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

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Headaches
Study type	Interventional

Summary

ID

NL-OMON47489

Source
ToetsingOnline

Brief title
I5Q-MC-CGAR

Condition

- Headaches

Synonym
cluster headache, headache

Research involving
Human

Sponsors and support

Primary sponsor: Eli Lilly

Source(s) of monetary or material Support: De sponsor van het onderzoek (Lilly)

Intervention

Keyword: CGRP neutralizing antibody, Cluster headache, Galcanezumab, Open-label

Outcome measures

Primary outcome

Primary objective (safety evaluation):

Analysis of:

- TEAEs

- SAEs

- Suicidal ideation and behaviors assessed by solicited questioning using the

C-SSRS

Secondary outcome

Secondary objective (discontinuation and AEs of interest):

The discontinuation rates will be measured.

Secondary objective (Immunogenicity):

Analysis of :

- Injection-site reactions

- Allergy/hypersensitivity

- Infections

- The development and consequences of ADAs to galcanezumab, their relationship

with AEs, and neutralizing ADAs to galcanezumab.

Tertiary objective (effectiveness):

The proportion of patients reporting a score of 1 (*very much better*) or 2 (*much better*) on the PGI-I 1 month after receiving their first dose will be reported.

Tertiary objective (effect of galcanezumab on health values):

EQ-5D-5L Analysis of:

- Health state index values
- Each dimension of the descriptive system and dichotomized level responses
- EQ-VAS current health score
- Correlations with PGI-I, cluster headache status

Study description

Background summary

Cluster headache is a rare but disabling primary headache disorder characterized by episodic attacks of intense unilateral headache and the frequent association of autonomic symptoms such as lacrimation, conjunctival injection, and nasal congestion. There are significant unmet needs for just about every clinical aspect of the patient with cluster headache, particularly related to the severity of the disease and treatment options. The majority of patients experiencing cluster headache attacks rate their pain intensity as near to or at the worst pain imaginable. Increased plasma or serum levels of calcitonin gene-related peptide (CGRP) have been associated with painful syndromes such as migraine and cluster headache. LY2951742 is a humanized monoclonal antibody that binds to and neutralizes CGRP. LY2951742 has been identified for clinical development in pain conditions relevant to the CGRP pathway such as migraine, and, in completed studies to date, LY2951742 was shown to alter plasma CGRP concentrations, which is consistent with the binding of the antibody (LY2951742) to CGRP. The similarities between migraine and cluster headache, the role of CGRP in both disorders and the clinical efficacy observed with LY2951742 to date for the preventive treatment of migraine support the evaluation of the CGRP neutralizing antibody LY2951742 for the treatment of cluster headache.

Study objective

The primary objective of this study is to evaluate the safety of open-label galcanezumab within the context of expected medical practice in eligible patients with episodic or chronic cluster headache.

The secondary endpoints are to characterize the reasons for discontinuation and AEs of interest for galcanezumab, and to characterize the immunogenicity of galcanezumab.

The tertiary endpoints are to evaluate the effectiveness of galcanezumab, and to evaluate the effect of galcanezumab on health values.

Study design

Study CGAR is a Phase 3b single-arm, open-label safety study of galcanezumab 300 mg in outpatients with episodic or chronic cluster headache who completed Study CGAL or Study CGAM. This study will consist of 2 study phases (SP): SP I is the screening phase to confirm patients meet the inclusion/exclusion criteria, and SP II is the open-label treatment phase during which patients can receive galcanezumab 300 mg administered subcutaneously (SC) up to once a month. Within the paradigm of a once-monthly dosing regimen, the decision to dose at each monthly interval will be determined by the investigator.

Intervention

All patients will receive galcanezumab 300 mg administered as 3 subcutaneous injections of 100 mg each, up to once a month as determined by the study investigator based on clinical symptoms and response.

Study burden and risks

The study drug is accompanied by certain risks.
Events seen most frequently (*10%) in patients with migraine and cluster headache who received LY2951742 are pain, redness, itching, bruising of skin, swelling, and/or hardening at the site of injection.

The study procedures, including blood draws, ECGs, subcutaneous injections and urine analysis, also have certain risks. The study drug, the study procedures and the combination may also have other, unknown risks.

Please refer to the subject information sheet and the Investigator*s Brochure for a detailed description of the risks.

Contacts

Public
Eli Lilly

Island House, Eastgate Business Park -
Little Island -
IE
Scientific
Eli Lilly

Island House, Eastgate Business Park -
Little Island -
IE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Patients who participated in and completed either Study CGAL or Study CGAM. For a definition of a study completer for each study, please refer to the protocol.
2. Investigator judges the patient as reliable to follow all study procedures, keep all study visits, and be compliant with study requirements.
3. Reproduction: Women of child-bearing potential may participate in the study if they test negative for pregnancy at the time of enrolment and if they agree to use either 1 highly effective method of contraception or a combination of 2 effective methods of contraception during the study. Women may choose to use a double barrier method of contraception (both barrier methods must include use of a spermicide). Women not of child-bearing potential may participate if they are infertile due to surgical sterilization or if they are post-menopausal. Male patients must agree to use at least 1 effective method of contraception during the study.

4. Throughout the study, agree to refrain from the use of drugs of abuse per United States Federal Guidelines such as, but not limited to, cannabinoids, cannabis, psilocybin (mushrooms), Lysergic acid diethylamide (LSD) and 2-bromo-LSD.
5. Agree not to post any personal medical data related to the study or information related to the study on any website or social media site until the entire trial has completed or if they are otherwise informed by the study investigator.
6. Have given written informed consent.

Exclusion criteria

7. Current enrollment in, or discontinuation within the last 30 days prior to V1 from, a clinical trial (with the exception of Study CGAL or Study CGAM) involving any investigational product or device, or concurrent enrollment in any other type of medical research judged not to be scientifically or medically compatible with this study. Adequate washout (*5 half-lives) of any investigational product is also required and may require >30 days depending on the half-life of the investigational product.
8. Use of therapeutic antibodies (except galcanezumab) during the course of the study. Prior use of other therapeutic antibodies is allowed if an adequate washout has occurred (*5 half-lives) prior to V2.
9. Lifetime history of migraine variants that could implicate or could be confused with ischemia; specifically, hemiplegic (sporadic or familial) migraine, ophthalmoplegic migraine, and basilar-type migraine defined by ICHD-3 beta.
10. Taking excluded medication(s) at V2. Excluded medications require an adequate washout (*5 half-lives) prior toV2.
11. Evidence of significant active or unstable psychiatric disease by medical history, such as bipolar disorder, schizophrenia, personality disorders or other serious mood or anxiety disorders. Patients with major depressive disorder or generalized anxiety disorder, whose disease state is considered stable and expected to remain stable throughout the course of the study, in the opinion of the investigator, may be considered for inclusion if they are not on excluded medication(s).
12. Patients who are considered by the investigator to be at significant risk for suicide.
13. Women who are pregnant or nursing.
14. Any of the following cardiovascular-related conditions are exclusionary:
a. Since enrolling in Study CGAL or Study CGAM or prior to V2 (enrollment), have ECGs showing acute abnormalities of:
i. evidence of delayed ventricular repolarization including but not limited to a corrected QT (Fridericia*s QT interval [QTcF]) interval >470 msec for women and >450 for men, and/or
ii. evidence of atrioventricular (AV) depolarization of PR>220, or conduction delay of QRS>120, and/or
iii. evidence of ischemia or any of the qualitative findings indicative of ST or J-point elevation, excluding those findings consistent with early repolarization (nonischemic).
NOTE: Patients who meet 1 of the 14(a) ECG criteria during Study CGAL or Study CGAM may enroll in Study CGAR if the study investigator deems the finding not clinically significant.
b. History of myocardial infarction (MI), unstable angina (UA), percutaneous coronary

intervention, coronary artery bypass graft, deep vein thrombosis/pulmonary embolism since enrolling in Study CGAL or Study CGAM and prior to V2 of Study CGAR, or have planned cardiovascular surgery or percutaneous coronary angioplasty or surgery for peripheral arterial disease.
c. Any lifetime history of vasospastic angina or stroke, or history of emergency room visit for chest pain in which an ischemic or cardiac event was not ruled out since enrolling in Study CGAL or Study CGAM and prior to V2 of Study CGAR.
d. Clinical evidence of peripheral vascular disease (e.g., Buerger*s Disease) or a diagnosis of Raynaud*s Disease or Raynaud*s Phenomenon.
e. Have any history of intracranial or carotid aneurysm, intracranial hemorrhage or stroke.
f. Have uncontrolled high blood pressure, characterized by systolic blood pressure >160 mmHg or diastolic blood pressure >100 mmHg on 2 or more blood pressure assessments prior to V2 of Study CGAR.
NOTE: Patients who meet the 14(f) blood pressure criteria during Study CGAL or Study CGAM may enroll in Study CGAR if the study investigator deems the finding not clinically significant.
15. Any of the following medical conditions are exclusionary:
a. Have a lifetime history of seizures (except for childhood febrile seizures).
b. Have a history or presence of any other medical illness including but not limited to any cardiovascular, hepatic, respiratory, hematological, endocrine, psychiatric or neurological disease, or any clinically significant laboratory abnormality, that in the judgment of the investigator indicates a medical problem that would preclude study participation.
c. Prior to V2, patients who have an elevation of *2× the upper limit of normal (ULN) for alanine aminotransferase (ALT), or *1.5× ULN for total bilirubin (TBL) or alkaline phosphatase (ALP) may be retested. The patient*s results must be discussed with Lilly Medical and judged not clinically significant prior to enrollment. See Protocol 6.2.15c for exceptions.
d. 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.
16. Any of the following drug- or alcohol-related conditions are exclusionary:
a. History of use of psilocybin (mushrooms), LSD, or 2-bromo-LSD within 2 months prior to V2.
b. Patients with a positive urine drug screen (UDS) for any substances of abuse prior to enrollment are excluded. If a patient fails eligibility due to a positive UDS, the patient may be considered for rescreen.
c. Drug, alcohol, opioid, or barbiturate abuse/dependence since completing either Study CGAL or Study CGAM (excessive or habitual use as judged by the investigator), or currently using drugs of abuse (including, but not limited to opioids, barbiturates and cannabis), or any prescribed or over the-counter medication in a manner that the investigator considers indicative of abuse/dependence. This exclusion criterion does not apply to tobacco and caffeine.
17. Employees of Lilly or investigational site personnel directly affiliated with this study and their immediate families.
18. Known hypersensitivity to multiple drugs, monoclonal antibodies or other therapeutic proteins, or to galcanezumab or to any of the inactive ingredients.
19. Patients who were inadvertently enrolled in study CGAL/CGAM may not be eligible for enrollment in CGAR. Approval from Lilly medical is required.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2017
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Galcanezumab
Generic name:	LY2951742

Ethics review

Approved WMO Date:	14-03-2017
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	08-05-2017
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	28-06-2017
Application type:	Amendment

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-08-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	13-12-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-12-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-03-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-04-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-01-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-01-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	11-02-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	13-02-2019
Application type:	Amendment

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	01-10-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-11-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2015-005234-21-NL
ClinicalTrials.gov	NCT02797951
CCMO	NL61088.028.17