Pediatric Options for Migraine Relief: A Randomized, Double-Blind, Placebo-Controlled Study of Lasmiditan for Acute Treatment of Migraine: PIONEER-PEDS1

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This study has been transitioned to CTIS with ID 2023-506253-38-00 check the CTIS register for the current data. Primary- To test the hypothesis that lasmiditan high dose is superior to placebo in the acute treatment of a migraine attack in...

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

Summary

ID

NL-OMON54273

Source
ToetsingOnline

Brief title
H8H-MC-LAHV (PIONEER-PEDS1)

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

Primary

- Proportion of patients >=6 to <18 years of age with pain freedom at 2 hours after dosing

Secondary outcome

Key Secondary

- Proportion of patients >=6 to <18 years of age with pain freedom at 2 hours after dosing

- Proportion of patients >=6 to <18 years of age with pain freedom at 2 hours after dosing

Secondary

- Proportion of patients with pain freedom at 2 hours after dosing in the subgroup of patients >=6 to <12 years of age and in the subgroup of patients 12 to <18 years of age

- Proportion of patients >=6 to <18 years of age with pain relief at 2 hours after dosing

- Proportion of patients >=6 to <18 years of age MBS-free at 2 hours after dosing

- In patients >=6 to <18 years of age:

* Proportion of patients nausea-free at 2 hours after dosing

* Proportion of patients photophobia-free at 2 hours after dosing

* Proportion of patients phonophobia-free at 2 hours after dosing

- Proportion of patients >=6 to <18 years of age with sustained pain freedom at 24 and 48 hours

- In patients >=6 to <18 years of age:

* Proportion of patients using additional medication for migraine within 24 and 48 hours

* Time to use of additional migraine medication

- In patients >=6 to <18 years of age:

* Proportion of patients with pain freedom at 30 minutes, 1, 1.5, and 2 hours after dosing

* Proportion of patients with pain relief at 30 minutes, 1, 1.5, and 2 hours after dosing

* Proportion of patients MBS-free at 30 minutes, 1, 1.5, and 2 hours after dosing

* Proportion of patients nausea-free at 30 minutes, 1, 1.5, and 2 hours after dosing

* Proportion of patients photophobia-free at 30 minutes, 1, 1.5, and 2 hours after dosing

* Proportion of patients phonophobia-free at 30 minutes, 1, 1.5, and 2 hours after dosing

- Proportion of patients >=6 to <18 years of age with PGIC rating of *a lot better,* *better,* *no different,* *worse,* and *a lot worse* at 2 hours

- Proportion of patients >=6 to <18 years of age with a rating of 0 (*not at

all*), 1 (*a little*), 2 (*a lot*), or 3 (*completely*) at 2 hours

Acceptability of the Formulation

- Proportion of patients >=6 to <18 years of age with a rating of *very easy,*

easy, *neither easy nor hard,* *hard,* or *very hard* at 24 hours after

dosing

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 2023-506253-38-00 check the CTIS register for the current data.

Primary
- To test the hypothesis that lasmiditan high dose is superior to placebo in the acute treatment of a migraine attack in pediatric patients >=6 to <18 years of age

Key Secondary
- To test the hypothesis that lasmiditan medium dose is superior to placebo in the acute treatment of a migraine attack in pediatric patients >=6 to <18 years of age
- To test the hypothesis that lasmiditan low dose is superior to placebo in the acute treatment of a migraine attack in pediatric patients >=6 to <18 years of age

Secondary
- To evaluate the efficacy of lasmiditan (low dose, medium dose, and high dose) compared with placebo with respect to pain freedom in age subgroups
- To evaluate the efficacy of lasmiditan (low dose, medium dose, and high dose) compared with placebo with respect to pain relief
- To evaluate the efficacy of lasmiditan (low dose, medium dose, and high dose) compared with placebo with respect to resolution of the MBS
- To evaluate the efficacy of lasmiditan (low dose, medium dose, and high dose) compared with placebo with respect to absence of individual associated symptoms of migraine
- To evaluate the efficacy of lasmiditan (low dose, medium dose, and high dose) compared with placebo with respect to sustained pain freedom
- To evaluate the efficacy of lasmiditan (low dose, medium dose, and high dose) compared with placebo with respect to use of additional medication within 24 and 48 hours
- To evaluate the efficacy of lasmiditan (low dose, medium dose, and high dose) compared with placebo with respect to time of onset of outcomes of pain freedom, pain relief, and freedom from associated symptoms of migraine, including the MBS
- To evaluate the efficacy of lasmiditan (low dose, medium dose, and high dose) compared with placebo with respect to patient-reported global measure of change
- To evaluate the efficacy of lasmiditan (low dose, medium dose, and high dose) compared with placebo with respect to the degree of migraine interference in normal activities

Acceptability of the Formulation
- To evaluate the acceptability of lasmiditan tablets (low dose, medium dose, and high dose) with respect to ease of swallowing of the tablets

Study design

Study LAHV is a multi-country, randomized, double-blind, parallel-group, placebo-controlled trial in patients of at least 6 to less than 18 years of age who meet International Classification of Headache Disorders criteria for a diagnosis of migraine. Study LAHV will assess the efficacy, safety, and tolerability of lasmiditan low dose, medium dose, and high dose compared to placebo in the treatment of a single migraine attack. Patients will treat a single migraine attack in 2 stages: a double-blind placebo challenge (Stage 1) prior to randomization in the efficacy analysis period (Stage 2). Patients will record characteristics of treated migraine and outcomes in an electronic diary prior to dosing and at specified intervals after dosing. Patients will record any AEs and concomitant use of medication throughout the Treatment Period in a paper diary. An End-of-Study Visit will be conducted within 28 days of dosing of study medication or after 12 weeks if no migraine attack is treated with study drug.

Intervention

This study involves a comparison of lasmiditan film-coated tablets with placebo. The study medication will be administered by mouth. To maintain the blind, each dose will require 3 tablets. The proposed lasmiditan dose, definitions of weight thresholds for this study, or both may be amended prior to the first enrollment, based on the PK and safety data from Study LAHX. The selected dose for each weight cohort is intended to reflect exposures comparable to the low, medium and high doses of lasmiditan in adults.

Study burden and risks

Migraine is a disabling and prevalent disorder that impacts children. There are few approved treatments for migraine in children and adolescents in the US, with only 1 approved treatment (rizatriptan) available for children aged at least 6 to less than 12 years. Current treatments are not sufficiently meeting the needs of all patients (El-Chammas et al. 2013). Lasmiditan is a highly selective 5-HT1F agonist that is being developed for the acute treatment of migraine attacks. Lasmiditan demonstrated efficacy and safety in 2 placebo-controlled, randomized, Phase 3 efficacy trials in adults (Kuca et al. 2018; Goadsby et al. 2019). If approved in a pediatric population, lasmiditan would provide another acute treatment option for children and adolescents with migraine. As a centrally penetrant 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.
It is generally well-tolerated, and the vast majority of events in adults are mild to moderate and of limited duration. Further information can be found in the Investigator*s Brochure. Patients who complete Visits 1, 2, 3, and 801 in Study LAHV may be eligible to participate in an open-label, 12-month, long-term safety study, Study LAHW. Treatment of a qualifying migraine during during the 12-week treatment period is not required to qualify for Study LAHW. In Study LAHW, patients will have the opportunity to treat multiple migraine attacks with lasmiditan.

Contacts

Public
Eli Lilly

Island House, Eastgate Business Park, Little Island na
Cork Co.
NL
Scientific
Eli Lilly

Island House, Eastgate Business Park, Little Island na
Cork Co.
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 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
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-06-2020
Enrollment:	4
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Lasmiditan
Generic name:	Lasmiditan

Ethics review

Approved WMO Date:	11-08-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-08-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-11-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-03-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-04-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	17-04-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-07-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-07-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-05-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-05-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-06-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-10-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-11-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	CTIS2023-506253-38-00
EudraCT	EUCTR2019-004378-24-NL
CCMO	NL73301.075.20