Clinical trial results:
A Phase 3b Multicenter, Single-Arm, Open-Label Safety Study of LY2951742 (galcanezumab) in Patients with Episodic or Chronic Cluster Headache

Summary

EudraCT number	2015-005234-21
Trial protocol	DE BE FI ES DK NL GR IT
Global end of trial date	21 January 2021

Results information

Result version number	v1 (current)
This version publication date	05 February 2022
First version publication date	05 February 2022

Trial information

Trial identification

Sponsor protocol code	I5Q-MC-CGAR

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02797951
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16351

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	21 January 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 January 2021
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 assess the long-term safety and tolerability of galcanezumab administered up to once monthly in participants with episodic or chronic cluster headache who have completed study I5Q-MC-CGAL (NCT02397473) or study I5Q-MC-CGAM (NCT02438826).

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	13 July 2016
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	Belgium: 17
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	Finland: 5
Country: Number of subjects enrolled	France: 23
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Greece: 2
Country: Number of subjects enrolled	Italy: 24
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 29
Worldwide total number of subjects	165
EEA total number of subjects	125

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	161
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants who completed one of the parent studies I5Q-MC-CGAL (NCT02397473) or I5Q-MC-CGAM (NCT02438826) were enrolled in this study.

Pre-assignment

Screening details:

Participants who continued until sponsor ended the study following regulatory approval or non-approval of study drug for cluster headache indication in a country/region were considered CGAR study completers.

Period 1

Period 1 title	Galcanezumab 300 mg SC (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Galcanezumab 300 mg SC

Arm description:

Participants received 300 milligram (mg) Galcanezumab administered subcutaneously (SC) up to once a month.

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:

300 mg Galcanezumab administered as SC injection up to once a month.

Number of subjects in period 1	Galcanezumab 300 mg SC
Started	165
Received at Least One Dose of Study Drug	164
Completed	116
Not completed	49
Adverse event, serious fatal	1
Consent withdrawn by subject	15
Physician decision	6
Adverse event, non-fatal	4
Lost to follow-up	4
Lack of efficacy	19

Baseline characteristics

Reporting groups	
Reporting group title	Galcanezumab 300 mg SC
Reporting group description:	
Participants received 300 mg Galcanezumab administered SC up to once a month.	

Reporting group values	Galcanezumab 300 mg SC	Total	
Number of subjects	165	165	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	161	161	
From 65-84 years	4	4	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	42	42	
Male	123	123	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	22	22	
Not Hispanic or Latino	118	118	
Unknown or Not Reported	25	25	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	1	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	5	5	
White	140	140	
More than one race	19	19	
Unknown or Not Reported	0	0	
Region of Enrollment Units: Subjects			
Belgium	17	17	
Canada	7	7	
Denmark	4	4	
Finland	5	5	
France	23	23	
Germany	25	25	

Greece	2	2	
Italy	24	24	
Netherlands	8	8	
Spain	17	17	
United Kingdom	4	4	
United States	29	29	

End points

End points reporting groups

Reporting group title	Galcanezumab 300 mg SC

Reporting group description:

Participants received 300 milligram (mg) Galcanezumab administered subcutaneously (SC) up to once a month.

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Serious AEs (SAEs)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Serious AEs (SAEs)[1]

End point description:

A TEAE is defined as the reported AEs that first occurred or worsened during the post-baseline phase compared with the baseline phase.
An SAE is any adverse event from this study that results in 1 of the following: Death, initial or prolonged inpatient hospitalization, a life-threatening experience (that is, immediate risk of dying), persistent or significant disability/incapacity, congenital anomaly/birth defect, Important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the subject or may require intervention to prevent 1 of the other outcomes listed in the definition above. A summary of serious and other non-serious adverse events regardless of causality is located in the reported adverse events module.

Analysis Population Description (APD): All participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline through End of Study (Up to 4 Years)

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: No inferential statistics were planned for this endpoint.

End point values	Galcanezumab 300 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	164			
Units: participants				
TEAEs	119			
SAEs	17			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Suicidal Ideation and Behaviours Collected by Columbia - Suicide Severity Rating Scale (C-SSRS)

End point title	Number of Participants With Suicidal Ideation and Behaviours Collected by Columbia - Suicide Severity Rating Scale (C-SSRS)[2]

End point description:

C-SSRS is a scale capturing occurrence, severity, and frequency of suicide-related thoughts and behaviours, and has a binary response (yes/no).

- Suicidal Ideation: a "yes" answer to any one of 5 suicidal ideation questions: Wish to be Dead, Non-specific Active Suicidal Thoughts, Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act, Active Suicidal Ideation with Some Intent to Act, without Specific Plan, Active Suicidal Ideation with Specific Plan and Intent.

- Suicidal Behaviour: a "yes" answer to any of 5 suicidal behaviour questions: Preparatory Acts or Behaviour, Aborted Attempt, Interrupted Attempt, Actual Attempt (non-fatal), Completed Suicide.

APD: All participants who received at least one dose of study drug and had at least one postbaseline C-SSRS assessment.

End point type	Primary

End point timeframe:

Baseline through End of Study (Up to 4 Years)

Notes:

[2] - 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: No inferential statistics were planned for this endpoint.

End point values	Galcanezumab 300 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	164			
Units: participants				
Suicidal Ideation	2			
Suicidal Behaviour	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment Emergent Anti-Drug Antibodies (TE-ADA) to Galcanezumab

End point title	Number of Participants with Treatment Emergent Anti-Drug Antibodies (TE-ADA) to Galcanezumab

End point description:

A participant is consider TE-ADA positive if:
- ADA “not present” baseline result and any subsequent “present” postbaseline ADA result with a titer of at least 1:20 (treatment-induced), or
- ADA “present” baseline result and any subsequent “present” postbaseline ADA result with a 4-fold or greater increase in titer from baseline (treatment-boosted).

APD: All participants who received at least one dose of study drug and had baseline and at least one post baseline ADA assessments.

End point type	Secondary

End point timeframe:

Baseline through End of Study (Up to 4 Years)

End point values	Galcanezumab 300 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	159			
Units: participants	8			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline through End of Study (Up to 4 Years)	
Adverse event reporting additional description:	
APD: All participants who received at least one dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Galcanezumab 300 mg SC
Reporting group description:	
Participants received 300 mg Galcanezumab administered SC up to once a month.	

Serious adverse events	Galcanezumab 300 mg SC		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 164 (10.37%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
bladder neoplasm			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 164 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
lung adenocarcinoma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 164 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
cartilage injury			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	1 / 164 (0.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
exposure to household chemicals				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 164 (0.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
rib fracture				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 164 (0.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
tibia fracture				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 164 (0.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
arterial occlusive disease				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 164 (0.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
cluster headache				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	3 / 164 (1.83%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
sciatica				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	1 / 164 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
chest discomfort			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 164 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
sarcoidosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 164 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 164 (0.61%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
completed suicide	Additional description: This event was not captured in the C-SSRS suicidal behaviour count as the participant's responses to suicidal ideation/behaviours were "no" for all completed assessments.		
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 164 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Renal and urinary disorders			
ureterolithiasis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 164 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue			

disorders			
intervertebral disc degeneration			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 164 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
gastroenteritis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 164 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Galcanezumab 300 mg SC		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	62 / 164 (37.80%)		
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	11 / 164 (6.71%)		
occurrences (all)	14		
back pain			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	11 / 164 (6.71%)		
occurrences (all)	13		
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	36 / 164 (21.95%)		
occurrences (all)	46		
influenza			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	16 / 164 (9.76%)		
occurrences (all)	21		
bronchitis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	10 / 164 (6.10%)		
occurrences (all)	16		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2017	1. Amendments were made to the exclusion criteria : - to allow for medical judgment in determining exclusion from Study CGAR based on abnormal ECG findings, blood pressure readings in Study CGAL or Study CGAM. - to allow participants with a history of intracranial tumor or head trauma to be enrolled in the study based on medical discretion. - to allow participants who fail eligibility due to an elevation of ≥2X ULN for ALT, or ≥1.5X ULN TBL or ALP to be retested and enrolled based on medical discretion if the results are not clinically significant. - to allow for rescreening of patients who fail eligibility due to a positive urine drug screen. 2. Amended the protocol to clarify study discontinuation for those patients whose dosing is temporarily interrupted for potential safety concerns.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported