Single-center, open label, multiple dose study to investigate the pharmacokinetics of RO5186582 given BID over 28 days, and in addition, the excretion and metabolism of [13C]-labelled IV microdoses and an oral [14C]-labelled dose of RO5186582 in Healthy Male Volunteers

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Primary:* To determine the absolute oral bioavailability and further characterize the PK of RO5186582 using a stable isotope technique.* To explore the routes and rates of elimination of [14C] labelled RO5186582.Secondary:* To identify and quantify…

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

Summary

ID

NL-OMON36981

Source
ToetsingOnline

Brief title
[13C]- and [14C]-RO5186582 absolute bioavailability study

Condition

- Chromosomal abnormalities, gene alterations and gene variants

Synonym
Down Syndrome, trisomy 21

Research involving
Human

Sponsors and support

Primary sponsor: Hoffmann-La Roche
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: ADME, Bioavailability

Outcome measures

Primary outcome

Plasma levels of RO5186582 and its metabolites as appropriate, will be determined. Plasma concentrations will be determined by a validated assay. The stable isotope [13C]-labelled RO5186582 and RO5271857 will be measured in plasma by a specific LC/MS-MS method.

Radioactivity concentrations in blood, plasma, urine and feces will be determined by conventional methods and AMS as appropriate.

Secondary outcome

adverse events, vital signs, ECG-parameters, laboratory parameters, physical examination, C-SSRS and Leeds Sleep Questionnaire

Study description

Background summary

RO5186582 is a new investigational compound that may eventually be used for the

treatment of cognitive, functional, and/or adaptive behavioural deficits in individuals with Down syndrome (DS) aged 6 to 30 years. The studymedication influences a receptor protein (GABAA *5) involved in the learning functions.

Study objective

Primary:
* To determine the absolute oral bioavailability and further characterize the PK of RO5186582 using a stable isotope technique.
* To explore the routes and rates of elimination of [14C] labelled RO5186582.

Secondary:
* To identify and quantify circulating and excreted metabolites of RO516582 in plasma and fecal samples based on radioactive metabolic profiling, using conventional analytical methods and AMS if necessary.
* To investigate the safety and tolerability of 28 days of twice-daily dosing of RO5186582

Study design

open label with [14C] and [13C] labeled study medication

Intervention

Oral Treatments:
Days 1-27
160mg RO5186852
orally as 4x40mg tablets twice daily (Day 1: evening only)
Day 1 morning only
160mg RO5186852 single dose
as capsule [14C]-labelled RO5186582 containing 2.80MBq

Intravenous Treatments:
Day 1 and Day 28
0.1mg [13C]-labelled RO5186852
as solution by constant rate infusion over 15 minutes

All these doses will be administered within 10 minutes after completion of a standard meal or snack.

Study burden and risks

During this study several assessments will be performed that may be considered a burden.

Contacts

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Scientific
Hoffmann-La Roche

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GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

healthy male
30-55 yrs, inclusive
BMI: 18.0-30.0 kg/m2, inclusive
non-smoking or smoking < 5 cigarettes/day

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 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):	16-08-2012
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	01-08-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-08-2012
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	EUCTR2012-001434-34-NL
CCMO	NL41103.056.12