Clinical trial results:
Biomarker and Genetic Predictors of Erenumab Treatment Response, a Phase 4 Investigational Open-label Study (INTERROGATE)

Summary

EudraCT number	2019-002331-28
Trial protocol	DK IS
Global end of trial date	18 January 2023

Results information

Result version number	v1 (current)
This version publication date	28 December 2023
First version publication date	28 December 2023

Trial information

Trial identification

Sponsor protocol code	20190006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04265755
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States,
Public contact	Study Director, Amgen Inc., +1 8665726436, medinfo@amgen.com
Scientific contact	Study Director, Amgen Inc., +1 8665726436, medinfo@amgen.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	18 January 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to explore the relationship between clinical response to erenumab and genetic biomarkers.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation Good Clinical Practice and other regulations/guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 October 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 696
Country: Number of subjects enrolled	Iceland: 710
Worldwide total number of subjects	1406
EEA total number of subjects	1406

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)	1366
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 1406 participants were enrolled in Denmark and Iceland between October 2020 and January 2023.

As pre-specified, the primary objective of the study was to assess the relationship between migraine polygenic risk score (mPRS) and the reduction in mean monthly migraine days (MMD) after using erenumab, regardless of erenumab dose received.

Pre-assignment

Screening details:

The study consisted of the following:
- A Screening Period of up to 3 weeks.
- A Baseline Period of 4 - 5 weeks to collect data on migraine headaches and acute headache medication use.
- A 24-week, Open-label Treatment Period.

Period 1

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

Arms

Arm title	Erenumab 70 mg/140 mg

Arm description:

Participants were enrolled into the Open-label Treatment Period and received erenumab 70 mg or 140 mg administered subcutaneously (SC) once every 4 weeks (Q4W) at the discretion of the investigator. Per protocol, dose switching between erenumab 70 mg and 140 mg was permitted at Week 12. However, participants could switch dose before or after Week 12 if needed based on investigator discretion. Dose comparison was not pre-specified.

Arm type	Experimental
Investigational medicinal product name	Erenumab
Investigational medicinal product code	AMG 334
Other name	AIMOVIG
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered via autoinjector pen.

Number of subjects in period 1	Erenumab 70 mg/140 mg
Started	1406
Dose switch from Baseline dose	504 [1]
Completed	1353
Not completed	53
Adverse event, serious fatal	1
Consent withdrawn by subject	39
Lost to follow-up	11

Decision by sponsor	2

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone includes only participants who switched from Baseline dose.

Baseline characteristics

Reporting groups	
Reporting group title	Erenumab 70 mg/140 mg

Reporting group description:

Participants were enrolled into the Open-label Treatment Period and received erenumab 70 mg or 140 mg administered subcutaneously (SC) once every 4 weeks (Q4W) at the discretion of the investigator. Per protocol, dose switching between erenumab 70 mg and 140 mg was permitted at Week 12. However, participants could switch dose before or after Week 12 if needed based on investigator discretion. Dose comparison was not pre-specified.

Reporting group values	Erenumab 70 mg/140 mg	Total	
Number of subjects	1406	1406	
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	42.5		
standard deviation	± 11.9	-	
Sex: Female, Male Units:			
Female	1228	1228	
Male	178	178	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	22	22	
Not Hispanic or Latino	1384	1384	
Unknown or Not Reported	0	0	
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	2	2	
Asian	17	17	
Black or African American	2	2	
Multiple	9	9	
Native Hawaiian or Other Pacific Islander	0	0	
White	1353	1353	
Other	23	23	
MMDs During the Baseline Period			
A migraine day was defined as a calendar day (00:00 to 23:59) in which the participant reported any migraine headache or took any triptan-based acute migraine-specific medication. Monthly migraine days were calculated as the number of migraine days in the 4 - 5 week Baseline Period.			
Units: days / month			
arithmetic mean	12.82		
standard deviation	± 5.92	-	

End points

End points reporting groups

Reporting group title	Erenumab 70 mg/140 mg

Reporting group description:

Participants were enrolled into the Open-label Treatment Period and received erenumab 70 mg or 140 mg administered subcutaneously (SC) once every 4 weeks (Q4W) at the discretion of the investigator. Per protocol, dose switching between erenumab 70 mg and 140 mg was permitted at Week 12. However, participants could switch dose before or after Week 12 if needed based on investigator discretion. Dose comparison was not pre-specified.

Primary: Percentage of Participants Achieving at Least a 50% Reduction From Baseline in Mean Monthly Migraine Days Over Months 4, 5, and 6 in relation to mPRS

End point title	Percentage of Participants Achieving at Least a 50% Reduction From Baseline in Mean Monthly Migraine Days Over Months 4, 5, and 6 in relation to mPRS[1]

End point description:

A migraine day was defined as a calendar day (00:00 to 23:59) in which the participant reports any migraine headache or takes any triptan-based acute migraine-specific medication.

At least a 50% reduction from Baseline in monthly migraine days was determined if: (average number of migraine days per month during the last 3 months [months 4, 5, and 6] of the 24-week Open-label Treatment Period minus number of migraine days during the 4-week Baseline Period) / number of migraine days during the 4-week Baseline Period * 100, was less than or equal to -50%.

The odds ratio of achieving ≥ 50% reduction from Baseline in mean MMD over months 4, 5, and 6 in relation to mPRS was 1.01 (95% confidence interval = 0.90, 1.13; p = 0.86).

End point type	Primary

End point timeframe:

4-week Baseline Period and the last 3 months (Months 4, 5, and 6) of the 24-week Open-label Treatment Period

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Additional statistics added to endpoint description due to system limitations inhibiting presentation for single arm studies.

End point values	Erenumab 70 mg/140 mg			
Subject group type	Reporting group			
Number of subjects analysed	1368[2]			
Units: percentage of participants				
number (confidence interval 95%)	54.9 (52.22 to 57.56)			

Notes:

[2] - EAS: participants in FAS who received at least 1 dose of investigational product.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 24 weeks

Adverse event reporting additional description:

All-cause mortality is reported for all participants enrolled/randomized in the study. Serious adverse events and other adverse events are reported for all participants who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Erenumab 70 mg

Reporting group description:

Participants who were initially enrolled into the Open-label Treatment Period and received erenumab 70 mg administered SC Q4W at the discretion of the investigator.

Reporting group title	Erenumab 140 mg

Reporting group description:

Participants who were initially enrolled into the Open-label Treatment Period and received erenumab 140 mg administered SC Q4W at the discretion of the investigator.

Reporting group title	Erenumab 140 mg Switch to 70 mg

Reporting group description:

Participants who initially received erenumab 140 mg administered SC Q4W and were dose switched to erenumab 70 mg per investigation's discretion.

Reporting group title	Erenumab 70 mg Switch to 140 mg

Reporting group description:

Participants who initially received erenumab 70 mg administered SC Q4W and were dose switched to erenumab 140 mg per investigation's discretion.

Serious adverse events	Erenumab 70 mg	Erenumab 140 mg	Erenumab 140 mg Switch to 70 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 214 (3.74%)	14 / 688 (2.03%)	1 / 7 (14.29%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Vascular disorders			
Raynaud's phenomenon			
subjects affected / exposed	0 / 214 (0.00%)	0 / 688 (0.00%)	0 / 7 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	1 / 214 (0.47%)	1 / 688 (0.15%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 214 (0.00%)	0 / 688 (0.00%)	0 / 7 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 214 (0.47%)	0 / 688 (0.00%)	0 / 7 (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
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 214 (0.00%)	0 / 688 (0.00%)	0 / 7 (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
Suicide attempt			
subjects affected / exposed	1 / 214 (0.47%)	0 / 688 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 214 (0.47%)	0 / 688 (0.00%)	0 / 7 (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
Upper limb fracture			

subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (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
Spinal compression fracture			
subjects affected / exposed	1 / 214 (0.47%)	0 / 688 (0.00%)	0 / 7 (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
Pneumothorax traumatic			
subjects affected / exposed	0 / 214 (0.00%)	0 / 688 (0.00%)	0 / 7 (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
Wound			
subjects affected / exposed	0 / 214 (0.00%)	0 / 688 (0.00%)	0 / 7 (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			
Coronary artery disease			
subjects affected / exposed	0 / 214 (0.00%)	0 / 688 (0.00%)	0 / 7 (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			
Cerebral haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (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
Paraesthesia			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychogenic seizure			
subjects affected / exposed	0 / 214 (0.00%)	0 / 688 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sensory disturbance			

subjects affected / exposed	0 / 214 (0.00%)	2 / 688 (0.29%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis haemorrhagic			
subjects affected / exposed	1 / 214 (0.47%)	0 / 688 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Inflammatory bowel disease			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (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
Gastric ulcer			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (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
Abdominal pain upper			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (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
Cholelithiasis			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (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
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (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

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (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
Diverticulitis			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	0 / 7 (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
COVID-19			
subjects affected / exposed	1 / 214 (0.47%)	0 / 688 (0.00%)	0 / 7 (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
Appendicitis			
subjects affected / exposed	1 / 214 (0.47%)	0 / 688 (0.00%)	0 / 7 (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	Erenumab 70 mg Switch to 140 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 497 (1.61%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Vascular disorders			
Raynaud's phenomenon			

subjects affected / exposed	1 / 497 (0.20%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 497 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 497 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	1 / 497 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			

Ankle fracture				
subjects affected / exposed	0 / 497 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	0 / 497 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	0 / 497 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax traumatic				
subjects affected / exposed	1 / 497 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wound				
subjects affected / exposed	1 / 497 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Coronary artery disease				
subjects affected / exposed	1 / 497 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebral haemorrhage				
subjects affected / exposed	0 / 497 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Paraesthesia				
subjects affected / exposed	0 / 497 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Psychogenic seizure			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sensory disturbance			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis haemorrhagic			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inflammatory bowel disease			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	1 / 497 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	2 / 497 (0.40%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Erenumab 70 mg	Erenumab 140 mg	Erenumab 140 mg Switch to 70 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	172 / 214 (80.37%)	417 / 688 (60.61%)	7 / 7 (100.00%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	12 / 214 (5.61%)	12 / 688 (1.74%)	0 / 7 (0.00%)
occurrences (all)	13	14	0
Migraine			
subjects affected / exposed	6 / 214 (2.80%)	14 / 688 (2.03%)	1 / 7 (14.29%)
occurrences (all)	6	15	1
Psychogenic seizure			
subjects affected / exposed	0 / 214 (0.00%)	0 / 688 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	15 / 214 (7.01%)	47 / 688 (6.83%)	0 / 7 (0.00%)
occurrences (all)	15	53	0
Influenza like illness			
subjects affected / exposed	12 / 214 (5.61%)	14 / 688 (2.03%)	0 / 7 (0.00%)
occurrences (all)	14	17	0
Injection site bruising			
subjects affected / exposed	9 / 214 (4.21%)	0 / 688 (0.00%)	0 / 7 (0.00%)
occurrences (all)	10	0	0
Injection site erythema			
subjects affected / exposed	20 / 214 (9.35%)	1 / 688 (0.15%)	0 / 7 (0.00%)
occurrences (all)	20	1	0
Injection site pruritus			
subjects affected / exposed	1 / 214 (0.47%)	2 / 688 (0.29%)	1 / 7 (14.29%)
occurrences (all)	1	3	1
Pyrexia			
subjects affected / exposed	4 / 214 (1.87%)	5 / 688 (0.73%)	1 / 7 (14.29%)
occurrences (all)	4	5	1
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	17 / 214 (7.94%)	1 / 688 (0.15%)	0 / 7 (0.00%)
occurrences (all)	25	2	0

Gastrointestinal disorders			
Constipation			
subjects affected / exposed	92 / 214 (42.99%)	280 / 688 (40.70%)	5 / 7 (71.43%)
occurrences (all)	95	286	5
Gastrooesophageal reflux disease			
subjects affected / exposed	7 / 214 (3.27%)	7 / 688 (1.02%)	1 / 7 (14.29%)
occurrences (all)	7	7	1
Irritable bowel syndrome			
subjects affected / exposed	0 / 214 (0.00%)	1 / 688 (0.15%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	1 / 214 (0.47%)	0 / 688 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Alopecia			
subjects affected / exposed	37 / 214 (17.29%)	72 / 688 (10.47%)	1 / 7 (14.29%)
occurrences (all)	37	72	1
Pruritus			
subjects affected / exposed	5 / 214 (2.34%)	33 / 688 (4.80%)	3 / 7 (42.86%)
occurrences (all)	6	34	4
Psychiatric disorders			
Anxiety			
subjects affected / exposed	15 / 214 (7.01%)	3 / 688 (0.44%)	0 / 7 (0.00%)
occurrences (all)	15	3	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	12 / 214 (5.61%)	3 / 688 (0.44%)	0 / 7 (0.00%)
occurrences (all)	12	3	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	21 / 214 (9.81%)	17 / 688 (2.47%)	0 / 7 (0.00%)
occurrences (all)	24	20	0
Nasopharyngitis			
subjects affected / exposed	10 / 214 (4.67%)	15 / 688 (2.18%)	0 / 7 (0.00%)
occurrences (all)	10	15	0
Conjunctivitis			

subjects affected / exposed	0 / 214 (0.00%)	2 / 688 (0.29%)	1 / 7 (14.29%)
occurrences (all)	0	2	1
COVID-19			
subjects affected / exposed	49 / 214 (22.90%)	57 / 688 (8.28%)	1 / 7 (14.29%)
occurrences (all)	52	57	1

Non-serious adverse events	Erenumab 70 mg Switch to 140 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	391 / 497 (78.67%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	18 / 497 (3.62%)		
occurrences (all)	18		
Migraine			
subjects affected / exposed	8 / 497 (1.61%)		
occurrences (all)	9		
Psychogenic seizure			
subjects affected / exposed	0 / 497 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	37 / 497 (7.44%)		
occurrences (all)	42		
Influenza like illness			
subjects affected / exposed	16 / 497 (3.22%)		
occurrences (all)	16		
Injection site bruising			
subjects affected / exposed	34 / 497 (6.84%)		
occurrences (all)	38		
Injection site erythema			
subjects affected / exposed	36 / 497 (7.24%)		
occurrences (all)	38		
Injection site pruritus			
subjects affected / exposed	7 / 497 (1.41%)		
occurrences (all)	8		
Pyrexia			

subjects affected / exposed occurrences (all)	6 / 497 (1.21%) 6		
Immune system disorders Immunisation reaction subjects affected / exposed occurrences (all)	 35 / 497 (7.04%) 54		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Irritable bowel syndrome subjects affected / exposed occurrences (all)	 193 / 497 (38.83%) 206 2 / 497 (0.40%) 2 1 / 497 (0.20%) 1		
Skin and subcutaneous tissue disorders Night sweats subjects affected / exposed occurrences (all) Alopecia subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 0 / 497 (0.00%) 0 71 / 497 (14.29%) 71 9 / 497 (1.81%) 10		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	 14 / 497 (2.82%) 14		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 12 / 497 (2.41%) 12		
Infections and infestations			

Upper respiratory tract infection subjects affected / exposed occurrences (all)	76 / 497 (15.29%) 83		
Nasopharyngitis subjects affected / exposed occurrences (all)	35 / 497 (7.04%) 36		
Conjunctivitis subjects affected / exposed occurrences (all)	1 / 497 (0.20%) 1		
COVID-19 subjects affected / exposed occurrences (all)	103 / 497 (20.72%) 105		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 February 2021	- The Screening and Baseline Periods were separated. - Statistical analyses were updated. - Notes were added to the schedule of assessments (SOA) to clarify activities. - Optional substudy assessments were put under separate SOA. - References to some exploratory objectives were removed. - Benefit risk-assessment language was updated to reflect current assessments. - End of study language edited to reflect current template format. - Added exclusion criteria 215: "Initiation, discontinuation, or change of dosing of migraine prophylactic medications within 2 months prior to the start of the baseline period, during the baseline period or planned during the study". - Screen failure and rescreening language updated: a subject may be rescreened once if in the opinion of the investigator, the reason for the initial screen failure has been resolved or is no longer applicable. - Excluded treatments, medical devices, and/or procedures during the study period sections were updated. - Hepatotoxicity sections were removed per template language regarding it as optional.
23 February 2022	- Reduced the sample size from 2000 participants to 1400 participants throughout the protocol as the study centers were not able to achieve the enrollment target and it was determined that a lower sample would still provide sufficient analytical power. - Updated sample size determination to align with the sample size. - Updated section on serious adverse events after the protocol-required reporting period, product complaints, adverse device effect definition, serious adverse event reporting by electronic data collection tool as per the latest template text.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported