A Phase 1, Randomized, Double-Blind, Placebo Controlled, Single Dose Escalation Trial to Evaluate the Safety, Tolerability and Pharmacokinetics of Migalastat Hydrochloride given Intravenously to Healthy Volunteers with an Open-Label, Randomized, Two-Way Crossover Arm

Published: 04-03-2014
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Primary Objectives:* To investigate the pharmacokinetics of migalastat following a single 2hr IV infusion in healthy subjects.* To investigate the safety and tolerability of a single migalastat HCl 2hr IV infusion in healthy subjects.Secondary…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON40853

Source
ToetsingOnline

Brief title
Migalastat hydrochloride SAD study

Condition

- Chromosomal abnormalities, gene alterations and gene variants

Synonym
Fabry disease, lysosomal storage disease

Research involving
Human

Sponsors and support

Primary sponsor: Amicus Therapeutics, Inc.
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: intravenous, migalastat hydrochloride, phase 1, safety

Outcome measures

Primary outcome

1. Plasma pharmacokinetics

2. Safety: adverse events including infusion site reactions, clinically

significant changes in safety laboratory tests, vital signs, physical

examinations, and ECG

Secondary outcome

1. Plasma pharmacokinetics

2. Urinary pharmacokinetics

Study description

Background summary

Migalastat hydrochloride is a new investigational compound that may eventually be used for the treatment of Fabry disease. Fabry disease is a rare disorder caused by a mutation, which leads to reduced activity of a certain enzyme. Migalastat hydrochloride binds to this enzyme and as a result the enzyme activity will be increased. Migalastat hydrochloride is not approved as a drug in any country but has been given to humans before in other drug studies as an oral capsule formulation.

Study objective

Primary Objectives:
* To investigate the pharmacokinetics of migalastat following a single 2hr IV infusion in healthy subjects.
* To investigate the safety and tolerability of a single migalastat HCl 2hr IV infusion in healthy subjects.

Secondary Objectives:
* To assess dose proportionality of migalastat following a single 2hr IV infusion in healthy subjects (planned doses 0.3, 1.0, and 10.0 mg/kg), as data permit.
* To estimate the urinary excretion of unchanged migalastat following a single 2hr IV infusion in healthy subjects.
* To evaluate the absolute bioavailability of plasma migalastat.

Study design

This is a first in human study with a randomized, double blind, placebo controlled, single ascending dose escalation
design. Cohort 4 is an open-label, randomized, two-way crossover arm.

Intervention

The study will consist of 1 period during which you will receive migalastat hydrochloride once or placebo once. Migalastat hydrochloride and placebo will be given as a 2 hour intravenous infusion.

Please refer to the table below to see the planned dose levels for the groups. The dose for the next group will only be increased if the lower dose of the previous group was found to be well tolerated and after approval by the local Medical Ethics Review Committee. Should, in the opinion of the investigators, unacceptable adverse effects appear, the study may be discontinued.

The planning of the study is as follows:

Group Day Treatment How often
1 1 migalastat hydrochloride 0.3 mg/kg Once
2 1 migalastat hydrochloride 1.0 mg/kg* Once
3 1 migalastat hydrochloride 10 mg/kg* Once
*This indicated dose can be adapted dose is an indication, the final dose will be determined based on the results of previous groups

Cohort 4 will contain 2 sequential dosing periods with a 7 day washout between each administration. Five subjects will receive an oral dose of 150 mg

migalastat HCl during Period 1 then will return to the clinic for a 150 mg dose IV infusion of migalastat HCl during Period 2. Simultaneously, an additional five subjects will be receiving a 150 mg IV infusion of migalastat HCl during Period 1 then will return for a 150 mg oral dose of migalastat HCl. Thus, all Cohort 4 subjects will receive oral migalastat HCl and IV migalastat HCl to be considered as having completed the study.

Study burden and risks

- possible side-effect as described under E9
- blood draws via punction of the vena
- blood draws via indwelling cannula
- intraveneous administration
- screening and follow-up visit
- admission to the clinic
- study activities: physical examinations, vital signs, ECG and injection site reaction

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

- healthy male and female subjects
- 18-45 yrs, inclusive
- BMI: 18.5-29.9 kg/m2, inclusive
- non-smoking

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 60 days prior to dosing day or being a blood donor (>500 mL) within 60 days from the start of the study.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-03-2014
Enrollment:	31
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Migalastat Hydrochloride
Generic name:	n/a

Ethics review

Approved WMO Date:	04-03-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-03-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-04-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-04-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-05-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2013-005553-75-NL
CCMO	NL48251.056.14