A Long-Term, Open-Label, Safety and Efficacy Study of Cysteamine Bitartrate Delayed-release Capsules (RP103) in Patients with Cystinosis.

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The objective of this pivotal study is to assess the long-term safety, tolerability, pharmacokinetics and pharmacodynamics of RP103 in pediatric and adult patients with nephropathic cystinosis. Results of this Phase 3 study will be used to support...

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

Summary

ID

NL-OMON44053

Source
ToetsingOnline

Brief title
RP103-04

Condition

- Metabolism disorders NEC

Synonym
Nephropathic cystinosis; metabolic disorder in which the transport of cystine out of the lysosomes is abnormal

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cysteamine Bitartrate (INN : mercaptamine bitartrate) Delayed-release Capsules, Long-term, Nephropathic Cystinosis, Open-label

Outcome measures

Primary outcome

To assess safety and tolerability of RP103 using safety data collected during

the study (adverse events, physical exams, vital signs, VAS swallowing

assessments, ECG and clinical laboratory testing).

Secondary outcome

To assess the steady-state pharmacokinetics (PK) of RP103 using trough plasma

cysteamine concentrations 0.5 hours post-dose and to assess the steady-state

pharmacodynamics (PD) of RP103 using WBC cystine content meastured 0.5 hours

post-dose.

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 long-term safety, tolerability, pharmacokinetics and pharmacodynamics of RP103 in pediatric and adult 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 assess safety and tolerability of long-term repeat dosing of RP103 in patients with nephropathic cystinosis.

Secondary Objectives : to assess the steady-state pharmacokinetics (PK) and pharmacodynamics (PD) of RP103.

To assess the long-term quality of life using either PedsQL* and SF-36® instruments.

Study design

This is a long-term, open-label study of the safety, tolerability and steady-state pharmacokinetics and pharmacodynamics of RP103 in pediatric and adult patients with nephropathic cystinosis.

Intervention

This is an open-label study during which patients will receive RP103 for up to 8 years.

Study burden and risks

Up to 5 years of study participation, including up to 25 study visits; blood withdrawal (total max. of 290 mL 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 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 and female subjects must completed the last visit of Study RP103-03 and be willing to continue on RP103 treatment.;Or for patients who did not complete the RP103-03 study:;Male or female subject with a documented diagnosis of nephropathic cystinosis.
Subject must be on a stable dose of Cystagon® at least 21 days prior to Screening.
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

Patients enrolled in the previous Study RP103-03 who did not complete their last scheduled Study visit or who do not wish to continue on treatment with RP103.;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 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
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-01-2011
Enrollment:	5
Type:	Actual

Medical products/devices used

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:	14-12-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-04-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-06-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	10-11-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-11-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-02-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-04-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-09-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-01-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-07-2016
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	EUCTR2010-018365-34-NL
ClinicalTrials.gov	NCT01197378
CCMO	NL33066.091.10