A multi-center, open-label, uncontrolled, single-arm, extension study to determine the long-term safety and tolerability of oral lucerastat in adult subjects with Fabry disease

Published: 19-11-2018
Last updated: 12-04-2024

Primary objectiveThe primary objective of the study is to determine the long term safety and tolerability of lucerastat in subjects with Fabry disease (FD).Secondary objectives* To evaluate the effect of lucerastat on renal function and cardiac...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital and hereditary disorders NEC
Study type	Interventional

Summary

ID

NL-OMON55750

Source
ToetsingOnline

Brief title
OLE

Condition

- Congenital and hereditary disorders NEC

Synonym
alpha-galactosidase A deficiency, Fabry's disease

Research involving
Human

Sponsors and support

Primary sponsor: Idorsia Pharmaceuticals Ltd.
Source(s) of monetary or material Support: Idorsia Pharmaceuticals Ltd.

Intervention

Keyword: Adult, Fabry's disease, Lucerastat, Neuropathic pain

Outcome measures

Primary outcome

Safety endpoints

* Treatment-emergent adverse events (AEs) and serious AEs (SAEs) up to FU1 visit;

* AEs leading to premature discontinuation of study treatment;

* Change from baseline to each visit up to Month 48 in vital signs;

* Change from baseline to each visit up to Month 24 in 12 lead electrocardiogram (ECG) variables;

* Treatment-emergent marked abnormalities for quantitative 12 lead ECG variables at each visit up to Month 24;

* Change from baseline to each visit up to Month 48 in laboratory variables [see list in Section 7.2.4.2 of the protocol];

* Treatment-emergent marked abnormalities for selected laboratory variables at each visit up to Month 48.

Main efficacy endpoints

* Subject eGFR slope from baseline to Month 24 and from baseline to Month 48;

* Change from baseline to Month 24 in left ventricular mass index (LVMI) as measured by echocardiography;

* Change from baseline to Month 24 and Month 48 in plasma globotriaosylceramide

(Gb3).

Secondary outcome

Other efficacy endpoints

Other efficacy endpoints are described in Section 6.2.2.

Other endpoints (quality of life, other biomarkers)

Other endpoints are described in Sections 6.3 and 6.4.

Study description

Background summary

See protocol chapter 1 "Background" p. 29-37.

Study objective

Primary objective
The primary objective of the study is to determine the long term safety and tolerability of lucerastat in subjects with Fabry disease (FD).
Secondary objectives
* To evaluate the effect of lucerastat on renal function and cardiac parameters in subjects with FD;
* To evaluate the long-term effect of lucerastat on biomarkers of FD.
Other objectives
Other objectives are described in Section 2.3 and 6 of the protocol.

Study design

This is a prospective, multi-center, open-label, uncontrolled, single-arm, extension Phase 3 study.
Up to approximately 108 adult subjects with FD who completed the 6-month, double-blind treatment period in study ID-069A301 will be enrolled to receive lucerastat for approximately 48 months.
The study comprises the following consecutive periods:
Treatment period: Lasts about 48 months. These 48 months are split into part 1 and part 2. Part 1 begins with the signing of the informed consent form (during visit 1 day 1) and ends at the end of month 24. Then the patient will be asked if he/she wants to participate in part 2 of the study. This starts with the

last visit of part 1, and ends with the EOT visit after a total of 48 months
Post-treatment safety follow-up (FU) period: The FU period is applicable to all subjects. It starts on the day after the last dose of study treatment:
* For female and non-fertile male subjects it includes 1 safety FU telephone call (FU1) taking place approximately 1 month after the last dose of study treatment.
* For fertile male subjects it includes 2 safety FU telephone calls taking place approximately 1 month (FU1) and 3 months (FU2) after the last dose of study treatment.
In addition, any male subject who requires repeated male reproductive safety assessments will return at the time of the FU2 visit to the site and/or qualified local facility to perform those assessments as described in Sections 7.2.4.2.1 and 7.2.4.2.4. Subjects who discontinue study treatment prematurely for any reason should be subsequently treated according to local standard-of-care at the investigator*s discretion.

Intervention

Lucerastat is available for clinical study use in hard gelatin capsules containing 250 mg of lucerastat and inactive excipients (lactose anhydrous and talc).
The starting dose of the study treatment (lucerastat) will be based on the subject*s last available eGFR value, as reported in study ID-069A301 by the central laboratory [see Table 1].
During the study, the dose of the study treatment will be adjusted based on subject*s eGFR (as reported by the central laboratory during scheduled or unscheduled visits). The following rules apply:
a. Subject*s eGFR decreases and crosses the next lower eGFR boundary:
Upon receipt of the eGFR results from the central laboratory, the investigator/delegate will contact the subject to provide instruction to reduce the dose as needed. The date of the contact with the subject and the adjusted dose will be collected in the electronic case report form (eCRF).
b. Subject*s eGFR increases and crosses the next upper eGFR boundary:
Dose adjustment must not be performed until the eGFR increase is confirmed by a second central laboratory test (during scheduled or unscheduled visits performed at least 3 months after the first test). Upon receipt of the second laboratory results confirming the increase and boundary cross, the investigator/delegate will contact the subject to provide instruction to increase the dose as needed. The date of the contact with the subject and the adjusted dose will be collected in the eCRF.
Study treatment must be discontinued if one of the study treatment stopping criteria is met (see Section 5.1.8).

Study burden and risks

The following adverse reactionsside effects have been observed with treatment

with lucerastatseen with lucerastat in 4 or more subjects (out of 80 subjects):
* Abdominal complaints side effects (gastrointestinal complaintsside effects):
-nausea (11 persons, 14%)
* -diarrhoea, soft stools (9 persons, 11%)
-flatulence (gas development in intestines) (7 persons, 9%)
-vomiting (6 people, 8%)
-stomach pain (4 people, 5%)
-dry mouth (4 people, 5%)
* Other side effects were:
-headache (9 persons, 11%)
-itchy skin (6 persons, 8%)
-joint pain (5 persons, 6%)
-back pain (5 persons, 6%)
-vaccination complications (5 persons, 6%)

Blood draws: discomfort when inserting the needle. Taking blood with a needle can cause some pain and bruising
cause spots on the arm.

Contacts

Public
Idorsia Pharmaceuticals Ltd.

Hegenheimermattweg 91
Allschwil 4123
CH
Scientific
Idorsia Pharmaceuticals Ltd.

Hegenheimermattweg 91
Allschwil 4123
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Signed and dated ICF prior to any study-mandated procedure;
2. Subject completed the 6-month, double-blind treatment period in study ID 069A301.

Exclusion criteria

1. Pregnant / planning to become pregnant or lactating subject;
2. Subject considered to be at high risk of developing clinical signs of organ involvement within the time period of the study, as per investigator judgment;
3. Any known factor or disease that might interfere with treatment compliance, study conduct or interpretation of the results as per investigator judgment.,
In addition, the subject must not be enrolled in study ID-069A302 if at any time during study ID-069A301, one of the following criteria was met:
4. Subject*s eGFR per the Chronic Kidney Disease Epidemiology Collaboration creatinine equation < 15 mL/min/1.73 m2;
5. Subject experienced an event of acute kidney injury Common Terminology Criteria for Adverse Event (CTCAE) grade 2 or above;
6. Subject experienced an event of stroke CTCAE grade 3 or above;
7. Subject experienced an event of heart failure leading to in-patient hospitalization or prolongation of ongoing hospitalization.

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):	14-01-2020
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	lucerastat

Ethics review

Approved WMO Date:	19-11-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-04-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	08-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-05-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-03-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2018-002210-12-NL
ClinicalTrials.gov	NCT03425539
CCMO	NL67016.018.18