A Phase 3, Multicenter, Open-Label 156-Week Extension Study to Evaluate the Long-Term Safety and Tolerability of Oral Atogepant for the Prevention of Migraine in Participants with Chronic or Episodic Migraine

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This study has been transitioned to CTIS with ID 2023-507096-21-00 check the CTIS register for the current data. To evaluate the safety and tolerability of treatment with atogepant 60 mg once daily when administered over 156 weeks for the prevention...

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

Summary

ID

NL-OMON54251

Source
ToetsingOnline

Brief title
3101-312-002

Condition

- Headaches

Synonym
Migraine; Headache

Research involving

Human

Sponsors and support

Primary sponsor: AbbVie Deutschland GmbH & Co. KG
Source(s) of monetary or material Support: AbbVie B.V.

Intervention

Keyword: Atogepant, Chronic and Episodic Migraine, Long-Term, Prohylaxis

Outcome measures

Primary outcome

- Percentage of Participants with at Least 1 Treatment Emergent Adverse Event across the 156-week treatment period

Secondary outcome

- Percentage of Participants with Clinically Significant Laboratory Values (Chemistry, Hematology, Urinalysis) as assessed by the Investigator [Time Frame: 156 weeks]

- Percentage of Participants with Clinically Significant Electrocardiograms (ECGs) Findings as assessed by the Investigator [Time Frame: 156 weeks]

- Percentage of Participants with Clinically Significant Vital Sign Measurements as assessed by the Investigator [Time Frame: 156weeks]

- Columbia-Suicide Severity Rating Scale (C-SSRS) Assessing Suicidal Ideation and Behavior using 5-Point Scales [Time Frame: 156 weeks]

Study description

Background summary

Migraine affects 18% of women and 6% of men in the United States with peak

prevalence occurring between the ages of 25 to 55 years. Approximately one-third of these migraineurs have 3 or more migraine headaches per month, and over half report severe impairment or the need for bed rest. Prevalence is similar in Europe, with migraine headache affecting on average 17.6% of women and 8% of men. As of 2016, migraine is the second leading cause of disability worldwide. Migraine is typically characterized by attacks of throbbing, unilateral headache of moderate or severe pain intensity, associated with nausea, vomiting, and/or sensitivity to light (photophobia) and sound (phonophobia). In about 25% of individuals, the migraine headache is preceded by focal neurological dysfunction (aura). Improving diagnosis and optimizing treatments for migraine have been recognized as critically important to overcoming current barriers to reduce the global burden of migraine. Because there are no biological markers for migraine, diagnosis is based on clinical history, exam, and the exclusion of other headache disorders. Physicians apply clinical criteria to guide diagnoses and subsequent treatment. Episodic migraine (EM) can be divided into low frequency (LFEM) and high frequency episodic migraine (HFEM) depending on the headache days suffered per month (GBD 2017). Episodic migraine (EM) is a syndrome diagnosis applied to patients with migraine (with or without aura) who have 1 to 14 headache days per month. Chronic migraine is a specific ICHD-3diagnosis applied to a subset of patients with >=15 headache days per month. This study will include participants with episodic migraine who had failed 2-4 classes of prior oral prophylactic medications. The rationale for targeting this population is 2-fold. Firstly, patients on currently available oral prophylactic medications may experience poor tolerability; secondly, many of these treatments have shown insufficient efficacy (did not sufficiently reduce either severity or frequency) of migraine for many patients. The consequences of the limitations in current oral prophylactic migraine treatments amount to both poor adherence and reluctance to initiate prophylactic treatment. In fact, recent studies have indicated that approximately half of migraine patients discontinued their initial oral migraine prophylactic treatment within 60 days, which might be explained by poor tolerability or lack of efficacy. Moreover, in a US-based retrospective database study it was concluded that approximately 70% of patients who begin migraine prophylaxis with antidepressants, antiepileptics, or beta-blockers are no longer taking these medications at 6 months. Of those patients who continue to take a prophylactic medication, many still have substantial disease burden. Therefore, the proposed population for Study 3101-304-002 reflects clinical practice. There is severe unmet need in patients that have failed multiple migraine prophylactic oral medications, and these patients are currently often relying on ineffective treatments and many suffer from intolerability to currently available medications

Study objective

This study has been transitioned to CTIS with ID 2023-507096-21-00 check the CTIS register for the current data.

To evaluate the safety and tolerability of treatment with atogepant 60 mg once daily when administered over 156 weeks for the prevention of migraine in participants with Chronic Migraine (CM) or Episodic Migraine (EM).

Study design

This is a multicenter, open-label, 156-week, long-term safety extension study conducted in all eligible participants who complete either lead-in Study 3101-303-002 (Phase 3 CM study) or Study 3101-304-002 (Phase 3 EM study). All participants will be treated with atogepant 60 mg once daily. The study will consist of a 156-week open-label treatment period, and a safety follow-up period of 4 weeks.

Intervention

All participants will be treated with atogepant 60 mg once daily. The study will consist of an open-label treatment period of 156 weeks.

Study burden and risks

The study will include a total of 18 visits and will be up to 156 weeks in duration. Subjects are expected to undergo procedures/assessments as described in the section 1.3 of the study protocol, which include: Physical exam, vital signs, demographic and medical history; ECG; eDiary: reporting information on symptoms/signs of disease, (i.e. headache duration, frequency, characteristics, symptoms, acute medication use, etc.); Blood and urine tests (including urine drug screening); Completion of questionnaire and answering questions from the study team; Pregnancy tests in women of childbearing potential; Female patients: no breastfeeding allowed. Effective methods of birth control must be used from the time of signing the ICF, throughout the entire study; Male patients: due to the potential risk of the effect on the sperm appropriate method of contraception must be used starting at screening and throughout the entire study. The following risks were the most common side effects in a study of patients with migraine receiving atogepant or placebo (medically inactive substance) daily for 12 weeks: nausea, common cold, constipation, urinary tract infection, fatigue, increased creatine phosphokinase The risks involved in taking this study medication have been carefully assessed by previous testing done in animal and human studies. Overall, the risks are considered to be acceptable although some risks are unforeseeable. In addition to the risks listed above, there may be some infrequent and unforeseeable risks associated with the use of atogepant. Atogepant is investigational, when taken alone or in combination with other medications, so there may be other risks that are unknown. Older drugs in this class have been associated with an increased risk of liver problems. However, atogepant is a new drug that has been designed specifically to minimise this risk. Based on previous studies with this drug, no safety issues related to taking atogepant and liver problems have been

detected. Placebo Risks: If the study subject is in the group which is assigned placebo, study subject*s symptoms of migraine may not improve or may worsen. Even if the study subject is in the group that gets the active drug during the study, the symptoms may not improve or may worsen. Blood Sample Risks: Subjects may feel a slight needle prick when blood is drawn. Some participants may have a slight bruise that will go away within a few days. Sometimes, participants feel light headed or feel dizzy. Other rare complications associated with the blood sample collection include: infections, nerve lesions, accidental arterial puncture (when the needle pierces an artery instead of a vein) and bleeding, inflammation of vein, and dizziness. Electrocardiogram (ECG) Risks: The ECG procedure may cause minimal discomfort and skin irritation during or after the attachment/removal of the leads (and adhesive). Allergic Reaction Risks: As with taking any treatment, there is a risk of allergic reaction. Some symptoms of allergic reactions are: Rash; Wheezing and difficulty breathing; Dizziness and fainting; Swelling around the mouth, throat or eyes; A fast pulse; Sweating. This study will include participants with episodic migraine who had failed 2-4 classes of prior oral prophylactic medications. The rationale for targeting this population is 2-fold. Firstly, patients on currently available oral prophylactic medications may experience poor tolerability; secondly, many of these treatments have shown insufficient efficacy (did not sufficiently reduce either severity or frequency) of migraine for many patients. The consequences of the limitations in current oral prophylactic migraine treatments amount to both poor adherence and reluctance to initiate prophylactic treatment. In fact, recent studies have indicated that approximately half of migraine patients discontinued their initial oral migraine prophylactic treatment within 60 days, which might be explained by poor tolerability or lack of efficacy. Moreover, in a US-based retrospective database study it was concluded that approximately 70% of patients who begin migraine prophylaxis with antidepressants, antiepileptics, or beta-blockers are no longer taking these medications at 6 months. Of those patients who continue to take a prophylactic medication, many still have substantial disease burden. Current available data supports the efficacy of atogepant for the prevention of episodic migraine; in addition, atogepant has been well tolerated with no safety concerns to date. The protocol is designed to ensure that patient safety is assessed adequately throughout the study. An independent DSMB will review unblinded safety data throughout the trial and make recommendations to the sponsor, including modification or early termination of the trial, if emerging data show unexpected and clinically significant adverse effects of treatment. Overall the assessment of benefit/risk is favorable.

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

1. Written informed consent and participant privacy information (eg, written authorization for use and release of health and research study information) obtained from the participant prior to initiation of any study-specific procedures.
2. Participants must be using a medically acceptable and effective method of birth control during the course of the entire study, as defined in Section 4.5.2 of the protocol.
3. Eligible participants who completed the double-blind treatment period (Visit 7) and the follow-up period (Visit 8), if applicable, depending on the timing of study initiation, of Study 3101-303-002 or Study 3101-304-002 without significant protocol deviations (eg, noncompliance to protocol-required procedures) and who did not experience an AE that, in the investigator*s opinion, may indicate an unacceptable safety risk.

Exclusion criteria

1. Requirement for any medication, diet (ie, grapefruit or grapefruit juice),

or nonpharmacological treatment that is on the list of prohibited concomitant medications or treatments (see Section 4.5.1 and Attachment 12.1 of the study protocol) that cannot be discontinued or switched to an allowable alternative medication or treatment.
Exception: participants from lead-in Study 3101-303-002 taking only 1 migraine prevention medication (with demonstrated efficacy, as listed in Attachment 12.1 of the protocol) at a stable, well-tolerated dose during the lead-in study; the medication may be continued at the same dose or discontinued.
2. Female participant is pregnant, planning to become pregnant during the course of the study, or currently lactating. WOCBP must have a negative urine pregnancy test at Visit 1.
3. An ECG with clinically significant abnormalities at Visit 1 as determined by the investigator.
4. Hypertension as defined by sitting systolic BP > 160 mm Hg or sitting diastolic BP > 100 mm Hg at Visit 1. Vital sign measurements that exceed these limits may be repeated only once.
5. Significant risk of self-harm based on clinical interview and responses on the C-SSRS, orof harm to others in the opinion of the investigator; participants must be excluded if they report suicidal ideation with intent, with or without a plan (ie, Type 4 or 5 on the C-SSRS) since the last visit.
6. Participants with clinically significant hematologic, endocrine, cardiovascular, pulmonary, renal, hepatic, gastrointestinal, or neurologic disease.
7. Participant has a condition or is in a situation which in the investigator's opinion may put the participant at significant risk, may confound the study results, or may interfere significantly with participation in the study.
8. Any medical or other reasons (eg, unlikely to adhere to the study procedures, keep appointments, or is planning to relocate during the study) that, in the investigator*s opinion, might indicate that the participant is unsuitable for participation in the study.
9. History of acute hepatitis within 6 months of screening (Visit 1); or chronic liver disease (including nonalcoholic fatty liver disease, viral chronic hepatitis, and cirrhosis).

Study design

Design

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

Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-02-2022
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Atogepant
Generic name:	Atogepant

Ethics review

Approved WMO Date:	10-05-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-07-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	25-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-04-2023
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-05-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-06-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	CTIS2023-507096-21-00
EudraCT	EUCTR2020-002470-27-NL
ClinicalTrials.gov	NCT04686136
CCMO	NL76039.056.21