A Randomized, Crossover, Pharmacokinetic and Pharmacodynamic Study to Determine the Safety and Efficacy of Cysteamine Bitartrate Delayed-release Capsules (RP103), Compared to Cystagon® in Patients with Nephropathic Cystinosis

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Metabolism disorders NEC
Study type	Interventional

Summary

ID

NL-OMON34074

Source
ToetsingOnline

Brief title
RP103-03

Condition

- Metabolism disorders NEC

Synonym
metabolic disorder in which the transport of cystine out of the lysosomes is abnormal,

Nephropathic cystinosis

Research involving
Human

Sponsors and support

Primary sponsor: Raptor Pharmaceuticals Europe BV
Source(s) of monetary or material Support: door de opdrachtgever

Intervention

Keyword: crossover study, Cystagon®, Cysteamine Bitartrate (INN : mercaptamine bitartrate) Delayed-release Capsules, Nephropathic Cystinosis, Randomized

Outcome measures

Primary outcome

To demonstrate that at steady-state, patients receiving every 6 hour (Q6H)

treatment of Cystagon® can maintain a comparable depletion of white blood cell

(WBC) cystine levels after receiving every 12 hour (Q12H) treatment regimen of

RP103.

Secondary outcome

To assess safety and tolerability of RP103.

To assess the steady-state pharmacokinetics (PK) and pharmacodynamics (PD) of

RP103 compared to Cystagon®.

Study description

Background summary

Cysteamine bitartrate is currently marketed for treatment of nephropathic cystinosis under the trade name Cystagon® and is available for oral administration as immediate-release 50 mg or 150 mg capsules with a dosing interval of Q6H. Preliminary studies in healthy volunteers using a delayed-release formulation have shown that an extemporaneously prepared enteric-coated cysteamine product (i.e., EC-Cystagon, enteric-coated Cystagon®

Capsules) had a mean maximum concentration (Cmax) and area under the curve (AUC) similar to Cystagon®. Compared to the study period with Cystagon® which required dosing Q6H, the EC-Cystagon was taken only Q12H, eliminating the problem of disrupting sleep with a Q6H dosing schedule while still maintaining adequate reduction of WBC cystine levels. Raptor Pharmaceuticals (Raptor) is developing Cysteamine Bitartrate Delayed-release Capsules (RP103), 75 mg and 25 mg. Cysteamine Bitartrate Delayed-release Capsules (RP103) are enteric-coated beads that are further encapsulated and intended to be administered every 12 hours (Q12H).

Study objective

The objective of this pivotal study is to assess the PK and PD as well as safety and tolerability of RP103 compared to Cystagon® in patients with nephropathic cystinosis. Results of this Phase 3 study will be used to support the registration application for this new formulation of cysteamine bitartrate. Primary Objective: to demonstrate that patients on a stable Q6H regimen of Cystagon® can be switched to a Q12H regimen of RP103 and maintain comparable depletion of white blood cell (WBC) cystine levels after receiving Q12H treatment regimen of RP103. Secondary Objectives : to assess safety and tolerability of RP103; and to assess the steady-state pharmacokinetics and pharmacodynamics of RP103 compared to Cystagon®.

Study design

This is a randomized, crossover, out-patient study of the safety, tolerability, pharmacokinetics and pharmacodynamics of Cystagon® compared to RP103 in pediatric and adult patients with nephropathic cystinosis.

Intervention

This is a randomized, crossover treatment study. At the end of Run-in and prior to the start of Period 1, qualifying patients will be randomized to initially receive either Cystagon® or RP103. For Period 2, patients will crossover to receive the opposite treatment.

Study burden and risks

10-11 weeks of study participation, including up to 20 study visits; blood withdrawal (total of 125.5 to 127.5mL of blood) for clinical laboratory tests and PK/PD analyses, ECG examinations, physical examinations, vital signs, completion of at-home medications diary, completion of Quality of Life questionnaires, and treatment with Cystagon® and RP103.

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

Male or female subject with a documented diagnosis of nephropathic cystinosis.
Subject must be on a stable dose of Cystagon® sufficient to maintain their white blood cell (WBC) cystine level at <= 1.0 nmol/half-cystine/mg protein.
Subject must be able to swallow their typically administered Cystagon® capsule with the capsule intact.
Within the last 6 months, no clinically significant change from normal in liver function tests [i.e., 1.5 times ULN for ALT and AST, and/or 1.5 times ULN for total bilirubin] and renal function
[i.e., estimated GFR (corrected for body surface area)] at Screening as determined by the

Investigator.
Subject must have an estimated GFR (corrected for body surface area) > 30 mL/minute/1.73 m2.
Sexually active female subjects of childbearing potential (i.e., not surgically sterile [tubal ligation, hysterectomy, or bilateral oophorectomy] or at least 2 years naturally postmenopausal)
must agree to utilize the same acceptable form of contraception from Screening through completion of the study. The acceptable forms of contraception for this study include hormonal
contraceptives (oral, implant, transdermal patch, or injection) at a stable dose for at least 3 months prior to Screening, barrier (spermicidal condom, diaphragm with spermicide), IUD, or a
partner who has been vasectomized for at least 6 months. For pre-pubescent children, a documented attestation of abstinence from their parent or guardian will be acceptable.
Subject must be willing and able to comply with the study restrictions and requirements.
Subject or their parent or guardian must provide written informed consent and assent (where applicable) prior to participation in the study.

Exclusion criteria

Subject*s age < 6 years old or subjects weight < 21 kg.
Subjects with current history of the following conditions or any other health issues that make it, in the opinion of the Investigator, unsafe for them to participate:
- Inflammatory bowel disease (if currently active) or prior resection of small intestine;
- Heart disease (e.g., myocardial infarction, heart failure, unstable arrhythmias, or poorly controlled hypertension) 90 days prior to Screening;
- Active bleeding disorder 90 days prior to Screening;
- History of malignant disease within the last 2 years.
Subject with a hemoglobin level of < 10 g/dL at Screening or, in the opinion of the Investigator, a hemoglobin level that would make it unsafe for the subject to participate.
Subjects receiving any form of cysteamine medication through a gastric tube.
Subjects who are receiving maintenance dialysis or who have had a kidney transplant.
Subjects who are on an active kidney transplant list or who are planning to receive a kidney transplant within 3 months of Screening.
Subjects with known hypersensitivity to cysteamine and penicillamine.
Female subjects who are nursing, planning a pregnancy, known or suspected to be pregnant, or with a positive serum pregnancy screen.
Subjects who have a made a blood donation within 30 days of Screening.
Subjects who, in the opinion of the Investigator, are not able or willing to comply with the protocol.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-11-2010
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cystagon®
Generic name:	INN : mercaptamine bitartrate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	RP103
Generic name:	Cysteamine Bitartrate (INN mercaptamine bitartrate) Delayed-release Capsules

Ethics review

Approved WMO Date:	22-07-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-10-2010

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-10-2010
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-12-2010
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2009-017882-42-NL
ClinicalTrials.gov	NCT01000961
CCMO	NL32583.091.10