: that participants with a migraine on the day after the first dose and that 100% responder endpoints will be analysed using an extended CMH test.
30 November 2021	It included following changes: - Cancelled the planned interim analysis; - Clarified definitions for eligibility: migraine day, headache day, and eDiary compliant day. - Updated sections that described: • randomization stratified by MHDs and by country; • timing of exit interviews for participants who withdrew prior to Week 24; • definitions for calculating the number of episodic migraine (EM)/chronic migraine (CM) participants and low/high frequency EM participants for subgroup analyses; • unscheduled visits - Added that: • participants could attend up to two Screening Visits to complete all screening assessments; • vaccination against COVID-19 is allowed during the study; • following the database lock for the Placebo-controlled Period, Sponsor personnel involved in the development of the Clinical Study Report were unblinded to individual treatment codes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported