Clinical trial results:
Head-to-head study of Erenumab against topiRamate-a double-blind, double dummy Migraine study to assess tolerability and efficacy in a patiEnt –centered Setting

Summary

EudraCT number	2018-000943-15
Trial protocol	DE
Global end of trial date	29 July 2020

Results information

Result version number	v1 (current)
This version publication date	04 August 2021
First version publication date	04 August 2021

Trial information

Trial identification

Sponsor protocol code	CAMG334ADE01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03828539
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 July 2020
Global end of trial reached?	Yes
Global end of trial date	29 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate the tolerability of 70 mg and 140 mg Erenumab compared to Topiramate in the highest tolerated dose assessed by the rate of patients discontinuing treatment due to AE during the double-blind epoch of the study.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 February 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 776
Worldwide total number of subjects	776
EEA total number of subjects	776

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)	772
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

82 centers in Germany enrolled patients.

Pre-assignment

Screening details:

A total of 777 patients were randomized to receive either erenumab (389 patients) or topiramate (388 patients).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Erenumab

Arm description:

70 mg and 140 mg Erenumab

Arm type	Experimental
Investigational medicinal product name	Erenumab
Investigational medicinal product code	
Other name	AMG334
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

70mg/1mL (70 mg) or 2x70mg/1mL (140 mg) in pre-filled syringe, administered every 4 weeks

Investigational medicinal product name	Erenumab matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Erenumab matching placebo pre-filled syringue administered every 4 weeks

Arm title	Topiramate

Arm description:

Topiramate in the highest tolerated dose (50 - 100 mg/day)

Arm type	Active comparator
Investigational medicinal product name	Topiramate matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Topiramate matching placebo administered daily

Investigational medicinal product name	Topiramate
Investigational medicinal product code	
Other name	Topamax

Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Film-coated tablet taken orally: 25 mg administered once daily (first week of titration phase). After the first week, titration was done according to the summary of product characteristics (SmPC) in 25 mg increments each week and aimed to reach the recommended daily treatment dose of 100 mg (50/75/100 mg). 50/75/100 mg were administered twice daily during titration phase and maintenance phase.

Number of subjects in period 1	Erenumab	Topiramate
Started	388	388
Full Analysis set (FAS)	388	388
Safety Analysis Set (SAF)	388	388
Completed	372	366
Not completed	16	22
Adverse event, non-fatal	3	12
Patient’s/guardian’s decision	3	5
Lost to follow-up	4	2
Withdrawal of informed consent	2	1
New therapy for study indication	1	-
Protocol deviation	3	2

Baseline characteristics

Reporting groups	
Reporting group title	Erenumab
Reporting group description:	
70 mg and 140 mg Erenumab	
Reporting group title	Topiramate
Reporting group description:	
Topiramate in the highest tolerated dose (50 - 100 mg/day)	

Reporting group values	Erenumab	Topiramate	Total
Number of subjects	388	388	776
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	385	387	772
From 65-84 years	3	1	4
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	40.8	40.7	
standard deviation	± 12.4	± 12.4	-
Sex: Female, Male Units: Participants			
Female	331	335	666
Male	57	53	110
Race/Ethnicity, Customized Units: Subjects			
Caucasian	383	387	770
Asian	1	0	1
Unknown	1	0	1
Other	3	1	4
Baseline Monthly Migraine Days (MMDs) categories			
Monthly migraine days at baseline are the number of migraine days in the baseline period that are normalized in a 28-day interval. Monthly migraine days after baseline are the number of migraine days between each monthly IMP dose that are normalized in a 28-day interval. Days without eDiary data in each normalized monthly interval were prorated.			
Units: Subjects			
< 4 days	2	0	2
4 to 7 days	94	92	186
8 to 14 days	248	254	502
>= 15 days	43	42	85
Missing	1	0	1

End points

End points reporting groups	
Reporting group title	Erenumab
Reporting group description:	
70 mg and 140 mg Erenumab	
Reporting group title	Topiramate
Reporting group description:	
Topiramate in the highest tolerated dose (50 - 100 mg/day)	

Primary: Proportion of patients with treatment discontinuation due to an Adverse Event (AE) during the double-blind treatment epoch/period (DBTE)	
End point title	Proportion of patients with treatment discontinuation due to an Adverse Event (AE) during the double-blind treatment epoch/period (DBTE)
End point description:	
The primary objective was to demonstrate the tolerability of 70 mg and 140 mg erenumab compared to topiramate in the highest tolerated dose assessed by the rate of patients discontinuing treatment due to AE during the double-blind epoch of the study.	
End point type	Primary
End point timeframe:	
24 Weeks	

End point values	Erenumab	Topiramate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	388	388		
Units: Participants	41	151		

Statistical analyses

Statistical analysis title	Treatment discontinuation due to an AE during DBTE
Comparison groups	Erenumab v Topiramate
Number of subjects included in analysis	776
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	0.27

Secondary: Number of patients with at least 50% reduction from baseline in monthly migraine days (MMD) over the last three months (month 4, 5, and 6)

End point title	Number of patients with at least 50% reduction from baseline in monthly migraine days (MMD) over the last three months (month 4, 5, and 6)

End point description:

The secondary objective of this study was to evaluate the effect of erenumab compared to topiramate on the proportion of patients with at least 50% reduction from baseline in MMDs. The Baseline period was defined as the period between Week -4 and the day prior to first dose. This was analyzed by logistic regression over the last 3 months (months 4, 5, and 6) of treatment. All the subjects' data collected regarding 50% response in MMD was used in the analysis regardless of whether subjects discontinue study treatment or not. Subjects with missing response information on this endpoint were imputed as non-response (non-responder imputation).

End point type	Secondary

End point timeframe:

Baseline, Last three months (month 4, 5, and 6)

End point values	Erenumab	Topiramate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	388	388		
Units: Participants	215	121		

Statistical analyses

Statistical analysis title	Reduction in MMDs over the last three months
Comparison groups	Erenumab v Topiramate
Number of subjects included in analysis	776
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.06
upper limit	3.71

Other pre-specified: EXPLORATORY ENDPOINT: Proportion of patients achieving at least a 5 points reduction in the Headache Impact Test (HIT-6) from baseline to week 24

End point title	EXPLORATORY ENDPOINT: Proportion of patients achieving at

	least a 5 points reduction in the Headache Impact Test (HIT-6) from baseline to week 24

End point description:

The HIT-6 is a widely used patient-reported outcome measure that assesses the negative effects of headaches on normal activity. Six items assess the frequency of pain severity, headaches limiting daily activity (household, work, school, and social), wanting to lie down when headache is experienced, feeling too tired to work or do daily activities because of headache, feeling "fed up" or irritated because of headache, and headaches limiting ability to concentrate or work on daily activities. Each of the 6 questions is responded to using 1 of 5 response categories: "never," "rarely," "sometimes," "very often," or "always." For each HIT-6 item, 6, 8, 10, 11, or 13 points, respectively, are assigned to the response provided. These points are summed to produce a total HIT-6 score that ranges from 36 to 78. HIT-6 scores are categorized into 4 grades: little or no impact (49 or less), some impact (50 – 55), substantial impact (56 – 59), and severe impact (60 – 78) due to headache.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 24

End point values	Erenumab	Topiramate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	388	388		
Units: Participants	280	209		

Statistical analyses

Statistical analysis title	5 points reduction in HIT-6 from BL to Week 24
Comparison groups	Erenumab v Topiramate
Number of subjects included in analysis	776
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	3.12

Other pre-specified: EXPLORATORY ENDPOINT: Proportion of patients achieving at least a 5 points increase in the Medical Outcome Short Form Health Survey Version 2 (SF-36) from baseline to week 24

End point title	EXPLORATORY ENDPOINT: Proportion of patients achieving at least a 5 points increase in the Medical Outcome Short Form Health Survey Version 2 (SF-36) from baseline to week 24

End point description:

The SF-36 is a widely used and extensively studied instrument to measure health-related quality of life (HRQoL) among healthy subjects and patients with acute and chronic conditions. It consists of eight

subscales that can be scored individually: Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, and Mental Health. Two overall summary scores, the Physical Component Summary (PCS) and the Mental Component Summary (MCS) also can be computed. The SF-36 has proven useful in monitoring general and specific populations, comparing the relative burden of different disease, differentiating the health benefits produced by different treatments, and in screening individual patients. The purpose of the SF-36 in this study was to assess the HRQoL of patients. Given the nature of this disease and the 4-weekly assessment, the SF-36 version 2, with a 4-week recall period, was used in this study.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 24

End point values	Erenumab	Topiramate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	388	388		
Units: Participants				
Physical Component Summary (PCS)	185	145		
Mental Component Summary (MCS)	98	65		

Statistical analyses

Statistical analysis title	5 points increase in SF-36 from BL to Week 24
Statistical analysis description: Physical Component Summary (PCS)	
Comparison groups	Erenumab v Topiramate
Number of subjects included in analysis	776
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	2.43

Statistical analysis title	5 points increase in SF-36 from BL to Week 24
Statistical analysis description: Mental Component Summary (MCS)	
Comparison groups	Erenumab v Topiramate

Number of subjects included in analysis	776
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.005
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.29
upper limit	2.69

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first dose of study treatment until 8 weeks after the last Investigational Medicinal product (IMP) injection, assessed up to approximately 33 weeks (treatment duration ranged from 4.0 to 25.1 weeks).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Erenumab

Reporting group description:

Erenumab

Reporting group title	Topiramate

Reporting group description:

Topiramate

Serious adverse events	Erenumab	Topiramate	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 388 (2.58%)	19 / 388 (4.90%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroadenoma of breast			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dysmenorrhoea			
subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometriosis			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Weight decreased			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			

subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sternal fracture			
subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			
subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine with aura			

subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhegmatogenous retinal detachment			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ileus			
subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive defaecation			

subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteriuria			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Influenza			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papilloma viral infection			
subjects affected / exposed	1 / 388 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parasitic gastroenteritis			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 388 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Erenumab	Topiramate	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	253 / 388 (65.21%)	331 / 388 (85.31%)	
Investigations			
Weight decreased			
subjects affected / exposed	5 / 388 (1.29%)	22 / 388 (5.67%)	
occurrences (all)	5	23	

Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	18 / 388 (4.64%)	63 / 388 (16.24%)	
occurrences (all)	19	65	
Dizziness			
subjects affected / exposed	28 / 388 (7.22%)	60 / 388 (15.46%)	
occurrences (all)	31	66	
Dysgeusia			
subjects affected / exposed	3 / 388 (0.77%)	23 / 388 (5.93%)	
occurrences (all)	3	23	
Paraesthesia			
subjects affected / exposed	17 / 388 (4.38%)	159 / 388 (40.98%)	
occurrences (all)	22	196	
Taste disorder			
subjects affected / exposed	0 / 388 (0.00%)	26 / 388 (6.70%)	
occurrences (all)	0	26	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	44 / 388 (11.34%)	74 / 388 (19.07%)	
occurrences (all)	48	87	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	20 / 388 (5.15%)	24 / 388 (6.19%)	
occurrences (all)	24	28	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	22 / 388 (5.67%)	23 / 388 (5.93%)	
occurrences (all)	25	23	
Constipation			
subjects affected / exposed	48 / 388 (12.37%)	12 / 388 (3.09%)	
occurrences (all)	50	12	
Diarrhoea			
subjects affected / exposed	20 / 388 (5.15%)	29 / 388 (7.47%)	
occurrences (all)	21	30	
Nausea			

subjects affected / exposed	36 / 388 (9.28%)	71 / 388 (18.30%)	
occurrences (all)	44	75	
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	20 / 388 (5.15%)	8 / 388 (2.06%)	
occurrences (all)	21	9	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	21 / 388 (5.41%)	20 / 388 (5.15%)	
occurrences (all)	23	20	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	145 / 388 (37.37%)	150 / 388 (38.66%)	
occurrences (all)	189	197	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 388 (2.06%)	39 / 388 (10.05%)	
occurrences (all)	8	40	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 March 2019	Amendment 01: Implementation of further safety procedures in line with topiramate SmPC, adjustment of safety follow-up, correction and clarification of certain criteria and procedures.
06 June 2019	Amendment 02: Inclusion of patients with chronic migraine, correction and clarification of certain criteria and procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

1 patient in the erenumab treatment group was mis-randomized (no intake of active study medication) and was excluded from all analysis.

Notes: