A Randomized, Double-Blind, Placebo-Controlled Study of Galcanezumab in Adults with Treatment-Resistant Migraine - The CONQUER Study

Published: 28-06-2018
Last updated: 11-04-2024

The primary objective is to test the hypothesis that galcanezumab is superior to placebo in the prevention of migraine in patients with treatment-resistant migraine.The key secondary objective are:- To compare galcanezumab with placebo with respect…

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

Summary

ID

NL-OMON46150

Source
ToetsingOnline

Brief title
I5Q-MC-CGAW (CONQUER)

Condition

- Headaches

Synonym
migraine

Research involving
Human

Sponsors and support

Primary sponsor: Eli Lilly

Source(s) of monetary or material Support: Eli Lilly and Company

Intervention

Keyword: CGRP neutralizing antibody, migraine, migraine prevention, treatment-resistant migraine

Outcome measures

Primary outcome

The overall mean change from baseline in the number of monthly migraine headache days during the 3-month double-blind treatment phase in the total population (episodic and chronic migraine).

Secondary outcome

- Comparing galcanezumab with placebo in prevention of migraine in episodic subpopulation: the overall mean change from baseline in the number of monthly migraine headache days during the 3-month double-blind treatment phase in patients with episodic migraine.
- Comparing galcanezumab with placebo with regard to 50%, 75% or 100% response rate: the percentage of patients with respectively *50%, *75%, or *100% reduction from baseline in monthly migraine headache days during the 3-month double-blind treatment phase.
- Comparing galcanezumab with placebo with respect to change in functioning: the mean change from baseline in the Role Function-Restrictive domain score of the Migraine-Specific Quality of Life Questionnaire version 2.1 at Month 3.

For other secondary and for tertiary endpoints, see pages 18-20 of the protocol.

Study description

Background summary

Migraine is a chronic, debilitating neurological disease found to be one of the top 10 causes of disability worldwide. Despite the availability of preventive medications for migraine, many patients do not respond to these treatments or are unable to tolerate them. Among patients with episodic or chronic migraine who are undergoing oral preventive treatment, side effects and a lack of efficacy are the most common reasons for discontinuation. Among patients whose disease is not adequately managed, the negative impact on patient functioning increases, leading to losses in work/school and home productivity, missing or restricting family and social activities, and an overall decrease in quality of life. Therefore, new treatment options are needed, particularly for those patients who have previously failed multiple preventive medications.

Galcanezumab is a humanized monoclonal antibody that potently and selectively binds to CGRP and prevents its biological activity without blocking the CGRP receptor. The efficacy of galcanezumab for the prevention of migraine has been demonstrated in three Phase 3 randomized, double-blind trials which found statistically significant and clinically meaningful mean reduction of monthly migraine headache days and improvement in patient function compared to placebo in patients with episodic and chronic migraine. However, the Phase 3 studies excluded patients who had failed medications from 3 or more classes of migraine preventives due to inadequate efficacy among those medications with Level A or Level B evidence (defined as those listed in Silberstein et al. [2012] or botulinum toxin A or B).

Study I5Q-MC-CGAW is a Phase 3, multicenter, randomized, double-blind, parallel, placebo controlled study of galcanezumab in patients who meet ICHD-3 criteria for a diagnosis of migraine with or without aura or chronic migraine, and have a history of 2 to 4 prior migraine preventive treatment failures due to inadequate efficacy or tolerability. Study CGAW will thus enable a comprehensive clinical assessment of galcanezumab in a broader treatment-resistant patient population, including patients who may potentially have failed up to 4 different classes of standard-of-care migraine preventives.

Study objective

The primary objective is to test the hypothesis that galcanezumab is superior to placebo in the prevention of migraine in patients with treatment-resistant migraine.

The key secondary objective are:
- To compare galcanezumab with placebo with respect to prevention of migraine

in the episodic migraine subpopulation
- To compare galcanezumab with placebo with respect to 50% response rate, the 75% response rate, and the 100% response rate
- To compare galcanezumab with placebo with respect to change in functioning

For other secondary and for tertiary objectives, see pages 18-20 of the protocol.

Study design

Study CGAW is a multicenter, randomized, double-blind, parallel, placebo-controlled study of
galcanezumab in patients who meet International Classification of Headache Disorders (ICHD)
criteria for a diagnosis of migraine with or without aura or chronic migraine, and who have
previously failed 2 to 4 standard-of-care treatments for migraine prevention. The study has
4 Study Periods (SP):
- SP1: Screening (3-30 days)
- SP2: Prospective Baseline (30-40 days)
- SP3: 3-month double-blind treatment phase, where patients will be randomized in a 1:1 ratio to receive 120 mg/month galcanezumab (with an initial 240-mg loading dose) or placebo.
- SP4: Patients who complete the double-blind treatment phase (Study Period III) can opt to enter an open-label treatment phase (Study Period IV) for 3 months of treatment with galcanezumab. Sites and patients will remain blinded to patients* previous treatment assignments.

Intervention

This study involves a comparison of galcanezumab 120 mg (with an initial 240-mg loading dose) administered by subcutaneous injection once monthly with placebo. Site staff will administer injections of galcanezumab or placebo at 3 office visits during the double-blind treatment phase and administer galcanezumab at 3 office visits during the open-label treatment phase.

In order to preserve the blind during the open-label phase but to allow for a loading dose to be administered to previous placebo patients, all patients who enter the open-label treatment phase will receive 2 injections at Visit 6, and sites and patients will remain blinded to the dose administered at Visit 6; patients previously assigned to galcanezumab will receive 1 injection of 120 mg and 1 injection of placebo, while those patients previously assigned to placebo will receive an initial loading dose of galcanezumab 240 mg (2 injections of 120 mg each).

Study burden and risks

Risks:
Unwanted events of galcanezumab. The unwanted events that were determined related to galcanezumab in people with migraine, are listed in section E9. The study procedures, including blood draws, also come with certain risks. The risks are described in more detail in the subject information sheet and the Investigator's Brochure. The study drug, the study procedures and a combination thereof may include other, unknown risks.

Burden:
A total of approximately 8 months of participation, with a treatment period of max. 3 months where subjects receive monthly injections of galcanezumab/placebo, followed by an optional open-label treatment period of max. 3 months, where subjects receive monthly injections of galcanezumab. Visit duration mostly 1-2 hours.
Patients may experience a return or worsening of their symptoms at any time during this study. It may happen during the treatment period or at other times during the study when they do not receive study drug, such as the washout screening period.

Diary entries: patients are requested to make daily entries into their electronic diary device and headache medication log.

Blood draws: patients will have max. 5 visits where blood will be drawn (5-27 ml each).

ECG: patients will have max. 5 visits where an ECG is recorded.

Contacts

Public
Eli Lilly

Papendorpseweg 83
Utrecht 3528 BJ
NL
Scientific
Eli Lilly

Papendorpseweg 83
Utrecht 3528 BJ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Patients are 18 to 75 years of age (inclusive) at the time of screening.
2. Have a diagnosis of migraine as defined by IHS ICHD-3 guidelines (1.1, 1.2, or 1.3) (ICHD-3 2018), with a history of migraine headaches of at least 1 year prior to Visit 1, and migraine onset prior to age 50.
3. Prior to Visit 1, have a history of at least 4 migraine headache days and at least 1 headache-free day per month on average within the past 3 months.
4. Prior to Visit 1, have documentation (medical or pharmacy record or by physician*s confirmation) of previous failure to 2 to 4 migraine preventive medication categories in the past 10 years from the following list due to inadequate efficacy (that is, maximum tolerated dose for at least 2 months) and/or safety/tolerability reasons.
- propranolol or metoprolol
- topiramate
- valproate or divalproex
- amitriptyline
- flunarizine
- candesartan
- botulinum toxin A or B (if documented that botulinum toxin was taken for chronic migraine)
- medication locally approved for prevention of migraine;Note: Patients only qualifying under the above criteria with f) and h) should
not exceed 20% of the total study population.;5. From Visit 2 to Visit 3 (prospective baseline period), have a frequency of 4 or more migraine headache days and at least 1 headache-free day per 30-day period.
6. From Visit 2 to Visit 3 (prospective baseline period), must achieve sufficient compliance with ePRO daily headache entries as demonstrated by completion of at least 80% of daily diary entries.
7. Are able and willing to give signed informed consent.
8. Are reliable and willing to follow study procedures.
9. Women of child-bearing potential must test negative for pregnancy at the time of

enrollment based on a serum pregnancy test.
10. All females must agree to use a reliable method of birth control during the study as well as for 5 months after the last dose of investigational product. For acceptable methods of birth control for this study, see inclusion criterion 10 in the Clinical Protocol.
11. 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.

Exclusion criteria

12. Are currently enrolled in any other clinical trial involving an investigational product or any other type of medical research judged not to be scientifically or medically compatible with this study.
13. Have participated within the last 30 days or within 5 half-lives (whichever is longer) in a clinical trial involving an investigational product. If the investigational product*s half-life is not known, 6 months should have passed prior to Visit 1.
14. Prior use of galcanezumab or another CGRP antibody or CGRP receptor antibody, including those who have previously completed or withdrawn from this study.
15. Known hypersensitivity to monoclonal antibodies or other therapeutic proteins, or to galcanezumab.
16. A re currently receiving medication or other treatments for the prevention of migraine headaches. Patients must have discontinued such treatment at least 5 days prior to Visit 2. Botulinum toxin A and B that has been administered in the head or neck area for therapeutic use must be discontinued at least 3 months prior to Visit 2. Nerve blocks or device use (such as transcranial magnetic stimulation) in the head or neck area or for migraine prevention must be discontinued at least 30 days prior to Visit 2.
17. Have previously failed more than 4 migraine preventive medication categories from the list in Inclusion Criterion [4] due to inadequate efficacy (that is, maximum tolerated dose for at least 2 months) and/or safety/tolerability reasons. Previous failures to medications not on the above list will not count toward this exclusion.
18. History of cluster headache or migraine subtypes including hemiplegic (sporadic or familial) migraine, ophthalmoplegic migraine, and migraine with brainstem aura (basilar-type migraine) defined by IHS ICHD-3.
19. In the 3 months prior to randomization, have other types of headache besides migraine, tension type headache, or medication overuse headache (MOH) as defined by IHS ICHD-3.
20. History of head or neck injury within 6 months prior to Visit 1.
21. History of traumatic head injury associated with significant change in the quality or frequency of their headaches.
22. Have centralized reading of ECG at Visit 1 showing abnormalities compatible with acute cardiovascular events and/or serious cardiovascular risk, or have had myocardial infarction, unstable angina, percutaneous coronary intervention, coronary artery bypass graft, or stroke within 6 months of screening, or have planned cardiovascular surgery or percutaneous coronary angioplasty. Fridericia-corrected QT interval (QTcF) >450 msec for males or >470 msec for females based on the centralized reading of the ECG at Visit 1 must be discussed and judged not clinically significant by the principal investigator and Lilly Medical prior to enrollment.

23. Any liver tests outside the normal range at Visit 1 that are clinically significant. Alanine aminotransferase (ALT) >2X upper limit of normal (ULN), or total bilirubin (TBL) >1.5X ULN, or alkaline phosphatase (ALP) >2X ULN must be discussed and judged not clinically significant by the principal investigator and Lilly Medical prior to enrollment.
24. 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. Note: Patients with major depressive disorder (MDD) or generalized anxiety disorder (GAD) 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 medications.
25. Patients who, in the clinician*s judgment, are actively suicidal and therefore deemed to be at significant risk for suicide, or have had clinically significant suicidal ideation within the past month (eg, includes some plan or intent to act), or have had any suicidal behavior within the past month.
26. Women who are pregnant or nursing.
27. Patients who have used opioids or barbiturate containing analgesic >4 days per month for the treatment of pain in more than 2 of the past 3 months.
28. History of drug or alcohol abuse/dependence within 1 year prior to Visit 1 (excessive or compulsive use as judged by the investigator), or currently using drugs of abuse (including opioids, barbiturates, and marijuana), or any prescribed or over-the-counter medication in a manner that the investigator considers indicative of abuse/dependence.
29. Have a positive urine drug screen for any substances of abuse at Visit 1.
30. Have an acute, serious, or unstable medical condition that, in the judgment of the investigator, indicates a medical problem that would preclude study participation.
31. In the opinion of the investigator, have other issues which would interfere with compliance with the study requirements and completion of evaluations required for this study.
32. Are investigator site personnel directly affiliated with this study and/or their immediate families.
33. Are Lilly employees.
34. Are unwilling or unable to comply with the use of a data collection device.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-12-2018
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	emgality
Generic name:	galcanezumab, LY2951742

Ethics review

Approved WMO Date:	28-06-2018
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	31-08-2018
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	07-01-2019
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	11-01-2019
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	14-01-2019

Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	11-02-2019
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)

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	EUCTR2018-000600-42-NL
CCMO	NL65789.075.18