A Phase 3, 12-Month, Open-Label Study of Lasmiditan in Pediatric Patients with Migraine - PIONEER-PEDS2

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This study has been transitioned to CTIS with ID 2023-506724-85-00 check the CTIS register for the current data. Primary- To evaluate the safety and tolerability of long-term intermittent use of lasmiditan for the acute treatment of migraine in...

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

Summary

ID

NL-OMON49166

Source
ToetsingOnline

Brief title
H8H-MC-LAHW (PIONEER-PEDS2)

Condition

- Headaches

Synonym
Headache; migraine

Research involving
Human

Sponsors and support

Primary sponsor: Eli Lilly

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

Intervention

Keyword: Lasmiditan, Migraine, Pediatric

Outcome measures

Primary outcome

- Nature, proportion, and severity of TEAEs by treated attack.

- Proportion of discontinuation due to AEs.

Secondary outcome

- Proportion of treated attacks with pain freedom at 2 hours after dosing for

each 3-month period.

- Proportion of treated attacks with pain relief at 2 hours after dosing for

each 3-month period.

- Proportion of treated attacks with freedom of the most bothesome symptom, at

2 hours after dosing for each 3-month period.

Study description

Background summary

Migraine is one of the most common neurological conditions in pediatrics. Migraine attacks are characterized by intense pain and associated symptoms, resulting in substantial negative impacts on daily life. In children and adolescents, migraine can have a negative impact on function (including missed school days and poorer academic performance) and quality of life.
The goal of migraine treatment in the pediatric population is quick resolution of the headache with minimal side effects, allowing the child to resume normal activities. There are few positive trials of acute medication for the treatment of migraine in children, particularly in the population less than 12 years old. High placebo response rates, as well as shorter attack length in this population, have complicated efforts to demonstrate efficacy of treatments. Lasmiditan is a novel therapy for the acute treatment of migraine. Lasmiditan

is a high-affinity, centrally penetrant, selective 5-HT1F receptor agonist developed specifically for the acute treatment of migraine. Lasmiditan selectively targets 5-HT1F receptors on neurons in the central and peripheral trigeminal system, decreasing neuropeptide release and inhibiting pain pathways (including the trigeminal nerve) (Nelson et al. 2010; Vila-Pueyo 2018). Lasmiditan is structurally and mechanistically distinct from other approaches for the acute treatment of migraine, such as triptans, and lacks the vasoconstrictive effects of triptans that result from 5-HT1B activity. In 2 placebo-controlled, randomized, Phase 3 efficacy trials of a single migraine attack in adults, lasmiditan low dose, medium dose, and high dose were associated with a greater proportion of patients achieving pain freedom and freedom from their most bothersome associated symptom at 2 hours (Kuca et al. 2018; Goadsby et al. 2019). Lasmiditan may provide therapeutic benefit to children and adolescents from at least 6 to less than 18 years of age.

Study objective

This study has been transitioned to CTIS with ID 2023-506724-85-00 check the CTIS register for the current data.

Primary
- To evaluate the safety and tolerability of long-term intermittent use of lasmiditan for the acute treatment of migraine in pediatric patients.

Key Secondary
- To evaluate the efficacy of intermittently dosed lasmiditan in the treatment of multiple migraine attacks over time in pediatric patients.

Study design

This is a prospective, randomized, open-label, 12-month study in children and adolescents with a diagnosis of migraine who previously enrolled in and completed Study H8H-MC-LAHX (LAHX) or Study H8H-MC-LAHV (LAHV). Study participants will be stratified by age group (6 to <12 years and 12 to <18 years based on age at time of enrollment into Study LAHX or LAHV) and randomized in a 1:1 ratio to treatment with weight-based doses comparable to medium dose and high dose adult exposure.
During a 12-month open-label treatment period, study participants may use lasmiditan to treat up to 8 migraine attacks per month on an outpatient basis. Dosing with lasmiditan, outcomes, use of concomitant medications, and adverse events will be recorded in a paper diary. Rescue medication may be used beginning 2 hours after lasmiditan dosing. Patients may use 1 dose of lasmiditan in a 24-hour period. Participants may use their usual treatment in the event they choose not to take lasmiditan for an individual attack

Intervention

Participants will be randomized in a 1:1 ratio at study entry to treatment with weight-based doses corresponding to the medium dose- and the high dose adult exposure (referred to throughout as lasmiditan medium dose and lasmiditan high dose). The lasmiditan dose may be reduced 1 time during study participation in the event of tolerability concerns, after treatment of at least 3 migraine attacks at the randomized dose (see Section 6.6 of the Protocol). Study participants may use lasmiditan to treat up to 8 migraine attacks per month on an outpatient basis.

Study burden and risks

Lasmiditan may provide therapeutic benefit to children and adolescents with migraine. Lasmiditan is approved in the United States for the acute treatment of migraine, with or without aura, in adults. In adults with migraine with or without aura, lasmiditan (low dose, medium dose and high dose) has been shown to be an effective treatment based on the primary endpoints of pain freedom and freedom from the most bothersome symptom (selected from nausea, photophobia, or phonophobia at the beginning of the migraine attack) at 2 hours postdose (Kuca et al. 2018; Goadsby et al. 2019). Additional evidence of efficacy was observed on multiple secondary measures of pain relief (2 hours), sustained pain freedom (24 hours), functioning (2 hours), and Patient Global Impression of Change (2 hours), as well as time to onset of pain relief, pain freedom, and freedom from associated symptoms.
In Study LAHW, pediatric patients will have the option to treat up to 8 migraine attacks a month with lasmiditan for 12 months. Patients will be initially randomized to receive weight-based doses comparable to medium dose and high dose exposures in adult patients. However, patients may request 1 dose adjustment for tolerability after treating at least 3 migraine attacks at the randomized dose.
As a centrally penetrant and neurally active drug, lasmiditan use is associated with neurologic treatment-emergent adverse events (TEAEs), with the most common being dizziness, paresthesia, somnolence, fatigue, nausea, hypoesthesia, and muscle weakness. Lasmiditan is generally well-tolerated, and the vast majority of adverse events (AEs) are mild to moderate in severity and of limited duration.
More information about the known and expected benefits, risks, serious adverse events (SAEs), and reasonably anticipated AEs of lasmiditan can be found in the Investigator*s Brochure (IB).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Type of Patient and Disease Characteristics
[1] Patient is at least 6 and less than 18 years of age at Screening (Visit 1).
[2] Patient must have a minimum body weight of 15 kg.
[3] Patient has a history of migraine with or without aura as defined by International Headache Society International Classification of Headache Disorders, 3rd edition (ICHD-3) (ICHD-3 2018) diagnostic criteria 1.1 or 1.2.1 and meets the following criteria:
- History of migraine attacks for more than 6 months
- Reports at least 2 and no more than 8 moderate-to-severe migraine attacks per month in the 2 months prior to Screening Visit
- Duration of a typical untreated migraine attack (excluding sleep) is greater than or
equal to*3 hours
- Patient has not, by history, experienced satisfactory response with a previous migraine therapy, in the opinion of the investigator.
[4] Patient must be able to swallow a tablet.
[5] For patients taking migraine preventive medication, treatment regimen is

stable and has been taken for at least 3 months prior to Visit 1.

Informed Consent and Patient Agreements
[6] The patient and patient*s parent or guardian must understand the nature of the
study. The patient*s parent or guardian must sign an ICF, and the patient must sign an informed assent document as required by local regulations.
[7] The patient and patient*s parent or guardian are reliable and willing to make
themselves available for the duration of the study and are willing to follow study procedures.
[8] Patient is male or female; if female, must agree to abide by the following guidance:
- Females of childbearing potential (started menses, to include any duration or amount of spotting) must agree to use a highly effective method of contraception (that is, one with less than 1% failure rate) such as
o combination oral contraceptives
o implanted/injected contraceptives
o intrauterine devices, or
o sterile partner until 30 days after the last dose of study medication.
- Females of childbearing potential who are abstinent (if this is complete abstinence,
as their preferred and usual lifestyle) or in a same-sex relationship (as part of their
preferred and usual lifestyle) must agree to either remain abstinent or stay in a
same-sex relationship without sexual relationships with males. Periodic abstinence
(for example, calendar, ovulation, symptothermal, and postovulation methods), declaration of abstinence just for the duration of a trial, and withdrawal are not
acceptable methods of contraception.
[9] The patient and patient*s parent or guardian must 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 notification that the study has been completed. Examples of these sites include
- Facebook
- Twitter
- Snapchat
- Instagram, and
- Google+.

Exclusion criteria

Medical Conditions

[10] Patient has a history or clinical evidence of congenital heart disease, suspected
or confirmed.
[11] ECG showing abnormalities compatible with acute cardiovascular events, serious cardiovascular disease risk, or both.
[12] Within 6 months of screening, patient had
- myocardial infarction
- unstable angina
- percutaneous coronary intervention, and
- coronary artery bypass graft.
[13] Patient has planned cardiovascular surgery or percutaneous coronary angioplasty, or has a history of stroke.
[14] Patient has any liver tests outside the normal range at screening that are clinically
significant. Alanine aminotransferase (ALT) greater than 2x upper limit of normal
(ULN), or total bilirubin level (TBL) greater than 1.5x ULN, or alkaline phosphatase
(ALP) greater than 2x ULN must be discussed and judged not clinically significant by
Lilly Medical prior to enrollment.
NOTE: Patients with TBL at least 1.5x ULN are not excluded if they meet all of the
following criteria for Gilbert syndrome:
*- Bilirubin is predominantly indirect (unconjugated) at Screening (direct bilirubin within normal limits)
* - Absence of liver disease
* - ALT, aspartate aminotransferase (AST), and ALP no greater than 1x ULN at screening, and
* Hemoglobin not significantly decreased at screening.
[15] Patient has, in the judgement of the investigator, a psychiatric disorder as
defined by the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, that would interfere with adherence to study requirements or safe participation in the trial. This includes a current or historical diagnosis of a substance use disorder.
[16] Patient is, in the judgment of the investigator, actively suicidal and therefore
deemed to be at significant risk for suicide.
[17] At Screening:
- patient has answered *yes* to either Question 4 or Question 5 on the *Suicidal Ideation* portion of the Columbia-Suicide Severity Rating Scale (C-SSRS) or has answered *yes* to any of the suicide-related behaviors on the *suicidal behavior*
portion of the C-SSRS, and
- the ideation or behavior occurred within the past month.
[18] Patient is pregnant or breastfeeding.

[19] Patient has, in the judgment of the investigator, an acute, serious, or unstable
medical condition or a history or presence of any other medical illness that would preclude study participation.
Prior and Concomitant Therapy/Substances of Abuse
[20] Patient has used opioids or barbiturate-containing analgesic more than 3 times
per month for the treatment of pain in more than 2 of the past 6 months.
[21] Patient has known allergies to lasmiditan, related compounds, or any components of the formulation.
[22] Patient has a positive urine drug screen for any substances of abuse.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-06-2020
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lasmiditan
Generic name:	Lasmiditan

Ethics review

Approved WMO Date:	11-08-2020
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	24-08-2020
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	05-10-2020
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	29-10-2020
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	01-03-2021
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	17-04-2021
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	09-07-2021
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	13-07-2021
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	11-05-2022
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO	

Date:	19-05-2022
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	05-07-2023
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
EU-CTR	CTIS2023-506724-85-00
EudraCT	EUCTR2019-004379-38-NL
CCMO	NL73491.075.20