# Microdose (intravenous and oral) and oral dose of S 47445 to assess absolute bioavailability, pharmacokinetic parameters and excretion balance of S 47445 in healthy young male volunteers.

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Other condition |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON36963

**Source**
ToetsingOnline

**Brief title**
14C-S 47445 microdosing study

### Condition

- Other condition

**Synonym**
Alzheimer's disease; dementia

**Health condition**

Ziekte van Alzheimer

**Research involving**
Human

## Sponsors and support

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

## Intervention

**Keyword:** Alzheimer's disease, microdose, S 47445

## 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

n/a

# Study description

### Background summary

S 47445 is a new investigational compound that may eventually be used for the treatment of Alzheimer*s disease. Alzheimer*s disease is associated with disturbances in the exchange of *messenger* molecules (neurotransmitters) between cells in the brain and the nervous system. S 47445 is developed to enhance this exchange.
S 47445 is not registered as a drug but has been given to humans before.

### Study objective

The purpose of the study is to investigate how quickly and to what extent S 47445 is absorbed, distributed, metabolized (broken down) and eliminated from the body (this is called pharmacokinetics). S 47445 will be labeled with 14-Carbon (14C) and is thus radioactive. This enables the investigator to trace S 47445 in blood, urine and feces. The safety and tolerability of S 47445 will

also be evaluated. In addition, the bioavailability (measurements of the amount of drug that is actually absorbed) of S 47445 will be investigated.

## Study design

Procedures and assessments
Screening and follow-up:
clinical laboratory, full physical examination, ECG, weight, vital signs (BP, temperature HR) and adverse events; only at screening: medical and surgical history, relevant previous treatments, psychological examination, alcohol and drug screen, HBsAg, anti HCV and anti-HIV 1/2, height, EEG and CYP2D6 genotyping; upon admission: medical and surgical history, alcohol and drug screen and ADME genotyping

Observation period:
two periods in clinic from -17 h up to 144 h (Day 7) after drug administration

Blood sampling:
for pharmacokinetics of S 47445 and total radioactivity in plasma: Period 1 and 2: pre-dose and until 96 hrs post dose
for CYP2D6 genotyping: once during screening
for ADME genotyping: once at Day -1 of period 1

Urine sampling:
for pharmacokinetics of S 47445 and total radioactivity: period 1 and 2: pre-dose and until 120-144 h post-dose

Faeces sampling:
for pharmacokinetics of S 47445 and total radioactivity: period 1 and: pre-dose and until 120-144 h post-dose

Safety assessments:
adverse events: throughout the study; physical exam, vital signs (including body temperature and respiratory rate) and 12-lead ECG: pre-dose and several time points during the study.

## Intervention

In period 1 the subjects will receive a single oral dose of 20 mg as 4 tablets of unlabeled S 47445 after an overnight fast (at least 10 hours) with 250 mL of water. Three hours later, you will receive 50 mcg radio labeled S 47445 in 2.5-mL solution as a single intravenous (IV) infusion over 15 min.

In period 2, the subjects will receive a single oral dose of 50 mcg radio labeled S 47445 after an overnight fast (at least 10 hours) as a 2.5-mL oral solution.

**Study burden and risks**

Registration of adverse effects

Blood sampling, indwelling cannula: During this study less than 500 ml of blood will be drawn. It is anticipated that an indwelling cannula will be inserted for blood samplings on Day 1 and Day 2 of both periods. The blood samplings on the other days will be drawn by direct puncture of the vein.

IV administration: For the IV administration an indwelling cannula will be inserted specifically for this purpose in addition to the indwelling cannula used for blood sampling.

Collection of urine and feces: In both periods urine and feces will be collected until 144 hours after administration of S 47445 (thus until Day 7). A blank urine and faeces sample will be obtained before drug administration.

Heart trace (ECG*s): ECG*s will be made regularly: specifically on Day 1.

Electro Encephalogram (EEG): The study medication is expected to act on the brain, so in order to avoid problems during the study the brain activity is studied before administration of the study medication.

Genotyping for CYP2D6: Part of the screening visit will be to perform genotyping in order to assess liver*s capacity to metabolize certain drugs.

Blood sample for DNA tests: On Day 0 an additional blood sample will be taken in order to perform analyses on genetic material (DNA).

In previous clinical studies with S 47445 in 100 healthy volunteers, with doses up to 800 mg (single dose) and up to 100 mg (multiple dose, 21 days) the following adverse events were reported: feeling of thirst, dizziness and low blood pressure when standing-up, hematoma on the back of the foot, headache, hot flush, and redness of the skin. Drugs with a comparable action sometimes induce unrest, anxiety or sleeplessness.

# 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 Caucasian subjects,
non-smoking,
EM for CYP2D6,
18 - 45 yrs, inclusive,
19.0 * 28.0 kg/m2, inclusive

## 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

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|---|---|
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 28-08-2012 |
| Enrollment: | 6 |
| Type: | Actual |

# Ethics review

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|---|---|
| Approved WMO Date: | 15-08-2012 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 24-08-2012 |
| 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 | EUCTR2012-002405-21-NL |
| CCMO | NL41753.056.12 |