A Phase 2/3, double-blind, randomized, placebo-controlled, multi-center study to evaluate the efficacy and safety of OxabactTM to reduce urinary oxalate in subjects with Primary Hyperoxaluria.

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Primary Objective:To evaluate the efficacy of OxabactTM to reduce urinary oxalate levels (molar oxalate to creatinine ratio) from Baseline to Week 24 in subjects with Primary Hyperoxaluria (PH).Secondary Objectives- To evaluate the safety of...

Ethical review	Approved WMO
Status	Pending
Health condition type	Inborn errors of metabolism
Study type	Interventional

Summary

ID

NL-OMON32604

Source
ToetsingOnline

Brief title
Phase 2/3 Oxabact Study

Condition

- Inborn errors of metabolism
- Renal disorders (excl nephropathies)

Synonym
Primary Hyperoxaluria (PH)

Research involving
Human

Sponsors and support

Primary sponsor: OxThera IP AB
Source(s) of monetary or material Support: OxThera IP AB

Intervention

Keyword: Oxabact TM, Primary Hyperoxaluria (PH), urinary oxalate

Outcome measures

Primary outcome

Primary endpoint:

- Percentage change in urinary oxalate levels (expressed as molar oxalate to creatinine ratio) from Baseline to Week 24.

Secondary outcome

Secondary endpoints:

- Percentage change in urinary oxalate levels (expressed as molar oxalate to creatinine ratio) from Baseline to Week 8

- Percentage change in urinary oxalate levels (expressed as molar oxalate to creatinine ratio) from Baseline to Week 24 in subsets of subjects

- Percentage of subjects who have *20% reduction from Baseline urinary oxalate at Week 24.

- Percentage change in plasma oxalate levels.

- Frequency of Stone Events (i.e. nephrolithiasis or markers thereof)

- Correlation between percentage change in plasma oxalate levels and percentage change in urinary oxalate levels, from Baseline to Week 24

- Frequency of adverse events (AEs) and abnormal lab results.

Study description

Background summary

Primary Hyperoxaluria is a metabolic disorder, characterized by excess endogenous oxalate synthesis and excretion in the urine. Raised oxalate excretion leads to calcifications in the kidneys. Primary Hyperoxaluria is an inborn error of metabolism, and symptoms occur as early as the first month of age. Calcifications in the urinary tract can lead to decreased kidney function, and 50% of patients need dialysis by 25 years.

The use of OxabactTM is supposed to lead to increased degradation of oxalate in the intestine. This generates a suitable trans-epithelial gradient to promote the removal of endogenously produced plasma oxalate by enteric elimination. Animal studies have shown that enteric elimination of oxalate occurs both by the passive flow of oxalate across the gut epithelia in response to a concentration gradient, as well as by its active flux mediated by specific transporters. Enteric elimination is expected to reduce the levels of urinary oxalate in both PH1 and PH2 patient populations.

Previous similar phase 2/3 study has shown that the collected 24-hour urine was not always effective for evaluating the study objectives (incorrectly performed method) and that the capsules did not release all the active ingredients as was predicted per study design.
Therefore this phase 2/3 study will be executed again with more strict coherence and more precise guidelines in the study protocol for the collection and processing of the urine and with a new (powder shape) formula.

Study objective

Primary Objective:
To evaluate the efficacy of OxabactTM to reduce urinary oxalate levels (molar oxalate to creatinine ratio) from Baseline to Week 24 in subjects with Primary Hyperoxaluria (PH).

Secondary Objectives
- To evaluate the safety of OxabactTM administered for 24 weeks in subjects with Primary Hyperoxaluria (PH).
- To evaluate the efficacy of OxabactTM from Baseline to Week 24 as regards:
o reduction in urinary oxalate levels in subsets of subjects, based on disease characteristics and age.
o percentage of subjects who have *20% reduction in urinary oxalate levels.
o reduction in plasma oxalate levels and any correlation to reduction in urinary oxalate levels.
o frequency of Stone Events.

- To evaluate the efficacy of OxabactTM from Baseline to Week 8.

Study design

This study is a double-blind, randomized, placebo-controlled, multi-center, international study to evaluate the efficacy and safety of OxabactTM in the reduction of urinary oxalate in subjects with PH. Following screening, 30-35 eligible subjects will be randomized 1:1 to receive OxabactTM or placebo twice daily for 24 weeks. The randomization will be stratified by GFR.

Urinary oxalate levels will be measured during the baseline and in weeks 8, 16 and 24.
Plasma oxalate levels will be measured during baseline, week 8 and week 24.
Routine lab assessments will be measured during baseline, week 8 and week 24.

All patients in the double-blind study will be monitored for safety and concomitant medication usage throughout the study period, with the last assessment of safety 4 weeks post-treatment.

Intervention

One group receives during 24 weeks twice a daily the study drug. The study drug is supplied as two separate sachets, one containing lyophilized O. formigenes (NLT 107 CFU) and the other containing a buffer powder (1.5 g sodium bicarbonate and 0.5 g citric acid), to be mixed and reconstituted prior to administration.
The other group receives during 24 weeks twice daily a placebo and the buffer (1.5 g sodium bicarbonate and 0.5 g citric acid).
The randomisation is 1:1.
Dosing will be on fasted stomach 30-60 minutes before breakfast and dinner, i.e. twice daily.

Study burden and risks

The bacterium in this drug has previously been given to about 60 people without any major side effects. There may be side effects that are unknown at this time. Theu can get stomach problems such as abdominal pain, nausea, vomiting, diarrhea, constipation and flatulence. There is also a risk of the bacteria getting in the blood and causing an infection. So far there have been no reports of such infections caused by the bacterium.

Some of the commonly observed side effects noted with the acid suppressing medication are diarrhea, headache, abdominal pain, nausea and somnolence. There may also be a slightly increased risk for stomach infection.

De flessen waarin de urine wordt verzameld bevatten een gesloten buis, waarin

het bijtende zoutzuur zit. Deze stof zorgt ervoor dat de urine een aantal dagen kan worden bewaard. Het grootste risico van deze stof voor mensen is schade aan de ogen, aan de huid en aan onderhuids weefsel. Als de bijtende stof wordt ingeademd of ingeslikt kan schade ontstaan aan de ademhalingsorganen en aan het maag-darmkanaal. Vanwege de veiligheid mag het zuur uit het buisje pas in de fles worden gedaan, nadat de eerste urine erin is gegoten. De flessen die bij dit onderzoek worden gebruikt zijn speciaal ontworpen voor het veilig verzamelen van 24-uurs-urine .
Taking blood from your arm may cause discomfort and can leave a bruise.
Collecting urine may cause you some discomfort or embarrassment, but it will be done in private.
Deze risico's worden doorgaands bij medische onderzoeken als gering beschouwd.

Contacts

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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

De deelnemers wordt volledige informatie gegeven1. Signed informed consent (as applicable for the age of the subject)
2. Male or female subjects * 2 years of age
3. A diagnosis of PH I or PH II (as determined by standard diagnosis methods)
4. A mean urinary oxalate excretion of > 1.0 mmol/1.73m2/day at collections performed during screening.
5. Renal function defined as an estimated GFR * 40 ml/min normalized to 1.73m2 body surface area, or a creatinine clearance of * 40 ml/min normalized to 1.73m2 body surface area.
6. Subjects receiving pyridoxine must be receiving a stable dose for at least 3 months prior to entry into the study and must remain on the stable dose during the study. Subjects not receiving pyridoxine at study entry must be willing to refrain from initiating pyridoxine during study participation.

Exclusion criteria

1. Inability to collect two complete 24-hour urine samples. Each urine collection will be evaluated for completeness based on the urine acceptance criteria outlined in section 11.1.
2. Subjects diagnosed as PH I who are pyridoxine naïve.
3. Subjects that have undergone transplantation (solid organ or bone marrow).
4. The existence of secondary hyperoxaluria, e.g. chronic gastrointestinal diseases such as cystic fibrosis, chronic inflammatory bowel disease and short-bowel syndrome.
5. Current systemic (oral, IM, IV) antibiotic use or received systemic antibiotics within 14 days of study enrolment.
6. History of a recurrent infection requiring >2 courses of systemic antibiotics in the past 6 months, or chronic antimicrobial suppression.
7. Subjects who require immune suppressive therapy (including prednisone > 10mg daily for more than 2 weeks).
8. Current treatment with a separate ascorbic acid preparation. Ascorbic acid up to 250mg/day as a component of a multivitamin formulation is not excluded.
9. Known hypersensitivity to esomeprazol (or any of the other ingredients of this medicine), or to any other proton pump inhibitor medicine. (Nexium contraindication)
10. Concomitant treatment with atazanavir. (Nexium contraindication)
11. Pregnancy.
12. Women of child-bearing potential who are not using adequate contraceptive precautions. Sexually active females, unless surgically sterile or at least 2 years post-menopausal, must be using a highly effective contraception (including oral, transdermal, injectable, or implanted contraceptives, IUD, abstinence, use of a condom by the sexual partner or sterile sexual partner) for 30 days prior to the first dose of OxabactTM and must agree to continue using such precautions during the clinical study.

13. Presence of a medical condition that the Principal Investigator considers likely to make the subject susceptible to adverse effect of study treatment or unable to follow study procedures. Note: Subjects from correctional facilities or asylums and subjects who are mentally handicapped are not to be included in the study.
14. Participation in any study of an investigational product, biologic, device, or other agent within 30 days prior to randomization 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:	Pending
Start date (anticipated):	01-11-2009
Enrollment:	6
Type:	Anticipated

Ethics review

Approved WMO

Date:	18-11-2009
Application type:	First submission
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	EUCTR2009-015817-31-NL
CCMO	NL29887.018.09