A phase III double-blind, randomized study to evaluate the long-term efficacy and safety of Oxabact® in patients with primary hyperoxaluria

Published: 10-08-2017
Last updated: 04-01-2025

Primary:- To evaluate the efficacy of Oxabact® following 52 weeks treatment in patients with maintained kidney function but below the lower limit of the normal range (eGFR < 90 ml/min/1.73 m2) and a total plasma oxalate concentration >= 10...

Ethical review	Approved WMO
Status	Completed
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON47491

Source
ToetsingOnline

Brief title
ePHex

Condition

- Metabolic and nutritional disorders congenital
- Inborn errors of metabolism
- Renal disorders (excl nephropathies)

Synonym
Primary Hyperoxaluria

Research involving
Human

Sponsors and support

Primary sponsor: OxThera Intellectual Property AB.
Source(s) of monetary or material Support: Industry;OxThera Intellectual Property AB;Sweden

Intervention

Keyword: Oxabact®, Primary Hyperoxaluria

Outcome measures

Primary outcome

Primary endpoint

* Change from baseline in plasma oxalate concentration after 52 weeks of

treatment (total plasma oxalate concentration).

Secondary outcome

Secondary endpoints:

* Change from baseline in kidney function (eGFR) after 52 weeks of treatment.

* Change from baseline in plasma oxalate concentration (total plasma oxalate

concentration) after 52 weeks of treatment in different subgroups

of patients:

• Patients with a baseline urinary oxalate excretion above and equal to

or below 1.87 mmol/L/24h/1.73 m2 respectively (mean of the two first values

during screening/baseline).

• Patients above or equal toand below 18 years of age.

• Patients with a baseline eGFR above or equal to and below 60

ml/min/1.73m2 respectively (mean of the obtained values during

screening/baseline calculated by the Schwartz/CKD-EPI

equation).

* Change from baseline in kidney function (eGFR) after 52 weeks of treatment in different subgroups of patients:

• Patients with a baseline urinary oxalate excretion above and equal to or below 1.87 mmol/L/24h/1.73 m2 respectively (mean of the two values during screening/baseline).

• Patients above or equal to and below 18 years of age.

• Patients with a baseline eGFR above or equal to and below 60 ml/min/1.73m2 respectively (mean of the obtained values during screening /baseline calculated by the Schwartz/CKD-EPI equation).

* Change from baseline in myocardial function as measured by Speckle Tracking Echocardiography and traditional Echocardiography.

* Change from baseline in score of Quality of Life questionnaire.

* Change from baseline in free plasma oxalate concentration after 52 weeks of treatment.

* Change from baseline in free plasma oxalate concentration after 52 weeks of treatment in different subgroups of patients:

• Patients with a baseline urinary oxalate excretion above and equal to or below 1.87 mmol/L/24h/1.73 m2 respectively (mean of the two first values during screening/baseline).

• Patients above or equal to and below 18 years of age.

• Patients with a baseline eGFR above or equal to and below 60

ml/min/1.73m2 respectively (mean of the obtained values during

screening/baseline calculated by the Schwartz/CKD-EPI equation.

Study description

Background summary

See § 4.1, and § 4.2, and § 4.3 and § 4.5 of the protocol (OC5-DB-02, version 8, 28-Mar-2018).

Study objective

Primary:
- To evaluate the efficacy of Oxabact® following 52 weeks treatment in patients with maintained kidney function but below the lower limit of the normal range (eGFR < 90 ml/min/1.73 m2) and a total plasma oxalate concentration >= 10 µmol/L at baseline.

Secondary:
- To obtain additional safety data from 52 weeks continuous treatment with Oxabact®.

Study design

This is a Phase III, double-blind, randomised international multi-center study.

After the baseline period (at visit 3), 18 eligible patients will be randomised to start on twice daily dosing of Oxabact® or placebo in a 1:1 ratio.

Patients will be stratified in a first step in an attempt to evenly distribute PH type 2/type 3 patients, if the patient is not PH type 2 or PH type 3, the patient will be stratified for baseline urinary oxalate excretion above or below or equal to 1.87 mmol/24h/1.73 m2 (based on the mean of the two values from screening/baseline).

Intervention

The active treatment group receives a capsule with study medication (Oxabact®) twice daily with breakfast and dinner for 52 weeks.

The control group receives a placebo capsule twice daily with breakfast and

dinner for 52 weeks.*

The randomisation is 1:1.

Study burden and risks

See § 4.6 of the protocol (OC5-DB-02, version 8, 28Mar2018) and § 2.4 of the IMPD (version 7, 20Mar2017) and §5 "Summary of data and guidance for the investigator" in the IB (version 7, 26Mar2018).

Patients will be burdened with 10 study visits and all applicable study procedures as well as 4x stool sampling at home and 6x 24 hour urine collection at home. There seems a small risk for serious adverse events.
The patient could benefit from the treatment or future PH patients could benefit from the study results. Patients can be asked to participate in an open-label, follow-up study compassionate use programme when they have finished the study.

Contacts

Public
OxThera Intellectual Property AB.

c /o KLara Papper Box 1062
Stockholm SE-101 39
SE
Scientific
OxThera Intellectual Property AB.

c /o KLara Papper Box 1062
Stockholm SE-101 39
SE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

1. Signed informed consent (as applicable for the age of the subject).
2. A diagnosis of PH (as determined by standard diagnostic methods).
3. eGFR < 90 ml/min/1.73 m2. The Schwartz formula will be used to estimate GFR for children (age below 18), and CKD-EPI formula will be used for adults (age 18 or above).
4. Plasma oxalate concentration >=10 µmol/L in total plasma oxalate.
5. Male or female patients >= 2 years of age.
6. Patients receiving vitamin B6 must be receiving a stable dose for at least 3 months prior to screening and must not change the dose during the study. Patients not receiving vitamin B6 at study entry must be willing to refrain from initiating pyridoxine during study participation.

Exclusion criteria

7. Inability to swallow size 4 capsules.
8. Subjects that have undergone transplantation (solid organ or bone marrow).
9. Patients requiring dialysis or at immediate risk for kidney failure or expected to be in need of dialysis during the study period.
10. The existence of secondary hyperoxaluria, e.g. hyperoxaluria due to bariatric surgery or chronic gastrointestinal diseases such as cystic fibrosis, chronic inflammatory bowel disease and short-bowel syndrome.
11. Use of antibiotics to which O. formigenes is sensitive, including current antibiotic use, or antibiotics use within 14 days of initiating study medication.
12. Current treatment with a separate ascorbic acid preparation.
13. Pregnant women (or women who are planning to become pregnant) or lactating women.
14. Women of childbearing potential who are not using adequate contraceptive precautions. Please see section 7.3 regarding requirements for contraception.
15. Presence of a medical condition that the Investigator considers likely to make the subject susceptible to adverse effect of study treatment or unable to follow study procedures or any condition that is likely to interfere with the study drug mechanism of action (such as abnormal GI function).
16. Participation in any interventional study of another investigational product, biologic, device, or other agent within 60 days prior to the first dose of OC5 or not willing to forego other forms of investigational treatment during this study.

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:	Completed
Start date (anticipated):	09-01-2018
Enrollment:	2
Type:	Actual

Ethics review

Approved WMO Date:	10-08-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-10-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-05-2018

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-05-2018
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	EUCTR2017-000684-33-NL
ClinicalTrials.gov	NCT03116685onClinicalTrials.Gov
CCMO	NL60845.018.17

Study results

Date completed:	01-10-2019
Results posted:	20-09-2021

First publication
30-08-2021