Interventional, randomized, double-blind, parallel-group, placebo-controlled study of add-on eptinezumab treatment to brief educational intervention for the preventive treatment of migraine in patients with dual diagnosis of migraine and Medication Overuse Headache

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This study has been transitioned to CTIS with ID 2024-510729-24-00 check the CTIS register for the current data. Primary Objective• To evaluate the efficacy of eptinezumab as add-on to BI for the prevention of migraine and treatment of MOHSecondary…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Headaches
Study type	Interventional

Summary

ID

NL-OMON51647

Source
ToetsingOnline

Brief title
RESOLUTION/

Condition

- Headaches

Synonym
migraine and Medication Overuse Headache, severe headache and drug-induced headaches

Research involving
Human

Sponsors and support

Primary sponsor: Lundbeck
Source(s) of monetary or material Support: Pharmaceutical company

Intervention

Keyword: eptinezumab, Medication Overuse Headache, Migraine, Resolution

Outcome measures

Primary outcome

Primary endpoint:

* Change from baseline in the number of MMDs (Weeks 1-4)

Secondary outcome

Key secondary endpoints:

* Change from baseline in MMDs (Weeks 1-12)

* Change from baseline in the number of MHDs (Weeks 1-4)

* Change from baseline in MHDs (Weeks 1-12)

* Not fulfilling the ICHD-3 diagnostic criteria for CM nor MOH (Week 4)

* Not fulfilling the ICHD-3 diagnostic criteria for CM nor MOH (Week 12)

* Change from baseline in average Daily Pain assessment score (Weeks 1-2)

* Change from baseline in monthly days with acute medication use (Weeks 1-4)

* Change from baseline in monthly days with acute medication use (Weeks 1-12)

Secondary endpoints:

* Not fulfilling the ICHD-3 diagnostic criteria for CM (Week 4, Week 12)

* Not fulfilling the ICHD-3 diagnostic criteria for MOH (Week 4, Week 12)

* Change from baseline in MMDs with use of acute medication (Weeks 1-12)

* Change from baseline in monthly days with triptan or ergotamine medication use (Weeks 1-12)

* Change from baseline in monthly days with individual non-opioid analgesics or NSAID medication use (Weeks 1-12)

* Change from baseline in monthly days with combination non-opioid analgesics medication use (Weeks 1-12)

* Migraine on the day after dosing (Day 1)

* Response: >=50% reduction from baseline in MMDs (Weeks 1-4, Weeks 1-12)

* Response: >=75% reduction from baseline in MMDs (Weeks 1-4, Weeks 1-12)

* Response: >=50% reduction from baseline in MHDs (Weeks 1-4, Weeks 1-12)

* Response: >=75% reduction from baseline in MHDs (Weeks 1-4, Weeks 1-12)

* Change from baseline in rate of migraines with severe pain intensity (Weeks 1-4, Weeks 1-12)

* Change from baseline in rate of headaches with severe pain intensity (Weeks 1-4, Weeks 1-12)

* PGIC score at Week 4 and Week 12

* MBS score at Week 12

Secondary endpoints

* Change from baseline to Week 4, and from baseline to Week 12 in the HIT-6 total score

* Change from baseline to Week 4 and from baseline to Week 12 in the mMIDAS total score

* Change from baseline to Week 4, and from baseline to Week 12 in the MSQ v2.1 sub-scores (Role Function-Restrictive, Role Function-Preventive, Emotional Function)

* Change from baseline to Week 4, and from baseline to Week 12 in the EQ-5D-5L VAS score

* Migraine specific HCRU at Baseline and at Week 12

* Change from baseline to Week 12 in the WPAI:M sub-scores (Absenteeism, Presenteeism, Work productivity loss, Activity impairment)

* Change from baseline to Week 4, and from baseline to Week 12 in HADS - depression, and anxiety subscale scores

* Change from baseline to Week 4, and from baseline to Week 12 in TSQM-9

* Change from baseline to Week 24 in the HIT-6 total score

* Change from baseline to Week 24 in the mMIDAS total score

* Change from baseline to Week 24 in the MSQ v2.1 sub-scores

* Change from baseline to Week 24 in the EQ-5D-5L VAS score

* Migraine specific HCRU at Week 24

* Change from baseline to Week 24 in the WPAI:M sub-scores

* Change from baseline to Week 24 in HADS - depression and anxiety subscale scores

* PGIC score at Week 24

* MBS score at Week 24

* Change from baseline to Week 24 in TSQM-9

* Change from baseline to Week 24 in MMDs

* Change from baseline to Week 24 in MHDs

* Not fulfilling the ICHD-3 diagnostic criteria for CM nor MOH (Week 24)

* Change from baseline to Week 24 in monthly days with acute medication use

* Change from baseline to Week 24 in average Daily Pain assessment score

* Change from baseline to Week 24 in monthly days with triptan or ergotamine medication use

* Change from baseline to Week 24 in monthly days with individual non-opioid analgesics or NSAID medication use

Safety Endpoints

* Adverse events

* Absolute values and changes from baseline in vital signs

* Potentially clinically significant vital signs changes

Study description

Background summary

Eptinezumab is approved for migraine prevention and a substantial proportion of migraine patients have a dual diagnosis of migraine and MOH. These patients generally constitute the most burdensome population, accounting for approximately 80% of all health care costs generated by the patients with CM. MOH is a global health problem with a prevalence in the general adult population of different countries ranging from 0.5% to 7.6%. Robust data from Scandinavia indicate a prevalence of 1% to 2%, representing around 50% of all patients with chronic daily headache. There is a substantial proportion of patients with a dual diagnosis of migraine and MOH worldwide5, who do not respond to, or cannot tolerate, existing treatments. None of the new CGRP mAbs have been investigated as add-on treatment to education or medication withdrawal. Therefore, it is of high clinical relevance to explore if BI would benefit from combination with a preventive treatment that has rapid onset of action and long-lasting effect.
This study is a placebo-controlled study in patients with a dual diagnosis of migraine and MOH. The study is intended to evaluate the effect on MMDs, of

eptinezumab as add-on treatment to BI, for the prevention of migraine and treatment of MOH in patients with a dual diagnosis of migraine and MOH.

Study objective

This study has been transitioned to CTIS with ID 2024-510729-24-00 check the CTIS register for the current data.

Primary Objective
• To evaluate the efficacy of eptinezumab as add-on to BI for the prevention of migraine and treatment of MOH

Secondary Objectives
• To evaluate the efficacy of eptinezumab as add-on to BI on health-related quality of life and work productivity
• To evaluate the efficacy of eptinezumab during the 12-week open label extension period

Exploratory Objectives
• To investigate the efficacy of eptinezumab as add-on to BI on level of daily physical activity and sleep using a wearable digital device (subset
• To investigate efficacy of eptinezumab as add-on to BI on the level of analgesic dependence

Safety Objective
• To evaluate the safety and tolerability of eptinezumab

Study design

• This is a phase 4, interventional, multi-national, multi-site, randomized, double-blind, parallel-group, placebo controlled study designed to demonstrate the efficacy and safety of add-on eptinezumab treatment to BI, performed at baseline, for the prevention of migraine and treatment of MOH in patients with a dual diagnosis of migraine and MOH. The 12-week placebo-controlled period will be followed by a 12-week open-label period where all patients will receive eptinezumab to provide further relief and gain exploratory data on the durability of a potential remission of the MOH and CM. The safety and tolerability of eptinezumab will be also further assessed in this open-label period.
• Patients will be instructed at the Baseline Visit to stop taking acute headache medications during a semi structured educational conversation. However, acute headache medications are allowed for patients in severe need with an advice to not exceed 9 days per month. These headache medications include paracetamol, triptans, ergotamine, combination of non-opioid analgesics, individual non-opioid analgesics and NSAIDs. The use of barbiturates and/or opioid analgesics should not exceed 4 days per month.

• Eligible patients will be randomly allocated via a randomization system to one of the two treatment groups: BI and eptinezumab 100 mg, or BI and placebo, in a ratio of 1:1.
• Randomization will be stratified by country and number of previous preventive treatment failures (<=2; >2) occurring up to 5 years prior to Baseline Visit by using IRT system. Treatment failure is defined as treatment discontinuation due to lack of efficacy (no clinically meaningful improvement at the recommended or prescribed dose for at least 3 months), side effects, or general poor tolerability of the treatment.
• The total study duration from Screening Visit to Safety Follow-up Visit is approximately 36 weeks and includes a screening period (4 weeks), a placebo-controlled period (12 weeks), an open-label period (12 weeks), and a safety follow-up period (8 weeks).
• Patients will attend on-site visits at the Screening Visit, visits with IMP intravenous (IV) infusions (Baseline Visit and Week 12 Visit), and EoS Visit at Week 24. All other visits will be conducted as telephone or telemedicine visits.
• Patients will complete a daily headache eDiary from Screening Visit until EoS/Withdrawal Visit

Intervention

• Reference therapy: BI for MOH
* BI is a semi-structured educational conversation with the purpose on helping the patients to stop the medication overuse. The BI starts with five questions of the SDS:H (including an indication of the patient*s willingness and confidence to change his/her medication overuse). Then patient is shown a short-structured scheme bases presentation either on a flip-over or slides with information about MOH and the association between medication overuse and chronic headache. The interview will end with an agreed plan on how to stop the medication overuse.
The intervention will take approximately 10 minutes to complete and is performed at Baseline Visit before IMP infusion.

• IMP
* Dosage form
• Eptinezumab - 100 mg, Concentrate for Solution for Infusion
100 mg/mL added to 100 mL of 0.9% normal saline
• Placebo - 100 mL of 0.9% normal saline
The IMP will be administered at Baseline Visit and Week 12 Visit (Visit 5), by intravenous infusion over 30 minutes (+15 minutes).

Study burden and risks

Patients are asked to undergo procedures described on pages 12 - 15 of the study protocol. These procedures include physical and neurological examination,

blood draw (i.e. HIV, Hepatitis B and C testing, etc.) urine sampling (i.e. drug screen, etc.), vital signs, ECG, completion of an eDiary and several questionnaires, answer questions of investigator and study team and administration of study drug. Additionally, female subjects of childbearing potential will have pregnancy tests. Subject*s participation in this study will last approximately 36 weeks (about 9 months). This duration includes a screening period (4 weeks), a placebo-controlled period (12 weeks), an open-label period (12 weeks), and a safety follow-up period (8 weeks).The study medication is a registered medication. Possible known side effects are described in the SmPC and patient information and can also occur during this study.

Eptinezumab may cause side effects.
• Redness and swelling of the inside of the nose and back of the throat (nasopharyngitis) (may happen to up to 1 in 10 people).
This was most often seen after the first infusion of eptinezumab. The number of people with this problem went down after the first dose and remained about the same.
• Allergic reactions and reactions to the eptinezumab infusion (may happen to up to 1 in 10 people):
Symptoms of allergic reactions can include swelling, itching, flushing, and rash. Most allergic reactions happened during the infusion and were not serious, but often led to stopping of eptinezumab. Although uncommon (may happen to up to 1 in 100 people), serious or severe allergic reactions (which are also called anaphylactic reactions) may happen. These allergic reactions can happen quickly during the eptinezumab infusion. Symptoms of serious or severe allergic reactions may include difficulty breathing, a fast or weak pulse or a sudden drop in blood pressure, swelling of the lips or tongue, hives, and a severe itchy rash.
Other symptoms that may occur due to eptinezumab infusion include respiratory symptoms (such as blocked or runny nose, throat irritation, cough, sneezing, shortness of breath, and fatigue (feeling tired). These symptoms are usually not serious and don't last long.
Eptinezumab can also have other side effects that we do not know about at the moment.

Discomforts participants may experience with checks or measurements during the study:
• To give the study drug, an IV catheter is inserted into a vein and kept there for about 30 to 45 minutes.
• There are potential risks associated with inserting the IV catheter into a vein and giving the study drug through this catheter. Some people may have nausea, anxiety, feeling faint, or some temporary discomfort during the catheter placement.
• the participant may have pain, bleeding at the insertion location, or bleeding under the skin causing a bruise where blood is drawn, or the catheter is inserted.

• There is a possibility that the insertion location could get infected, with swelling, redness, and pain.
• Possible side effects from blood draws include feeling faint, redness and swelling of the vein, pain, and bruising or bleeding at the place where blood is drawn. These normally disappear a few days afterwards.
• It is rare but possible to have a serious infection of the bloodstream or heart valves, or a blood clot in the lungs. If these rare but serious conditions occur, you would have to go to the hospital for treatment.

Blood pressure measurement
• the participant may have some discomfort as the cuff inflates and squeezes your arm, but it should only last a few seconds. Sometimes there are tiny red spots that appear after the test, just below the location of the cuff; they should be painless.

Electrocardiogram
• The sticky pads used may be cold when applied and sometimes cause some discomfort (slight redness or itching). If there is hair in the area where patches need to be applied, this area will be shaved in order to complete the electrocardiogram. Shaving may cause irritation.

Participating in the study may lead to a reduction in migraine days for the participants, but an improvement is not guaranteed for all participants.

Contacts

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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 participant has a diagnosis of migraine and MOH as defined by IHS ICHD-3 guidelines confirmed at the Screening Visit.
- The participant has >= 8 migraine days per month for each month within the past 3 months prior to the Screening Visit.
- The participant has >=15 headache days per month for each month within the past 3 months prior to the Screening Visit.
- The participant has had an onset of migraine diagnosis at <=50 years of age.

Exclusion criteria

- The participant has confounding and clinically significant pain syndromes (for example, fibromyalgia, chronic low back pain, and complex regional pain syndrome).
- The participant has a diagnosis of acute or active temporomandibular disorders.
- The participant has a history or diagnosis of chronic tension-type headache, hypnic headache, cluster headache, hemicrania continua, new daily persistent headache, or unusual migraine subtypes such as hemiplegic migraine (sporadic and familial), recurrent painful ophthalmoplegic neuropathy, migraine with brainstem aura, and migraine with neurological accompaniments that are not typical of migraine aura (diplopia, altered consciousness, or long duration).
- The participant has psychosis, bipolar mania, dementia, or any other psychiatric conditions whose symptoms are not controlled or who has not been adequately treated for a minimum of 6 months prior to the Screening Visit.
- The participant 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).

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-10-2022
Enrollment:	30
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	VYEPTI
Generic name:	eptinezumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-05-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-08-2022

Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-11-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-12-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-12-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-12-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
EU-CTR	CTIS2024-510729-24-00
EudraCT	EUCTR2021-003049-40-NL
Other	IND no 114647
CCMO	NL80981.100.22