A Phase 1 Study of DCR-PH1 in Patients with Primary Hyperoxaluria Type 1 (PH1)

Published: 11-12-2015
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Primary Objective:- To determine the safety and tolerability of DCR-PH1 administered via intravenous (IV) infusion to patients with PH1.Secondary Objective:- To study the pharmacokinetics (PK) of DCR-PH1- To study the pharmacodynamics (PD) effects...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON44062

Source
ToetsingOnline

Brief title
DICERNA: DCR-PH1-101

Condition

- Other condition

Synonym
PH1

Health condition

Autosomal recessive disorder

Research involving
Human

Sponsors and support

Primary sponsor: Dicerna Pharmaceuticals, Inc
Source(s) of monetary or material Support: sponsor van het onderzoek (Dicerna)

Intervention

Keyword: DCR-PH1, Patient study, Phase 1, Primary Hyperoxaluria type I

Outcome measures

Primary outcome

Safety and tolerability as determined by number of subjects with adverse events

Secondary outcome

1) Determination of pharmacokinetics parameters

2) Change in plasma levels from baseline (BL) to each time point of oxalate and

glycolate

3) Change in urine levels from baseline (BL) of oxalate, oxalate to creatinine

ratio and glycolate

Study description

Background summary

DCR-PH1 is intended to minimize the excessive production of oxalate in patients diagnosed with PH1 by blocking the production of glyoxylate, a key precursor for the production of oxalate in the liver.

The SAD (Part A) portion of Study DCR-PH1 is designed to identify doses of DCR-PH1 that are safe, tolerated and suitable for subsequent clinical assessment in the MAD (Part B) portion of the study. Once the Part A (SAD portion) maximum tolerated dose (MTD) has been established, all available clinical and nonclinical data will be summarized and submitted to regulatory authorities and ethics committees, together with a protocol amendment to support dosing in Part B (MAD portion) of the study.

The MAD portion of the study will provide additional safety and tolerability

information as well as better characterization of the pharmacokinetic (PK) and PD effects of multiple DCR-PH1 doses.

Study objective

Primary Objective:
- To determine the safety and tolerability of DCR-PH1 administered via intravenous (IV) infusion to patients with PH1.

Secondary Objective:
- To study the pharmacokinetics (PK) of DCR-PH1
- To study the pharmacodynamics (PD) effects of DCR-PH1 including, but not limited to changes in plasma and urine oxalate and glycolate levels

Additional secondary objectives for Part B are:
- To study clinical and radiological changes related to hyperoxaluria during treatment with DCR-PH1
- To study the quality of life (QOL) in patients during treatment with DCR-PH1

Study design

This is a single-arm, open-label, dose escalation study of DCR-PH1 designed to define a safe and tolerable dose of DCR-PH1 for patients with PH1.

Intervention

For Part A (SAD):

Dose Level (Cohort) Dose (mg/kg) Percent increase
1
0.05 -
2 0.1
100%
3 0.2
100%
4 0.4
100%
5
0.7 75%
6
1.0 50%

Study burden and risks

DCR-PH1 has not been studied in humans. Since information on side effects has

been obtained only from studies in animals, little is known about the side effects it may cause in humans. There have, however, been studies in humans of drugs that are similar to DCR-PH1 (because they have the same type of *coating* around the active part of the drug), and the side effects from those studies are listed in the Patient Information Leaflet.

There are certain risks and discomforts that may be associated with this research:
There is a slight risk of side effects from the routine blood tests that will be required throughout the study. There could be pain, swelling, and/or bruising at the site where you get your blood drawn, as well as possible inflammation of the vein or an infection at this site.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Diagnosis of PH1, confirmed by genotyping for homozygosity or compound heterozygosity in the AGXT gene (historically available genotype information is acceptable for study eligibility).
- 24-hour urine oxalate excretion * 0.7 mmol per 1.73 m2 body surface area (BSA).
- Estimated glomerular filtration rate * 40 mL/min normalized to 1.73 m2 BSA calculated using
the Modification of Diet in Renal Disease (MDRD) formula in adults (age * 18 years).

Exclusion criteria

- Prior renal and/or hepatic transplantation.
- History of clinical signs and symptoms of systemic oxalosis other than nephrolithiasis or nephrocalcinosis.
- Participation in any clinical study involving administration of any investigational drug within the 30 days before enrollment

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-08-2016
Enrollment:	7
Type:	Actual

Ethics review

Approved WMO

Date:	11-12-2015
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-07-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR201500314251-NL
CCMO	NL54981.000.15