Cysteamine bitartrate PO-001

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26870

Source
NTR

Brief title
CHDR1516

Health condition

Cystinosis

Sponsors and support

Primary sponsor: Patient One
Source(s) of monetary or material Support: Sponsor

Intervention

Outcome measures

Primary outcome

Safety and tolerability endpoints
Treatment-emergent (serious) adverse events ((S)AEs) will be documented, regarding incidence, nature and severity from the time the subject signs the consent until the follow-up visit (End of Study Visit). The following endpoints will be determined at the time points indicated in the Schedule of Assessments.

Clinical laboratory tests

o Haematology
o Chemistry
o Urinalysis

Vital signs
o Pulse Rate (bpm)
o Systolic blood pressure (mmHg)
o Diastolic blood pressure (mmHg)
o Temperature

ECG
o Heart Rate (HR) (bpm), PR, QRS, QT, QTcB, QTcF

Abdominal Visual Analog Scales (VAS) to assess:
o Abdominal fullness (completely empty-intolerably full)
o Nausea (no nausea-intolerance nausea)
o Epigastric pain (no pain-inbearable pain)
o Hunger (not at all-intolerable)
o Desire to eat (very weak-intolerably strong)

Pharmacokinetic endpoints
The following endpoints will be determined for the study drug at time points indicated in the Schedule of Assessments. They will be derived by non-compartmental analysis of the plasma concentration-time data:
• Plasma maximum cysteamine concentration (Cmax)
• The time to reach maximum plasma concentration (Tmax)
• The area under the plasma concentration-time curve from zero to infinity (AUC0-inf)
• The area under the plasma concentration-time curve from zero to t of the last measured concentration above the limit of
• quantification (AUC0-last)
• The terminal disposition rate constant (λz) with the respective Half-life (T1/2)
• Clearance (CL/F) apparent oral clearance calculated from Dose/AUC0-inf)

Secondary outcome

N.A.

Study description

Background summary

Cystinosis is a rare inherited autosomal recessive disease caused by mutations in the CTNS gene on chromosome 17p13 which leads to intralysosomal cystine accumulation in cells throughout the body. It occurs in approximately 1 in 100,000–200,000 live births. Children

generally present between the age of 6–12 months with polyuria, polydipsia and failure to thrive due to generalized proximal tubular damage, called renal Fanconi syndrome. Cystinosis is the most prevalent cause of congenital renal Fanconi syndrome.
In the Netherlands patients with cystinosis are treated with Cystagon®, cysteamine bitartrate. Cysteamine reduces cystine accumulation in cells such as leukocytes, muscle and liver cells and, when treatment is started early, it delays the development of renal failure. Cysteamine reacts with cystine to form mixed disulfide cysteinecysteamine, which is then transported out of the lysosomes by an intact lycine and cysteine transport system. The primary endpoint of cysteamine treatment is to drop the white blood cells cystine levels until a steady state has reached below 1 nmol hemicystine/mg protein.
A downside of this medicament is the need of a strict regimen of intake every six hours in order to work optimally. In order to reach the sufficient concentration of cysteamine, patients furthermore have to take a high number of relatively large capsules. The strict regimen and the size of the capsules result in poor patient compliance. Secondly Cystagon® causes an unpleasant odour of patients. This has a negative impact on the social life of the patients, which likewise results in a poor patient compliance.

In this study, the pharmacokinetic properties of a new sustained-release cysteamine bitartrate (PO-001) preparation will be assessed in healthy volunteers in comparison with commercialized comparator products.

Study objective

Patient One aims to develop, produce and commercialize a sustained-release cysteamine bitartrate (PO-001) reparation for the treatment of cystinosis. The product is encapsulated with an improved slow-release coating to decrease dosing frequency. In addition, PO-001 is expected to have a lower Cmax, which may lead to less halitosis. It is expected that the improved pharmacokinetic profile would contribute to less disruptance of daily routines of patients and improves adherence. In this clinical study the pharmacokinetic properties of the new cysteamine bitartrate will be assessed in healthy volunteers in comparison with commercialized comparator products

Study design

- Screening
- Three study visits . Window between study visits is at least 7 days
- Follow-up: 7-21 days after the third study day

Intervention

PO-001, comparator drugs

Contacts

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Eligibility criteria

Inclusion criteria

1. Healthy male, and 18-55 years of age (inclusive);
2. Body Mass Index between 18 and 27 kg/m2 (inclusive) and body weight minimal 50 kg (inclusive);
3. Ability to read and understand the written consent form, complete study-related procedures, and communicate with the study staff;
4. All males must practice effective contraception during the study and be willing and able to continue contraception for at least 90 days after their last dose of study treatment;
5. Subjects must be able to swallow the drug-administered capsules with the capsule intact;
6. Willingness to comply with study restrictions and requirements.

Exclusion criteria

1. Clinically relevant abnormal history or presence of physical and mental health as determined by medical history taking and physical examinations obtained during the screening visit and/or at the start of the first study day (as judged by the investigator);
2. Clinically relevant abnormal laboratory results, ECG and vital signs at screening and/or at the start of the first study day (as judged by the investigator);
3. Acute disease state (e.g. nausea, vomiting, fever, or diarrhea) within 7 days before the first study day;
4. Abnormal renal function (eGFR (MDRD) < 60 mL/min/1.73m2);
5. Positive test for hepatitis B, C or HIV at screening;
6. History of alcoholism or substance abuse within three years prior to screening or current use of more than 21 units alcohol per week or drug abuse;
7. Subjects using, on average, more than 3 units of alcohol per day, and unable to refrain from alcohol use from 24 hours prior to screening, each study day and whilst in study unit;
8. Subjects smoking, on average, more than 5 cigarettes per day, and unable to refrain from smoking during the study days;

9. Positive drug- (i.e. positive for cocaine, opioids, amphetamines, opiates, cannabinoids, benzodiazepines, and/or methadone) or alcohol test at screening and/or first study day;
10. Inability to refrain from the use of concomitant (prescription and over the counter) medication which, in the opinion of the investigator, interferes with their ability to participate in the trial, from one week (or less than 5 half-lives (whichever is longer) prior to the first the first study day until the last study day;
11. Use of any dietary supplements within 7 days of study drug administration, or less than 5 half-lives (whichever is longer). Exceptions can be made as judged by the investigator;
12. A history of severe allergies, or has had an anaphylactic reaction or significant intolerability (hypersensitivity) to prescription or non-prescription drugs or food;
13. Hypersensitive (allergic) to cysteamine (mercaptamine) or any of the other ingredients, e.g. to penicillamine;
14. History or clinical evidence of any disease and/or existence of any surgical or medical condition which might interfere with the absorption, distribution, metabolism or excretion of the study drug;
15. Participation in an investigational drug study within 90 days prior to screening or more than 4 times a year;
16. Loss or donation of blood over 500 mL within 90 days prior to screening or intention to donate blood or blood products during the study;
17. Inadequate venous accessibility as judged by the physician or nurse;
18. Any known factor, condition, or disease or any reason that might interfere in the opinion of the medical responsible person with the well-being of the subject, treatment compliance, study conduct or interpretation of the results.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2019
Enrollment:	9
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion
Date: 18-06-2019
Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 48026
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL7809
CCMO	NL67638.056.18
OMON	NL-OMON48026

Study results