SINGLE-CENTER, SINGLE DOSE ORAL EXCRETION BALANCE STUDY OF RO5200628 IN HEALTHY MALE VOLUNTEERS

Published: 23-08-2010
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Primary:to explore the routes and rates of elimination of [14C]-radio labeled RO5200628 after oral administrationto determine the pharmacokinetics of total drug related material, RO5200628and its metabolites as appropriateSecundary:to investigate...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Mood disorders and disturbances NEC
Study type	Interventional

Summary

ID

NL-OMON34612

Source
ToetsingOnline

Brief title
[14C]-RO5200628 ADME study

Condition

- Mood disorders and disturbances NEC

Synonym
depression, Major depressive disorder

Research involving
Human

Sponsors and support

Primary sponsor: Hoffmann-La Roche

Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: ADME, Major depressive disorder, Pharmacokinetics, RO05200628

Outcome measures

Primary outcome

The primary study variable is the urinary and fecal recovery of total

radioactivity.

Secondary outcome

All other kinetic parameters and the safety data will be regarded as secondary.

Study description

Background summary

The drug to be given RO5200628 is a new, investigational compound that may eventually be used for the treatment of major depressive disorder. Depressive disorders are associated with a disruption in the levels of serotonin, norepinephrine and dopamine, substances that are present in the human brain. Normally conventional anti-depressants only effect serotonin levels. This compound, however, is expected to target the levels of all three substances. This expected triple action of the investigational drug may enhance the onset of action, which with anti-depressants currently on the market is usually up to 6 weeks. In addition, the investigational compound may have less effect on sexual functions and body weight compared to conventional anti-depressants.

Study objective

Primary:
to explore the routes and rates of elimination of [14C]-radio labeled RO5200628 after oral administration
to determine the pharmacokinetics of total drug related material, RO5200628and its metabolites as appropriate

Secundary:
to investigate metabolic profiles of the RO5200628 in plasma and excreta and

characterize any major metabolites

Study design

Procedures and assessments:
Screening and follow up visit:
clinical laboratory (including TSH and T4), vital signs (including body temperature), physical examination, 12-lead ECG (in triplicate); at eligibility screening: medical history, height, alcohol breath test, urine drug screen, coagulation (PT and aPTT), HBsAg, anti HCV, anti-HIV 1/2; vital signs, 12-lead ECG (in triplicate), clinical laboratory, alcohol breath test and urine drug screen to be repeated upon admission

Treatment period:
Involving administration of a single oral dose of RO5200628. One period in clinic from -17 h up to 366 h (Day 15) after drug administration; if discharge criteria (the radioactivity in urine and faeces (and plasma) has decreased to approximately twice background levels and after review of cumulative total recovery of radioactivity (at least 90% of the total radioactivity has been recovered in urine and feces or < 1% of the administered dose excreted over a 48-hour period) by the Investigator and Clinical Pharmacologist) are not met on Day 11 additional urine and faeces collection may be requested up to Day 15; if the subject fulfils the discharge criteria on Day 11, the subject can be released and no further sampling will be done; if the subject does not fulfil discharge criteria on Day 15, subject will be discharged and sampling will be collected at home for up to 5 days or until discharge criteria are met.

Blood sampling:
for pharmacokinetics of RO5200628 and its known metabolites in plasma: pre-dose and 0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 12, 14, 24, 26, 36, 38, 48, 72, 74, 96, 120 and 144 h post-dose
for total radioactivity in plasma and/or whole blood: pre-dose and 0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 12, 14, 24, 26, 36, 38, 48, and 72 h post-dose and will continue in 24 h intervals until discharge criteria are met
for metabolic profiling: pre-dose and 1, 3, 8, 14, 24 and 48 h post-dose
for genotyping: once on Day 1

Urine sampling:
for pharmacokinetics of RO5200628, total radioactivity and metabolic profiling: intervals 0-6, 6-12 and 12-24 h post-dose and in 24 h intervals thereafter until discharge criteria are met

Feces sampling:
for total radioactivity and metabolic profiling: 24 h intervals until discharge criteria are met

Safety assessments:

adverse events: throughout the study; vital signs: pre-dose and 5, 8, 24, 38 and 72 h post-dose and once of day of discharge; 12-lead ECG (in triplicate): pre-dose and 1, 1.5, 3, 5, 8, 12, 24, 38 and 72 h post-dose and once on day of discharge; clinical laboratory: 24 h post-dose

Bioanalysis:
analysis of plasma and urine RO5200628 and its known metabolites samples using validated methods by Sponsor
analysis of total radioactivity in plasma, whole blood, urine and faeces using validated methods by PRA
quick counts by PRA
metabolic profiling by Sponsor
genotyping by Sponsor

Intervention

Active substance: RO5200628

Study burden and risks

In single doses up to 130 mg, RO5200628 was very well tolerated by healthy volunteers. The most frequently reported adverse effects up to now were headache, nausea, dizziness and hot flush. The adverse effects were moderate in severity and resolved within a few hours after onset. In this study 45 mg of the study medication will be administered.

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

1. Age: between18 and 65 years of age;
2. BMI: between 18 and 30 kg/m2;
3. Non-smoker and moderate smokers

Exclusion criteria

1. History of any clinically significant hematological, hepatic, gastro-intestinal, endocrine, respiratory, cardiovascular, renal, urogenital, central nervous system (CNS), allergic, ophthalmologic disease, metabolic disorder, cancer or cirrhosis.
2. Diseases or surgical or medical conditions that are capable of altering the absorption, metabolism or elimination of drugs or of constituting a risk factor when taking the study drug in the judgment of the investigator.
3. Presence or history of any medically diagnosed, clinically significant psychiatric disorder

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):	01-09-2010
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	23-08-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-08-2010
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	EUCTR2010-020695-40-NL
CCMO	NL33342.056.10

Register	ID
Other	www.clinicaltrials.gov en www.rochetrials.com