A phase 1 study to investigate the absorption, metabolism and excretion of [14C] AT1001 (migalastat hydrochloride) following a single oral administration in healthy volunteers.

Published: 30-05-2011
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Primary :to assess the mass balance profile (i.e., excretion in urine and feces) of a single dose of AT1001 using 14C-labeled AT1001to characterize the absorption and elimination profiles of a single dose of AT1001 using 14C-labeled AT1001to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Inborn errors of metabolism
Study type	Interventional

Summary

ID

NL-OMON35820

Source
ToetsingOnline

Brief title
[14C]-AT1001 tracer label study

Condition

- Inborn errors of metabolism

Synonym
Metabolic disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: AT1001, Fabry disease

Outcome measures

Primary outcome

Criteria for evaluation

Radiokinetics : total radioactivity in plasma, urine and faeces, cumulative

excretion (also based on the area under the excretion rate versus time curves

in urine and faeces, metabolite elucidation and identification

Pharmacokinetics :

plasma, urine and faeces AT1001 concentrations, pharmacokinetic parameters

Safety : adverse events, vital signs, ECG-parameters, laboratory parameters,

physical examination

Secondary outcome

Not applicable.

Study description

Background summary

In a previous study in more than 100 healthy volunteers, with doses up to 2000 mg in single doses and up to 300 mg daily in multiple doses (150 mg twice daily) AT1001 was well tolerated. In studies with patients that were given

doses of up to 500 mg daily, the following adverse effects were reported: headache, arthralgia, diarrhea, and nausea. In all studies with AT1001, one serious adverse event has been reported (short heartblock) that is considered unlikely related to the study medication.
With the dose(s) used in this study no serious adverse effects are expected. However, the possibility that any of the above-mentioned or other adverse effects could occur cannot be entirely excluded.

Study objective

Primary :
to assess the mass balance profile (i.e., excretion in urine and feces) of a single dose of AT1001 using 14C-labeled AT1001
to characterize the absorption and elimination profiles of a single dose of AT1001 using 14C-labeled AT1001
to generate samples that will be used to characterize the metabolic profile, if feasible, of AT1001 in plasma, urine and/or feces, following administration of a single oral dose of AT1001 using 14C-labeled AT1001

Secondary :
to evaluate the safety and tolerability of a single oral dose of 150 mg AT1001/1 *Ci 14C AT1001 to healthy subjects

Study design

Design: an open-label, tracer label study in six healthy male subject receiving a single oral dose of [14C]-AT1001, containing approximately 37 kBq radiocarbon

Screening and follow-up: clinical laboratory (including coagulation), vital signs, physical examination, 12-lead ECG; at eligibility screening: medical history, height, weight, drug screen, HBsAg, anti HCV, anti-HIV 1/2; alcohol and drug screen, vital signs, physical examination, clinical laboratory (including coagulation) and 12-lead ECG to be repeated upon admission

Observation period: one period in clinic from -17 h up to 240 h after drug administration (=Day 11); follow-up on Day 29

Blood sampling : for pharmacokinetics of AT1001 and total radioactivity in plasma: pre-dose and 30 min, 1, 1.5, 2, 3, 4, 6, 8, 12, 16, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216 and 240 h post-dose
for metabolite elucidation and identification (20 mL samples): 1, 4, 6 and 24 h post-dose

Urine sampling: for pharmacokinetics of AT1001, total radioactivity and metabolite elucidation and identification: pre-dose (-12-0 hours) and intervals 0-12 and 12-24 post-dose, and thereafter at 24-hour intervals on Days 2-10; the

last sample will be collected before release from the clinical unit on Day 11
Faeces sampling: for pharmacokinetics of AT1001, total radioactivity and metabolite elucidation and identification: pre-dose (-24 to 0 hours); all bowel movements post-dose are to be collected on Days 2-10; the last sample will be collected before release from the clinical unit on
Day 11

Enterotest (bile sampling): once on Days -1 and 1

Safety assessments: adverse events: throughout the study; vital signs: once daily on Days 1-11; physical examination, clinical laboratory (including coagulation) and 12-lead ECG: once on Day 11

Bioanalysis : analysis of plasma, urine and faeces AT1001 samples using validated methods by Sponsor
analysis of total radioactivity in plasma, urine and faeces using validated methods by Sponsor
metabolite elucidation and identification by Sponsor

Intervention

Study Medication
Active substance: AT1001 and [14C]-AT1001
Activity : pharmacological chaperone for *-Gal A
Indication : Fabry disease
Dosage form: oral solution

Treatment
A single oral dose of 150 mg [14C]-AT1001, containing approximately 37 kBq radiocarbon, on Day 1 in the fasted state

Study burden and risks

Not applicable.

Contacts

Public
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Cranbury
US
Scientific

Amicus Therapeutics, Inc.

6 Cedar Brook Drive
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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy male subjects, 30 - 55 years, BMI of *18.0 to *30.0, no smoking.

Exclusion criteria

Suffering from: hepatitis B, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of this study or being a blood donor within 90 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

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):	08-08-2011
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	30-05-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-06-2011
Application type:	First submission
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	EUCTR2010-024583-17-NL
CCMO	NL35979.056.11