Clinical trial results:
A Phase 3 Randomized, Double-Blind, Placebo-Controlled Study of LY2951742 in Patients with Episodic Cluster Headache

Summary

EudraCT number	2015-000149-22
Trial protocol	DE GB DK BE FI ES NL GR
Global end of trial date	04 June 2018

Results information

Result version number	v1 (current)
This version publication date	30 June 2019
First version publication date	30 June 2019

Trial information

Trial identification

Sponsor protocol code	I5Q-MC-CGAL

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02397473
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 15780

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	04 June 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the efficacy and safety of the study drug known as Galcanezumab in participants with episodic cluster headache.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 May 2015
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	Greece: 3
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	United States: 34
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Spain: 13
Worldwide total number of subjects	106
EEA total number of subjects	70

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)	104
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects had screening/washout phase for minimum of 0 days to maximum of 12 months. Subjects who enter screening in an active cluster headache (CH) period & meet initial screening eligibility can move directly into baseline phase as long as they do not need to wash out of any excluded medications. Subjects who enter in remission remain in screening

Pre-assignment

Screening details:

until onset of their next CH period.Prospective baseline phase begins on the day that the Subject first records a CH attack in their electronic patient-reported outcome (ePRO) diary. Minimum duration is 10 days of daily ePRO diary recording prior to Visit 3, & the preferred maximum duration is 14 days of daily ePRO diary recording prior to visit 3.

Period 1

Period 1 title	Treatment Phase
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 once a month for 2 months by subcutaneous (SC) injection during treatment phase.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo administered subcutaneously once a month for 2 months.

Arm title	Galcanezumab 300mg

Arm description:

Participants received Galcanezumab 300mg once a month for two months by subcutaneous (SC) injection during treatment phase.

Arm type	Experimental
Investigational medicinal product name	Galcanezumab
Investigational medicinal product code	
Other name	LY2951742
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

300mg Galcanezumab administered by subcutaneous injection once a month for 2 months.

Number of subjects in period 1	Placebo	Galcanezumab 300mg
Started	57	49
Received at least one dose of study drug	57	49
Completed	45	45
Not completed	12	4
Consent withdrawn by subject	2	1
Adverse event, non-fatal	1	2
Lost to follow-up	1	-
Lack of efficacy	8	1

Period 2	
Period 2 title	Post Treatment Follow-up Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants did not receive any intervention during post treatment follow-up phase.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Galcanezumab 300mg

Arm description:

Participants did not receive any intervention during post treatment follow-up phase.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Placebo	Galcanezumab 300mg
Started	45	45
Completed	47	45
Not completed	3	2
Consent withdrawn by subject	-	1
Lost to follow-up	1	-
Lack of efficacy	1	1
Protocol deviation	1	-

Joined	5	2
Discontinued treatment phase and joined	5	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo once a month for 2 months by subcutaneous (SC) injection during treatment phase.	
Reporting group title	Galcanezumab 300mg
Reporting group description:	
Participants received Galcanezumab 300mg once a month for two months by subcutaneous (SC) injection during treatment phase.	

Reporting group values	Placebo	Galcanezumab 300mg	Total
Number of subjects	57	49	106
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	45.40	47.49	
standard deviation	± 11.32	± 10.74	-
Gender categorical Units: Subjects			
Female	10	8	18
Male	47	41	88
Lifetime suicidal ideation prior to screening Units: Subjects			
Lifetime suicidal ideation prior to screening	5	9	14
No Suicidal Ideation prior to screening	52	40	92
Lifetime suicidal behavior prior to screening Units: Subjects			
Lifetime suicidal behavior prior to screening	0	1	1
No suicidal behaviour prior to screening	57	48	105

Weekly Cluster Headache Attacks			
Units: Cluster Headache Attacks			
arithmetic mean	17.30	17.82	
standard deviation	± 10.05	± 10.12	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo once a month for 2 months by subcutaneous (SC) injection during treatment phase.	
Reporting group title	Galcanezumab 300mg
Reporting group description:	
Participants received Galcanezumab 300mg once a month for two months by subcutaneous (SC) injection during treatment phase.	

Reporting group title	Placebo
Reporting group description:	
Participants did not receive any intervention during post treatment follow-up phase.	
Reporting group title	Galcanezumab 300mg
Reporting group description:	
Participants did not receive any intervention during post treatment follow-up phase.	

Primary: Overall Mean Change from Baseline in Number of Weekly Cluster Headache Attacks

End point title	Overall Mean Change from Baseline in Number of Weekly Cluster Headache Attacks
End point description:	
Number of cluster headache attacks was recorded daily by study participants in their ePRO Diary. Overall mean change from baseline is derived from the average of weeks 1 to 3 from mixed model repeated measures (MMRM) analysis. Least Square (LS) means were calculated using MMRM model with treatment, sex, pooled investigative site, week, baseline, and treatment by week as fixed effects. Analysis Population Description (APD): All randomized participants who received at least one dose of study drug and had baseline and at least one post baseline measurement.	
End point type	Primary
End point timeframe:	
Baseline, Week 1 through Week 3	

End point values	Placebo	Galcanezumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	49		
Units: Cluster Headache Attacks per Week				
least squares mean (standard error)	-5.22 (± 1.33)	-8.69 (± 1.42)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Galcanezumab 300mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-3.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.72
upper limit	-0.23
Variability estimate	Standard error of the mean
Dispersion value	1.63

Secondary: Percentage of Participants with 50% or Greater Reduction From Baseline in the Weekly Number of Cluster Headache Attacks

End point title	Percentage of Participants with 50% or Greater Reduction From Baseline in the Weekly Number of Cluster Headache Attacks

End point description:

Number of cluster headache attacks was recorded daily by study participants in their ePRO Diary. Percentage of participants with 50% or greater reduction from baseline at week 3 was analyzed using Koch's nonparametric randomization-based analysis of covariance method. This method adjusted for pooled investigative site by including it as a stratification variable. It also adjusted for sex and baseline value.
APD: All randomized participants who received at least one dose of study drug and had baseline and at least one post baseline measurement.

End point type	Secondary

End point timeframe:

Baseline, Week 3

End point values	Placebo	Galcanezumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	49		
Units: percentage of participants				
number (not applicable)	52.63	71.43		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Koch's nonparametric randomization-based ANCOVA.

Comparison groups	Galcanezumab 300mg v Placebo

Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.046
Method	ANCOVA

Secondary: Overall Mean Change From Baseline in Number of Weekly Cluster Headache Attacks

End point title	Overall Mean Change From Baseline in Number of Weekly Cluster Headache Attacks

End point description:

Number of cluster headache attacks was recorded daily by study participants in their ePRO Diary. Overall mean change from baseline is derived from the average of weeks 1 to 8 from MMRM analysis. Least Square (LS) means were calculated using MMRM model with treatment, sex, pooled investigative site, week, baseline, and treatment by week as fixed effects.
APD:All randomized participants who received at least one dose of study drug and had baseline and at least one post baseline measurement.

End point type	Secondary

End point timeframe:

Baseline, Week 1 through Week 8

End point values	Placebo	Galcanezumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	49		
Units: Cluster Headache Attacks per Week				
least squares mean (standard error)	-9.97 (± 0.95)	-10.80 (± 1.00)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Galcanezumab 300mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.493
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.23
upper limit	1.57

Variability estimate	Standard error of the mean
Dispersion value	1.2

Secondary: Percentage of Participants Reporting a Score of 1 or 2 on the Patient Global Impression of Improvement (PGI-I)

End point title	Percentage of Participants Reporting a Score of 1 or 2 on the Patient Global Impression of Improvement (PGI-I)

End point description:

PGI-I requests participants to mark the box that best describes their cluster headache condition since they started taking the medicine. The options in the displayed boxes are represented on a 7-point scale, with 1 = very much better, 2 = much better, 3 = a little better, 4 = no change, 5 = a little worse, 6 = much worse, and 7 = very much worse. Percentage of participants were derived with a generalized linear mixed model repeated measures method with treatment, sex, baseline cluster headache attack category, month, and treatment by month as fixed effects.
APD:All randomized participants who received at least one dose of study drug and had PGI-I measurement at week 4.

End point type	Secondary

End point timeframe:

Week 4

End point values	Placebo	Galcanezumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	44		
Units: percentage of participants				
number (not applicable)	46.4	72.5		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Galcanezumab 300mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	3.046
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.242
upper limit	7.469

Secondary: Percentage of Participants Reporting a Score of 1 or 2 on the Patient Global Impression of Improvement (PGI-I)

End point title	Percentage of Participants Reporting a Score of 1 or 2 on the Patient Global Impression of Improvement (PGI-I)

End point description:

PGI-I requests participants to mark the box that best describes their cluster headache condition since they started taking the medicine. The options in the displayed boxes are represented on a 7-point scale, with 1 = very much better, 2 = much better, 3 = a little better, 4 = no change, 5 = a little worse, 6 = much worse, and 7 = very much worse. Percentage of participants were derived with a generalized linear mixed model repeated measures method with treatment, sex, baseline cluster headache attack category, month, and treatment by month as fixed effects.
APD: All randomized participants who received at least one dose of study drug and had PGI-I measurement at week 8.

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo	Galcanezumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	38		
Units: percentage of participants				
number (not applicable)	66.1	71.9		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Galcanezumab 300mg v Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.575
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	1.312
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.502
upper limit	3.426

Secondary: Percentage of Participants with 50% or Greater Reduction from Baseline in Number of Weekly Cluster Headache Attacks

End point title	Percentage of Participants with 50% or Greater Reduction from Baseline in Number of Weekly Cluster Headache Attacks

End point description:

Number of cluster headache attacks was recorded daily by study participants in their ePRO Diary. Mean

percentage of participants is derived from the average of weeks 1 to 8 from generalized linear mixed model repeated measures method with treatment, sex, week, treatment by week, and baseline as fixed effects.
APD:All randomized participants who received at least one dose of study drug and had baseline and at least one post baseline measurement.

End point type	Secondary

End point timeframe:

Baseline, Week 1 through Week 8

End point values	Placebo	Galcanezumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	49		
Units: percentage of participants				
number (not applicable)	70.4	69.6		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Galcanezumab 300mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.91
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	0.965
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.512
upper limit	1.819

Secondary: Percentage of Participants with 30% or Greater Reduction from Baseline in Number of Weekly Cluster Headache Attacks

End point title	Percentage of Participants with 30% or Greater Reduction from Baseline in Number of Weekly Cluster Headache Attacks

End point description:

Number of cluster headache attacks was recorded daily by study participants in their ePRO Diary. Mean percentage of participants is derived from the average of weeks 1 to 8 from generalized linear mixed model repeated measures with treatment, sex, week, treatment by week and baseline as fixed effects.
APD:All randomized participants who received at least one dose of study drug and had baseline and at least one post baseline measurement.

End point type	Secondary

End point timeframe:

Baseline, Week 1 through Week 8

End point values	Placebo	Galcanezumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	49		
Units: percentage of participants				
number (not applicable)	78.9	77.7		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Galcanezumab 300mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.841
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	0.929
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.449
upper limit	1.923

Secondary: Pharmacokinetics (PK): Serum Concentration of Galcanezumab

End point title	Pharmacokinetics (PK): Serum Concentration of

End point description:

APD: All randomized participants who received at least one dose of study drug and had measurable PK samples.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, Statistical analysis was not planned.

End point values	Galcanezumab 300mg			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Nanogram per Milliliter (ng/mL)				
arithmetic mean (standard deviation)	20200 (± 6880)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Serum Concentration of Galcanezumab

End point title	Pharmacokinetics (PK): Serum Concentration of

End point description:

APD: All randomized participants who received at least one dose of study drug and had measurable PK samples.

End point type	Secondary

End point timeframe:

Week 8

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, Statistical analysis was not planned.

End point values	Galcanezumab 300mg			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Nanogram per Milliliter (ng/mL)				
arithmetic mean (standard deviation)	26400 (± 11200)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Developing Anti-Drug Antibodies (ADA) to Galcanezumab

End point title	Percentage of Participants Developing Anti-Drug Antibodies (ADA) to Galcanezumab

End point description:

Treatment emergent (TE) ADA evaluable participant is considered to be TE ADA+ if the subject has at least one post-baseline titer that is a 4-fold or greater increase in titer from baseline measurement. If baseline result is ADA Not Present, then the participant is TE ADA+ if there is at least one post-baseline result of ADA present with titer >= 1: 20.
APD: All randomized participants who received at least one dose of study drug and had non-missing baseline ADA result, and at least one non-missing post baseline ADA result.

End point type	Secondary

End point timeframe:

Baseline through Week 8

End point values	Placebo	Galcanezumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	48		
Units: percentage of participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Suicidal Ideation Assessed by Columbia - Suicide Severity Rating Scale (C-SSRS)

End point title	Percentage of Participants With Suicidal Ideation Assessed by Columbia - Suicide Severity Rating Scale (C-SSRS)

End point description:

C-SSRS captures the occurrence, severity, and frequency of suicide-related thoughts and behaviors during the assessment period. The scale includes suggested questions to solicit the type of information needed to determine if a suicide-related thought or behavior occurred. Some questions are binary responses (yes/no) and some are on a scale of 1 (low severity) to 5 (high severity). Suicidal ideation: a "yes" answer to any of 5 suicidal ideation questions: wish to be dead, non-specific active suicidal thoughts, active suicidal ideation with any methods without intent to act, active suicidal ideation with some intent to act without specific plan, active suicidal ideation with specific plan and intent.
APD:All randomized participants who received at least one dose of study drug and had at least one post baseline C-SSRS assessment.

End point type	Secondary

End point timeframe:

Month 1 through Month 6

End point values	Placebo	Galcanezumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	49		
Units: percentage of participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Suicidal Behaviors Assessed by Columbia - Suicide Severity Rating Scale (C-SSRS)

End point title	Percentage of Participants With Suicidal Behaviors Assessed by Columbia - Suicide Severity Rating Scale (C-SSRS)

End point description:

C-SSRS captures the occurrence, severity, and frequency of suicide-related thoughts and behaviors during the assessment period. The scale includes suggested questions to solicit the type of information needed to determine if a suicide-related thought or behavior occurred. Some questions are binary responses (yes/no) and some are on a scale of 1 (low severity) to 5 (high severity). Suicidal behavior: a "yes" answer to any of 5 suicidal behavior questions: preparatory acts or behavior, aborted attempt, interrupted attempt, actual attempt, and completed suicide.
APD: All randomized participants who received at least one dose of study drug and had at least one post baseline C-SSRS assessment.

End point type	Secondary

End point timeframe:

Month 1 through Month 6

End point values	Placebo	Galcanezumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	49		
Units: percentage of participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire Study	
Adverse event reporting additional description:	
I5Q-MC-CGAL	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Placebo - Treatment Phase
Reporting group description: -	
Reporting group title	Galcanezumab 300mg - Treatment Phase
Reporting group description: -	
Reporting group title	Placebo - Post-treatment Phase
Reporting group description: -	
Reporting group title	Galcanezumab 300mg - Post-treatment Phase
Reporting group description: -	

Serious adverse events	Placebo - Treatment Phase	Galcanezumab 300mg - Treatment Phase	Placebo - Post-treatment Phase
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 57 (0.00%)	0 / 49 (0.00%)	2 / 50 (4.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
cluster headache			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 57 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
nephrolithiasis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 57 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Galcanezumab 300mg - Post-treatment Phase		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 47 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
cluster headache			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
nephrolithiasis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 47 (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: 5 %

Non-serious adverse events	Placebo - Treatment Phase	Galcanezumab 300mg - Treatment Phase	Placebo - Post-treatment Phase
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 57 (7.02%)	7 / 49 (14.29%)	3 / 50 (6.00%)
General disorders and administration site conditions			
injection site pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 57 (0.00%)	4 / 49 (8.16%)	0 / 50 (0.00%)
occurrences (all)	0	4	0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 57 (5.26%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences (all)	3	0	0
Infections and infestations			

nasopharyngitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 57 (1.75%)	3 / 49 (6.12%)	3 / 50 (6.00%)
occurrences (all)	1	3	3

Non-serious adverse events	Galcanezumab 300mg - Post-treatment Phase		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 47 (2.13%)		
General disorders and administration site conditions			
injection site pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 December 2015	Revised Inclusion Criteria 9 to allow oral triptans as an abortive medication to align with current clinical practice.
10 February 2017	Revised Exclusion Criterion 22e (Have any history of intracranial or carotid aneurysm, intracranial hemorrhage, or stroke.) and added Exclusion Criterion 23d (Patients with a history of an intracranial tumor or head trauma must be discussed and judged not to indicate a medical problem that would preclude study participation by Lilly Medical prior to enrollment.) because intracranial or carotid aneurysm, intracranial hemorrhage, and stroke are cardiovascular-related conditions, whereas intracranial tumor and significant head trauma are not cardiovascular related. Patients with either of the non-cardiovascular-related conditions mentioned here may be enrolled in the clinical trial if upon discussion with Lilly Medical it is judged not to indicate a medical problem that would preclude study participation. Revised exclusion criteria to allow patients who fail eligibility due to an elevation of ≥2X ULN for ALT, or ≥1.5X ULN TBL or ALP to be retested. Added a new rescreening allowance for Inclusion Criteria to allow patients who fail eligibility due to the occurrence of >8 cluster headache attacks per day to rescreen for the study during their current cluster headache period. Added a new rescreening allowance for Exclusion Criteria this change allows patients who fail eligibility due to a positive UDS to be rescreened during their current cluster headache period.
18 March 2018	Updated the primary endpoint to be the overall treatment effect across Weeks 1 to 3 in weekly cluster headache attack frequency rather than the treatment effect at a single time point (Week 3).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported