Excretion balance, pharmacokinetics and metabolism of S 38844 after single oral dose administration of [14C]-S 38844 in healthy male volunteers.

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Primary:To assess after administration of a single oral dose of 75 mg S 38844 containing 55 *Ci (2.035 MBq) of [14C]-S 38844:* The excretion balance of total radioactivity;* The pharmacokinetics of total radioactivity in blood and plasma;* The...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON36850

Source
ToetsingOnline

Brief title
14C-S 38844 ADME study

Condition

- Cardiac disorders, signs and symptoms NEC
- Vascular hypertensive disorders

Synonym
cardiovascular diseases, heart- and (blood) vessel diseases

Research involving
Human

Sponsors and support

Primary sponsor: Institut de Recherches Internationales Servier I.R.I.S
Source(s) of monetary or material Support: Pharmaceutische industrie.

Intervention

Keyword: ADME Study, cardiovascular diseases, S 38844

Outcome measures

Primary outcome

Pharmacokinetics: Total radioactivity in plasma, urine and faeces

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

physical examination

Secondary outcome

Pharmacogenetic sample on (DNA) of 2.5-mL blood at pre-dose on D01.

Study description

Background summary

S 38844 is a new investigational compound that may eventually be used for the treatment of cardiovascular diseases through a selective reduction of the heart rate. S 38844 is not registered as a drug but has been given to humans before.

Study objective

Primary:
To assess after administration of a single oral dose of 75 mg S 38844 containing 55 *Ci (2.035 MBq) of [14C]-S 38844:
* The excretion balance of total radioactivity;
* The pharmacokinetics of total radioactivity in blood and plasma;
* The metabolite profile of S 38844 in plasma, urine and faeces;
* The pharmacokinetics of S 38844 and its metabolite S 41015 in plasma and urine.

Secondary:
* To gain further information on the safety of S 38844;

* To perform a pharmacogenetic analysis of genes encoding for proteins involved in absorption, distribution, metabolism and excretion (ADME).

Study design

Phase I, non-randomised, monocentre, open-label study in 6 healthy caucasian male volunteers.

The volunteers will be once administered with S 38844 in the form of a syringe in the mouth.

Procedures and assessments

Screening and follow-up:
clinical laboratory, full physical and mental examination, BP, HR, body temperature, ECG; at eligibility screening: medical history, normal blood (haematology, biochemistry) and urine (qualitative chemistry), drug screen, HBsAg, anti HCV, anti-HIV *.

Observation period:
1 period in clinic from Day -1 to minimal Day 9 and maximum Day 13 after administration of the study medication in the clinical research center in Zuidlaren.

Blood sampling:
for pharmacokinetics : 18 venous blood samples for each volunteer, from just prior to dosing up to 168 h (7 days) after dosing, according to the following schedule: 0, 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 48, 72, 96, 120, 144, 168 h post IMP administration (volume comprised between 7 and 41.5 mL, depending on sampling time).

Urine Sampling:
Urine from prior to dosing up to 168 h (7 days) after dosing and longer if required, according to the following schedule:
For all subjects:]-12-0h],]0-4h],]4-8h],]8-12h],]12-24h],]24-48h],]48-72h],]72-96h],]96-120h],]120-144h],]144-168h];
For each individual subject, part or all of the following time periods if required:]168-192h],]192-216h],]216-240h],]240-264h],]264-288h],]288-312h],] 312-336h],]336-360h],]480-504h],]648-672h].

Feces sampling;
Feces, from prior to dosing up to 168 h (7 days) after dosing and longer if required, according to the following schedule:
For all subjects:]-48-0h],]0-24h],]24-48h],]48-72h],]72-96h],]96-120h],]120-144h],]144-168h];
For each individual subject, part or all of the following time periods if required:]168-192h],]192-216h],]216-240h],]240-264h],]264-288h],

]288-312h],] 312-336h],]336-360h],]480-504h],]648-672h].

Safety assessments:
Adverse events throughout the study;
12-lead resting ECG and blood pressure;
Laboratory tests (haematology, blood biochemistry, urine biochemistry).

Pharmacogenetic assessments:
Pharmacogenetic assessments on genes encoding for proteins involved in absorption, distribution, metabolism and
excretion (ADME): one 2.5-mL bloodsample at pre-dose on Day 01.

Intervention

The volunteer will receive one dose of 75 mg S 38844 as a 20-mL clear colourless drinking solution which will be dosed in the volunteers mouth by means of syringe.

Study burden and risks

Blood draw, indwelling canula:
During this study 436 ml of blood will be drawn. One time an indwelling canula will be used. The blood samplings on the other days of 7 in total will be drawn by direct puncture of the vein. Blood sample for DNA tests: on Day 1 at pre-dose a blood sample will be taken for possible DNA tests (this is not mandatory).

Collection of urine and feces:
Urine and feces will be collected until 168 hours after administration of S 38844 (thus until Day 8) with a possible extension to Day 29 (672 hours). A blank urine and feces sample will be obtained before drug administration.

Heart trace (ECG*s):
ECG*s will be made regularly: specifically on Days 0, on Day 1 at pre-dose, 3 and 24 hours after drug administration, before discharge and during post study examination.

Adverse events:
In previous phase 1 studies, the overall safety and tolerability of S 38844 were considered satisfactory at all doses and in all conditions tested, including a study with single administration up to 100 mg and repeated administration up to 50 mg twice a day for 10 days. The most important adverse events reported were: appearance of transient enhanced brightness in the eyes, excessive slow heart rate, headache, fatigue, dizziness and gastro-intestinal disorders.

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 Caucasian male volunteers, aged 18 - 64 years inclusive
18.5 * body mass index * 30.0 kg/m2
50 kg * body weight *100 kg

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 90 days from the start of the study. In case of donating of participating in another ADME study in the 12 months prior the start of this study, with a radiation burden of >0,1 mSv.

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):	15-01-2013
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	21-12-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-01-2013
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	EUCTR2012-004140-30-NL
CCMO	NL42761.056.12