Interventional, open-label, fixed-dose multiple administration study to evaluate long-term treatment with eptinezumab in patients with chronic cluster headache

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Primary Objective:To evaluate the long-term safety and tolerability of eptinezumab in patients with chronic cluster headache (cCH)Secondary ObjectivesTo evaluate the efficacy of eptinezumab in patients with cCHExploratory ObjectiveTo explore the...

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

Summary

ID

NL-OMON54055

Source
ToetsingOnline

Brief title
19385A

Condition

- Headaches

Synonym
chronic Cluster Headache

Research involving
Human

Sponsors and support

Primary sponsor: Lundbeck

Source(s) of monetary or material Support: Lundbeck

Intervention

Keyword: chronic cluster headache, eptinezumab

Outcome measures

Primary outcome

Endpoints for the primary objective:

-adverse events

-absolute values and changes from baseline in clinical

safety laboratory test values, vital signs, weight, and

electrocardiogram (ECG) parameter values

-potentially clinically significant (PCS) clinical safety

laboratory test values, vital signs, weight changes, and

ECG parameter values

-development of specific anti-eptinezumab antibodies

(ADA) including neutralizing antibodies (NAbs)

-Columbia-Suicide Severity Rating Scale (C-SSRS) score

Secondary outcome

Endpoints for the secondary objective (efficacy):

-Conversion from cCH to episodic cluster headache (Week 0 to Week 48): Number

of patients with no cluster

headache attacks for >=3 consecutive months (>=13 consecutive weeks)

-Change from baseline in weekly number of times an abortive therapy (oxygen

and/or triptans) was used

(calculated for each infusion with eptinezumab, taking the average across the

first 4 weeks after the infusion)

-Change from baseline in the average number of weekly attacks (calculated for

each infusion with eptinezumab,

taking the average across the first 4 weeks after the infusion)

-Change from baseline in the 5-point self-rating pain severity scale

(calculated for each infusion with

eptinezumab, taking the average across the first 4 weeks after the infusion)

-Response: >=30% reduction in number of weekly attacks

(calculated for each infusion with eptinezumab, based on the average across the

first 4 weeks after the infusion)

-Response: >=50% reduction in number of weekly attacks (calculated for each

infusion with eptinezumab, based on

the average across the first 4 weeks after the infusion)

-cCH remission (Week 0 to Week 48): Number of patients

with no cluster headache attacks for >=1 month (5 consecutive weeks)

-cCH remission (Week 0 to Week 12): Number of patients with no cluster headache

attacks for >=1 month

(5 consecutive weeks between the first and second infusion)

-cCH remission (Week 12 to Week 24): Number of patients with no cluster

headache attacks for >=1 month

(5 consecutive weeks between the second and third infusion)

-cCH remission (Week 24 to Week 36): Number of patients

with no cluster headache attacks for >=1 month (5 consecutive weeks between the

third and fourth infusion)

-cCH remission (Week 36 to Week 48): Number of patients with no cluster headache attacks for >=1 month
(5 consecutive weeks within the first 12 weeks after the fourth infusion)
-Number of patients who received a transitional therapy during the Treatment Period (Week 0 to Week 48)
-Patient Global Impression of Change (PGIC) score (assessed monthly after the first eptinezumab infusion)
-Change from baseline in Sleep Impact Scale (SIS) domain scores (at each infusion and 4 weeks after each infusion)
Exploratory endpoints for the secondary objective (efficacy):
-Change from baseline in the average number of monthly attacks (per 4-week intervals after each eptinezumab infusion)
-Change from baseline in the 5-point self-rating pain severity scale (taking the average across 4-week intervals after each eptinezumab infusion)
-Response: >=30% reduction in number of monthly attacks by 4-week intervals after each eptinezumab infusion, and for each of the periods between infusions with eptinezumab, and for 12 weeks after the last eptinezumab infusion
-Response: >=50% reduction in number of monthly attacks by 4-week intervals after each eptinezumab infusion, and for each of the periods between infusions with eptinezumab, and for 12 weeks after the last eptinezumab infusion
-Response: 100% reduction in number of monthly attacks

by 4-week intervals after each eptinezumab infusion, and for each of the

periods between infusions with

eptinezumab, and for 12 weeks after the last eptinezumab infusion

-Change from baseline in monthly number of times an abortive therapy (oxygen

and/or triptans) was used

(per 4-week interval after each eptinezumab infusion)

Study description

Background summary

See section 1.1 of the protocol

Study objective

Primary Objective:
To evaluate the long-term safety and tolerability of eptinezumab in patients with chronic cluster headache (cCH)
Secondary Objectives
To evaluate the efficacy of eptinezumab in patients with cCH
Exploratory Objective
To explore the target engagement of eptinezumab to calcitonin gene-related peptide (CGRP)

Study design

Study Methodology
This is an interventional, open-label, fixed-dose multiple administration study to evaluate the long-term
treatment with eptinezumab in patients with cCH.
The target population for this study is defined as patients with cCH, based on the International Headache
Society International Classification of Headache Disorders third edition (IHS ICHD-3) classification, with
documented evidence of cCH prior to screening and confirmed via prospectively-collected information in the
eDiary during the Screening Period.
The total study duration from the Screening Visit to the Safety Follow-up (SFU) Visit is approximately

60 weeks and includes Screening Period (4 weeks), Treatment Period (48 weeks), and SFU Period (8 weeks).
Eligible patients will receive four infusions with eptinezumab 400 mg at 12-week intervals at Day 0 (Visit 2), at the end of Weeks 12 (Visit 5), 24 (Visit 8) and 36 (Visit 11), administered as an intravenous (IV) infusion over 45 minutes (+15 minutes).
The SFU Visit will take place at Week 56 (Visit 15) that is 20 weeks (5 half-lives) after the last eptinezumab administration.
Patients who withdraw from the study, except for those who withdraw their consent, will be asked to attend a Withdrawal Visit as soon as possible and a further SFU Visit, scheduled 20 weeks (5 half-lives) after the last eptinezumab administration.
Patients who are withdrawn from the treatment will be given the opportunity to remain in the study at the discretion of the investigator. Patients will be expected to attend all scheduled study visits and procedures except eptinezumab administration. If patients refuse, they will be asked to attend a Withdrawal Visit as soon as possible and a further SFU Visit, scheduled 20 weeks (5 half-lives) after the last eptinezumab administration.
Eligibility will be assessed during the Screening Period and before the first administration of eptinezumab at the Baseline Visit (Day 0/Visit 2).
Study visits:
The following visits will be site visits: Screening Visit at Week -4 (Visit 1), Investigational Medicinal Product (IMP) Visits at Weeks 0, 12, 24 and 36 (Visits 2, 5, 8 and 11), Completion Visit at Week 48 (Visit 14) and SFU Visit at Week 56 (Visit 15) or Withdrawal Visit, if applicable.
All other study visits will be phone contact visits.
In exceptional situations to be approved by the Contract Research Organisation*s (CRO) medical monitor, site visits may only consist of blood and urine sampling (for clinical safety laboratory tests, exploratory eptinezumab quantification, ADA including NAb, and exploratory biomarkers), ECG, vital signs, physical and neurological examinations, adverse events recording, and eptinezumab administration, while the remaining assessments (eDiary, electronic patient-reported outcomes [ePROs], C-SSRS, and investigator evaluations) can be conducted remotely as virtual clinic visits in line with the United States Food and Drug

Administration (US FDA) and European Medicines Agency (EMA) guidance.
Patients will be assigned an eDiary at the beginning of the Screening Period (Visit 1, Week -4) and will be
required to complete it:
Daily - during the Screening Period (from Week -4 to Day 0) and during the first 4 weeks that follow each
eptinezumab infusion (Weeks 1 to 4, 13 to 16, 25 to 28, and 37 to 40).
Weekly - for Weeks 5 to 12, 17 to 24, 29 to 36, and 41 to 48.
During the study visits with eptinezumab infusion, eDiary and ePROs must be completed prior to infusion and
prior to any interaction with the clinical site staff.
At these visits, safety assessments will be performed before and after the infusion. Safety assessments before
eptinezumab infusion consists of vital signs including body temperature, weight, concomitant medications,
adverse events, ECG, blood sampling (for clinical safety laboratory tests, exploratory eptinezumab
quantification, and ADA including NAb), urine sampling (for clinical safety laboratory and pregnancy tests)
and C-SSRS. Safety assessments after eptinezumab infusion consists of vital signs including body
temperature, and adverse events.
Blood samples for exploratory eptinezumab quantification, and ADA and NAbs assessments will be collected
at Visits 2, 5, 8, 11, 14 (or at Withdrawal Visit for patients, who withdraw from the study) and at SFU Visit
(Visit 15).

Intervention

Investigational Medicinal Product, Dose and Mode of Administration
-Eptinezumab - 400 mg, concentrate for solution for infusion 100 mg/mL added to 100 mL of 0.9% normal
saline, intravenously.
Eptinezumab will be administered at Day 0 and at Weeks 12, 24 and 36, by IV infusion over 45 minutes
(+15 minutes).

Study burden and risks

Common side effects (may affect up to 1 in 10 people):
- Allergic reactions
- Reactions due to the infusion
- inflammation of the nose and throat; commonly known as a cold (Nasopharyngitis)

Uncommon (may affect up to 1 in 100 people)
• Anaphylactic reaction (serious allergic reaction, see below for further information)

Allergic reactions and reactions due to the infusion:
As with most medicines, there is a risk that could have an allergic reaction with the study drug. Symptoms of allergic reactions can vary from mild to severe and potentially life-threatening. Most allergic reactions that occurred in studies with eptinezumab in adult patients occurred while the study treatment was given and were not serious, but often required treatment or led to stopping the study treatment.

Mild symptoms may include one or more of the following and typically disappear within a few days:
• A rash/redness of the skin
• Itching
• Flushing
• Sudden sweating or cold sweat
Although uncommon (may affect up to 1 in 100 people), serious or severe allergic reactions (which may also be called anaphylactic reactions) may occur. These reactions could develop fast during the infusion. Symptoms of serious or severe allergic reactions may include:
• Swelling of your mouth, throat or eyes
• Hives or itchy rash
• Wheezing
• Difficulty breathing
• A fast or weak pulse
• A sudden drop in your blood pressure (making you feel dizzy or lightheaded).
Serious or severe allergic reactions may result in emergency treatment and patient should promptly seek medical attention or tell the study doctor right away if any of these symptoms occur.
Other symptoms that may occur due to the infusion include respiratory symptoms (such as blocked or runny nose, throat irritation, cough, sneezing, shortness of breath) and feeling tired. These symptoms are usually non-serious and of short duration.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-The patient has a diagnosis of cCH as defined by IHS ICHD-3 classification with a history of cCH of at least 12 months prior to the Screening Visit.
-The patient has medical history of onset of cluster headache at <50years of age.
-The patient has an adequately documented record of previous abortive, transitional and preventive medication use for cCH, for at least 12 months prior to the Screening Visit.
-The patient has during the Screening Period, based on prospectively-collected information in the eDiary, acluster headache attack frequency of (this requirement should not be shared with the patient):a.minimum of 14 cluster headache attacks for the 28-day Screening Period* The patient is able to distinguish cluster headache attacks from other headaches (such as tension-type headaches, migraine).
-The patient has demonstrated compliance with the eDiary by entry of data for at least 24 out of 28 days during the 4-week Screening Period.
-The patient is aged >=18 and <=75years at the Screening Visit

Exclusion criteria

-The patient has experienced failure on a previous treatment targeting the CGRP

pathway (anti-CGRP monoclonal antibodies [mAbs] and gepants).
-The patient has a history of severe drug allergy or hypersensitivity or known hypersensitivity or intolerance to the IMP or its excipients.
-The patient has confounding and clinically significant pain syndromes (for example, fibromyalgia, complex regional pain syndrome).
-The patient has a history or diagnosis of chronic paroxysmal hemicrania.
-The patient has a history or diagnosis of chronic tension-type headache, hypnic headache, hemicrania continua, new daily persistent headache, chronic migraine or unusual migraine subtypes such as hemiplegic migraine (sporadic and familial), recurrent painful ophthalmoplegic neuropathy, migraine with neurological accompaniments that are not typical of migraine aura (diplopia, altered consciousness, or longer than 1 hour).
-Patients with a history of epilepsy.* Patients with a lifetime history of psychosis, bipolar mania, or dementia. Patients with other psychiatric conditions whose symptoms are not controlled or who have not been adequately treated for a minimum of 6 months prior to the Screening Visit.
-The patient is, at the Screening Visit or at the Baseline Visit, at significant risk of suicide (either in the opinion of the investigator or defined, using the C-SSRS, as the patient answering: "yes" to suicidal ideation questions 4 or 5 or answering: "yes" to suicidal behaviour within the past month). Patients who do not meet this criterion, but who are considered by the investigator to be at significant risk for suicide, are excluded.
-The patient has a history of clinically significant cardiovascular disease, including uncontrolled hypertension, vascular ischaemia or thromboembolic events (for example, cerebrovascular accident, deep vein thrombosis, or pulmonary embolism).
-The patient has been previously tested positive for human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg) or Hepatitis C virus antibody (anti-HCV).

complete list of exlusion criteria can be found in protocol

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-02-2022
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Eptinezumab
Generic name:	Eptinezumab

Ethics review

Approved WMO

Date:	14-06-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	17-11-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	07-04-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	13-06-2022
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2020-001968-28-NL
CCMO	NL77833.058.21