Clinical Trial Protocol
Iranian Registry of Clinical Trials

31 May 2026

A phase III, randomized, two-armed, double-blind, single-center, parallel, active-controlled, non-inferiority clinical trial to compare efficacy and safety of Galcanezumab (CinnaGen Co.) versus Emgality® (Eli Lilly Co.) in adults with treatment-resistant migraine

Protocol summary

Study aim
Non-inferiority evaluation of Galcanezumab (CinnaGen) VS. Emgality® (Eli Lilly) in treatment-resistant migraine

Design
phase III, randomized, single-center, two-armed, parallel, double-blind, non-inferiority in comparison with originator brand

Settings and conduct
This phase 3 study will be conducted in migraine patients at Sina Hospital. Patients will be randomly assigned to two groups. The patient, medical staff, and other personnel will be unaware of the type of drug being administered. Blinding will be achieved through relabeling the contents of the labels in a way that they cannot be identified. Drug administration will occur at visits 1, 2, and 3. Total duration of the study for each patient, from screening visit to end of the study, is planned to be approximately 5 months. Throughout the study, adverse events will be evaluated at all visits, and immunogenicity will be assessed at the screening visit and visit 4.

Participants/Inclusion and exclusion criteria
Inclusion Criteria: 18-60 years; migraine at least 1 year prior with onset prior to age 50; history of at least 4 MHDs and 1 headache-free day within the past 3 months & run-in; previous failure to 2 to 4 migraine treatment; informed consent. Exclusion Criteria: receiving more than 1 preventive treatment in run-in; failure to respond to more than 4 migraine preventives; history of other types of headaches; history of cluster headache/migraine subtypes; history of head/neck injury within 6 months; history of traumatic head injury; history of CVD & interventions within 6 months, opioids/barbiturate more than 4 days per month; pregnancy/nursing or planning a pregnancy

Intervention groups
Intervention group: Galcanezumab (CinnaGen Co.)
Control group: Emgality® (Eli Lilly Co.) Galcanezumab 240 mg at day 0 and 120 mg at days 30 and 60 (SubQ)

Main outcome variables
Number of Migraine Headache Days (MHDs) Number of Headache Days (HDs)

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20150303021315N41**
Registration date: **2026-03-08, 1404/12/17**
Registration timing: **registered_while_recruiting**

Last update: **2026-03-08, 1404/12/17**
Update count: **0**

Registration date
2026-03-08, 1404/12/17

Registrant information

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Name of organization / entity
Orchid Pharmed

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Iran (Islamic Republic of)

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Recruitment status
recruiting

Funding source

Expected recruitment start date
2026-02-21, 1404/12/02
Expected recruitment end date
2028-01-22, 1406/11/02
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
A phase III, randomized, two-armed, double-blind, single-center, parallel, active-controlled, non-inferiority clinical trial to compare efficacy and safety of Galcanezumab (CinnaGen Co.) versus Emgality® (Eli Lilly Co.) in adults with treatment-resistant migraine

Public title
Non-inferiority evaluation of Galcanezumab (CinnaGen) VS. Emgality ® (Galcanezumab produced by Eli Lilly Co.)
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Patients are 18 to 60 years of age (inclusive) at the time of signing the informed consent form Have a diagnosis of migraine as defined by International Headache Society (IHS) International Classification of Headache Disorders (ICHD-3 2018) (migraine with or without aura), with a history of migraine of at least 1 year prior to screening, and migraine onset prior to age 50 Prior to screening, 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 Prior to screening, have previous failure to 2 to 4 migraine preventive medication categories in the past 10 years from the following list: a) propranolol or metoprolol, b) topiramate, c) valproate or divalproex, d) amitriptyline or nortriptyline, e) venlafaxine or duloxetine, f) flunarizine, g) botulinum toxin A or B During prospective baseline period, have a frequency of 4 or more migraine headache days and at least 1 headache-free day in the 30-day run-in period Ability to comprehend and willingness to sign the informed consent form for this study and adherence to the study protocol principles
Exclusion criteria:
Treatment with any investigational agent in the last 30 days prior to screening visit or passing less than five half-lives of the investigational agent (whichever is longer) or participating in clinical studies consisting of any investigational agent or procedure Prior exposure to Galcanezumab or another CGRP (Calcitonin gene-related peptide) antibody Have a history of known serious allergies to any components of the formulation Receiving more than one medication or other treatments for the prevention of migraine in the run-in visit. Patients must have discontinued such treatment(s) at least 30 days prior to entering the run-in period. 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 entering the run-in period. Failure to respond to more than 4 migraine preventive medication categories from the list in Inclusion Criterion [4]. Previous failures to medications not on the above list will not count toward this exclusion. History of other types of headaches besides migraine, tension type headache, or medication overuse headache (MOH) as defined by IHS ICHD-3 in the 3 months prior to randomization (In other words, patients can have migraine, tension type headache, or MOH in the 3 months prior to randomization, but they cannot have other types of headaches in that time.) 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 History of head or neck injury within 6 months prior to screening History of traumatic head injury associated with a significant change in the quality or frequency of headaches History of myocardial infarction, unstable angina, percutaneous coronary intervention, coronary artery bypass graft, deep vein thrombosis/pulmonary embolism, or stroke within 6 months of screening, or have planned cardiovascular surgery or percutaneous coronary intervention Patients who have used opioids or barbiturate >4 days per month for the treatment of pain in more than 2 of the past 3 months Alanine aminotransferase (ALT) >3-fold upper limit of normal (ULN), or total bilirubin (TBL) >2-fold ULN, or alkaline phosphatase (ALP) >3-fold ULN at the screening visit History of significant psychiatric disease, 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. Women who are pregnant, nursing, or planning a pregnancy during the study History of drug or alcohol abuse/dependence within 1 year prior to screening judged by the investigator Having any other condition such as major neurologic diseases which, in the opinion of the investigator, will make the subject inappropriate for enrolling the study
Age
From **18 years** old to **60 years** old
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

Sample size
Target sample size: **226**
Randomization (investigator's opinion)
Randomized
Randomization description

Randomization of patients will be conducted using R-CRAN software version 4.4.0, utilizing block randomization (with sizes of 2 and 4) stratified by the type of migraine (chronic/episodic), receiving concomitant prophylactic medication (yes/no) and number of previous failure to migraine preventive medication categories (two / more than two) for a total of 226 patients (with a 1:1 ratio). The randomization process will be performed centrally, meaning that each patient will be allocated to one of these strata upon entering the study based on their conditions. Then, by contacting the unit responsible for randomization, they will be assigned to a treatment group using the random list corresponding to that stratum. Once randomization is completed, each patient will be assigned a code that will identify them throughout the study. The assigned code will consist of four letters (the first two letters of the first name and the first two letters of the last name), three numbers (the center code), three letters representing the generic drug name (which is GLC), and three digits (corresponding to the randomization code), forming the patient code. For example: ABCD001GLC-001. The randomization numbers will be assigned sequentially.

Blinding (investigator's opinion)

Double blinded

Blinding description

Due to the identical appearance of the syringes in both products, the information about the type of drug is indistinguishable for patients and healthcare professionals. The same research label will be designed for both study drugs. The content of the labels is based on EMA regulation. The therapeutic drug galcanezumab (CinnaGen Research and Manufacturing Company) compared to Emgality® (galcanezumab manufactured by Eli Lilly) are relabelled and packaged completely identically before the study begins. Blinding codes will be included on the drug label and each drug will be linked to a patient through this unique code, ensuring that the patient, healthcare staff, and other personnel remain unaware of the drug type. The randomization of patients and their treatment arm will not be disclosed to the study administrators and the relevant information for each patient will be provided to the investigator at the center in sealed opaque envelopes. Furthermore, individuals reviewing results and analyzing data will not be aware of the patient group classifications. A nurse will be assigned at the center for this study, responsible for administering the medication throughout the entire study duration. For the nurse injecting the drug, due to the similarity of the pharmaceutical form, according to the developed executive process, the drug is injected exclusively by the nurse and it is not possible to identify the drug type. The route of administration of the drug is subcutaneous and is done through the identical syringes. After ensuring the patient's eligibility and signing the informed consent form, according to the randomization list, patients are placed in a specific treatment group and the randomization code is announced to the nurse responsible for injecting the drug via telephone call. Decoding or breaking the blinding of the entire study based on grouping is under special conditions and is the responsibility of the DSMB committee. A request for decoding for a specific patient by the center's researcher is made when all possible cases of a specific event have been examined and, by ruling out all cases, the type of brand of drug used is identified as the most important factor in the occurrence of an event or the management of its complications, and knowing the brand name leads to specific treatment for that patient and making a decision that is not possible without decoding.

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Research Ethics Committees of Neuroscience Institute

Street address

Neuroscience Institute, Imam Khomeini Hospital, The end of Keshavarz Boulevard, Tehran

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Province

Tehran

Postal code

1419733139

Approval date

2026-02-16, 1404/11/27

Ethics committee reference number

IR.TUMS.NI.REC.1404.071

Health conditions studied

1

Description of health condition studied

treatment-resistant migraine

ICD-10 code

G43.9

ICD-10 code description

Migraine, unspecified

Primary outcomes

1

Description

The overall proportion of patients with ≥50% reduction from run-in in monthly Migraine Headache days (MHDs) during the 3-month study period.

Timepoint

Beginning of study, 90 days after intervention.

Method of measurement

Assessment based on electronic Patient Reported

Outcome (ePRO) questionnaire

Secondary outcomes

1

Description
The overall mean change from run-in in the number of monthly Migraine Headache Days (MHDs) during the 3-month study period
Timepoint
Beginning of the study, 90 days after intervention.
Method of measurement
Assessment based on electronic Patient Reported Outcome (ePRO) questionnaire

2

Description
The overall mean change from run-in in the number of monthly MHDs leading to taking medication for the acute treatment of headache during the 3-month study period
Timepoint
Beginning of the study, during 90 days after intervention.
Method of measurement
Assessment based on ePRO questionnaire

3

Description
The overall mean change from run-in in the number of monthly headache days during the 3-month study period
Timepoint
Beginning of the study, during 90 days after intervention.
Method of measurement
Assessment based on ePRO questionnaire

4

Description
The proportion of patients who maintain 50% response criteria for all 3 months of study period
Timepoint
Beginning of the study, during 90 days after intervention.
Method of measurement
Assessment based on ePRO questionnaire

5

Description
Overall mean change from run-in in the migraine attacks monthly measures (during the 3-month study period) in patients with episodic migraine
Timepoint
Beginning of the study, during 90 days after intervention.
Method of measurement
Assessment based on ePRO questionnaire

6

Description
The overall mean change from run-in in the number of monthly moderate to severe headache days during the 3-month study period
Timepoint
Beginning of the study, during 90 days after intervention.
Method of measurement
Assessment based on ePRO questionnaire

7

Description
Change from run-in in the number of monthly MHDs with: •Nausea and/or vomiting •Photophobia and/or phonophobia
Timepoint
Beginning of the study, during 90 days after intervention.
Method of measurement
Assessment based on ePRO questionnaire

8

Description
Assessment of adverse events
Timepoint
During all scheduled visits
Method of measurement
Clinical monitoring

9

Description
Assessment of immunogenicity (Assessment of anti-drug antibody (ADA) development in patients)
Timepoint
Screening, Day 90.
Method of measurement
Affinity capture elusion Enzyme-linked immunosorbent assay (ELISA) technique

Intervention groups

1

Description
Group 1: Galcanezumab (CinnaGen Co.), Galcanezumab 240 mg (2 PFSs of 120 mg/ml) at day 0 and 120 mg (one PFS) at days 30 and 60 administered by subcutaneous injection
Category
Treatment - Drugs

2

Description
Group 2: Emgality® (Galcanezumab produced by Eli Lilly Co.), Galcanezumab 240 mg (2 PFSs of 120 mg/ml) at day 0 and 120 mg (one PFS) at days 30 and 60 administered by subcutaneous injection
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center
Sina Hospital

Full name of responsible person
Dr. Elham Jafari

Street address
Sina Hospital, next to Hasan Abad square, Imam Khomeini Street, Tehran

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
Cinnagen company

Full name of responsible person
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Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
Yes

Title of funding source
Cinnagen company

Proportion provided by this source
100

Public or private sector
Private

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
Industry

Person responsible for general inquiries

Contact

Name of organization / entity
Orchid Pharmed Co.

Full name of responsible person
Dr. Hamidreza Kafi

Position
Medical Department Manager

Latest degree
Ph.D.

Other areas of specialty/work
Medical Pharmacy

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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Undecided - It is not yet known if there will be a plan to make this available

Study Protocol

Undecided - It is not yet known if there will be a plan to make this available

Statistical Analysis Plan

Not applicable

Informed Consent Form

Undecided - It is not yet known if there will be a plan to make this available

Clinical Study Report

Undecided - It is not yet known if there will be a plan to make this available

Analytic Code

Undecided - It is not yet known if there will be a plan to make this available

Data Dictionary

Not applicable