A Phase 2/3, Double-Blind, Randomized, Placebo-Controlled, Multi-center, International Study to Evaluate the Efficacy and Safety of Oxabact(TM) to Reduce Urinary Oxalate in Subjects with Primary Hyperoxaluria.

Published: 18-09-2007
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Primary Objective:To evaluate the efficacy of Oxabact TM to reduce urinary oxalate levels from Baseline to Week 24 in subjects with Primary Hyperoxaluria (PH).Secondary Objectives:To evaluate:* Percentage of subjects who have 20% or greater...

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

Summary

ID

NL-OMON31288

Source
ToetsingOnline

Brief title
Study to see if Oxabact reduces urinary oxalate, the Phoenix study

Condition

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

Synonym
Primary Hyperoxaluria (PH)

Research involving
Human

Sponsors and support

Primary sponsor: OxThera Inc.
Source(s) of monetary or material Support: Bedrijf: OxThera Inc.

Intervention

Keyword: OxabactTM, Primary Hyperoxaluria (HP), urinary oxalate

Outcome measures

Primary outcome

* Percentage change in urinary oxalate (expressed as mmole/1.73m2 /day) from Baseline to Week 24 (Day 168).

Secondary outcome

* Percentage of subjects who are responders at Week 24 where response is defined as a 20% or greater reduction from Baseline urinary oxalate to Week 24
* Percentage change in urinary oxalate (expressed as molar oxalate to creatinine ratio) from Baseline to Week 24 (Day 168)
* Percentage change in urinary oxalate (expressed as mmole/1.73m2/day and as molar oxalate to creatinine ratio) from Baseline to Week 12 (Day 84)
* Percentage change in urinary oxalate (expressed as mmole/1.73m2/day and as molar oxalate to creatinine ratio) from Baseline to Average of Weeks 12 and 24
* Reduction of urinary calcium oxalate super saturation from Baseline to Week 24
* Reduction of urinary oxalate levels from Baseline to Week 24 in 2 subsets of subjects defined by GFR of > 80 mL/min/1.73m2 (normal renal function) and < 80 mL/min/1.73m2 (mild to moderate reduction in renal function).
* Plasma oxalate levels at Weeks 12 and 24 and correlation with urinary oxalate

at these time points.

* Frequency of AEs and SAEs; laboratory safety data.

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. Calcification 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.

Study objective

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

Secondary Objectives:
To evaluate:
* Percentage of subjects who have 20% or greater reduction from Baseline urinary oxalate at Week 24
* The effect of Oxabact TM on plasma oxalate levels
* The effect of Oxabact TM on reduction of calcium-oxalate supersaturation
* The safety of Oxabact TM administered for 24 weeks in subjects with PH

Study design

This study is a double-blind, placebo-controlled, multi-center, international, clinical study to evaluate the safety and efficacy of OxabactTM in the reduction of urinary oxalate levels in subjects with PH. Eligible subjects will be randomized (1:1) to receive either:
* NLT 10exp7 CFU of OxabactTM orally, twice daily with meals

* Placebo orally, twice daily with meals

Subjects will receive study drug for 24 weeks. Subjects who complete study treatment will be eligible to participate in an extension study where all subjects will receive open label OxabactTM.

Urinary oxalate will be measured at Baseline and at Weeks 4, 8, 12, 18, and 24. Plasma oxalate levels will be measured at Baseline and at Weeks 12 and 24. Laboratory safety assessments will be performed at Weeks 12 and 24.

All subjects in the randomized double-blind controlled study will be monitored for safety throughout the study period

Intervention

One group receives during 24 weeks twice daily a capsule with Lyophilized O. formigenes for oral administration. Strength: NLT 10exp7CFU/capsule
One group receives during 24 weeks twice daily a capsule withplacebo for oral administration.
Randomisation is 1:1.

Study burden and risks

The treatment may harm the unborn child. Therefore, pregnancy is ruled out at the start of the study. Male participants must be advise not to be enrolled in the study if their partner wishes to become pregnant during the study time.

There may be side effects that are unknown at this time, such as stomach problems, diarrhea, bloating, or flatus. Any stomach problems that are currently present may worsen. The bacteria present in Oxabact* may cause infection in blood. However, no such infections have been reported by the use of Oxabact* to date.

Taking blood from the arm may cause discomfort and can leave a bruise. The consequences related to the drawing of blood are usually considered to be of minimal discomfort.

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

1. The subject (or legally acceptable representative) must give written informed consent (and assent for subjects * 12 years). For subjects less than 18 years of age, parent or guardian will provide informed consent and the subject will provide witnessed verbal assent
2. Male or female subjects > 5 years of age
3. Urinary oxalate excretion of > 1.0 mmol/1.73m2/day at Baseline
4. Documentation of diagnosis of PH I or PH II by any one of the following:
a. Liver biopsy confirmation of deficient liver specific peroxisomal alanine-glyoxylate aminotransferase, (AGT) or mislocalization of AGT from peroxisomes to mitochondria (PH I) or deficient glyoxylate reductase/hydroxypyruvate reductase (GR/HPR) activity (PH II)
b. Homozygosity or compound heterozygosity for a known mutation in the causative genes for PH I and PH II
c. Increased glycolate excretion for PH I or increased L-glycerate excretion for PH II
d. Family history in a sibling with a definitive diagnosis of PH
5. Subjects receiving pyridoxine must be receiving a stable dose for at least 3 months prior to entry in to 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.

6. Renal function defined as an estimated GFR * 50 ml/min normalized to 1.73m2 body surface area.

Exclusion criteria

1. Pregnant, lactating, or actively menstruating women and women of child-bearing potential who are not using adequate contraceptive precautions. Sexually active females, unless surgically sterile or at least 1 year post-menopausal, must be using a medically acceptable method of contraception (including oral, transdermal, injectable, or implanted contraceptives, IUD, female condom, diaphragm with spermicide, cervical cap, 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.
2. Positive serum pregnancy test
3. 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
4. Subjects on hemodialysis or peritoneal dialysis
5. Subjects that have undergone transplantation (solid organ or bone marrow)
6. Chronic gastrointestinal disease associated with enteric hyperoxaluria, e.g., history of inflammatory bowel disease, colostomy
7. Current systemic (oral, IM, IV) antibiotic use or received systemic antibiotics within 14 days of study enrolment
8. History of chronic, recurrent infections requiring >2 courses of antibiotics in the past 6 months
9. History of malignancy except for basal or squamous cell skin cancer that has been excised
10. Unable to collect 24-hour urine samples or follow other study procedures
11. Subjects who cannot swallow a size 2 capsule
12. 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
13. Subjects who require immune suppressive therapy (including prednisone of > 10mg daily for more than 2 weeks).

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):	15-09-2007
Enrollment:	7
Type:	Anticipated

Ethics review

Approved WMO Date:	18-09-2007
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-01-2008
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	EUCTR2007-002328-14-NL
CCMO	NL18410.018.07