Single center, open-label, non-randomized, non-placebo-controlled study to investigate the pharmacokinetics, metabolic disposition and mass balance after single administration of 5 mg [14C]BAY 1021189 (oral solution) in healthy male subjects

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON40889

Source
ToetsingOnline

Brief title
BAY 1021189 Mass Balance Study

Condition

- Heart failures

Synonym
Cardiovascular diseases, heart failure

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Excretion Pattern, Mass Balance, Metabolism

Outcome measures

Primary outcome

Pharmacokinetics:

plasma drug concentrations, pharmacokinetic parameters.

Secondary outcome

Safety and tolerability:

AEs, vital signs, ECG parameters, laboratory values**, physical examination.

Study description

Background summary

BAY 1021189 is a new investigational compound that may eventually be used for the treatment of heart failure. BAY 1021189 is a stimulator of the enzyme *soluble guanylate cyclase*, which plays an important role in the regulation of the cardiovascular system.
BAY 1021189 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 BAY 1021189 is absorbed, distributed, metabolized (broken down) and eliminated from the body (this is called pharmacokinetics). The compound to be administered

will be labeled with 14-Carbon (14C) and is thus radioactive (also called radiolabeled). This enables the investigator to trace the compound in blood, urine and feces. The safety and tolerability of the compound will also be evaluated.

Study design

The actual study will consist of 1 period during which you will stay in the clinical research center in Zuidlaren for a minimum of 12 days (11 nights) and a maximum of 16 days (15 nights), possibly followed by a maximum of 2 additional short visits.

During the study the volunteer will receive the study medication after an overnight fast (at least 10 hours) as an oral solution. After this the volunteer is also required to drink an additional amount of 240 milliliters water. Fasting will continue until 4 hours after administration of study medication. During fasting and after intake of the study medication, the volunteer is allowed to drink water ad libitum with the exception of 2 hours prior to until 1 hour after administration of the study medication.

Intervention

On day 1, a single dose of 5 mg radio-labeled study medication in the form of an oral solution of 10 milliliters.

Study burden and risks

Blood draw, indwelling canula:
During this study blood will be drawn. In one period 1 time an indwelling canula will be used and a number of blood draws
will be drawn by direct puncture of the vein. The insertion of the canula may be associated with pain, minor bleeding,
bruising, possible infection.

As BAY 1021189 is under development there may be side effects, including allergies, that have not been reported before. Therefore you must notify us of any new symptoms that you might have, even if you do not think it is related to the study medication.
BAY 1021189 is under development to treat heart failure. The dose determined for use in this study has been selected under the premise to avoid serious side effects.

Approximately 158 healthy male volunteers have received BAY 1021189 in different studies. In the studies conducted so far the dose range between 0.5 and 10 mg of BAY 1021189 was safe and well tolerated by healthy male volunteers. The most commonly reported side effects so far were diarrhea,

nausea, and abdominal discomfort. In addition, headache, postural dizziness, spontaneous penile erection, orthostatic hypotension, ocular hyperemia (red eyes), and nasal congestion were reported.

At the highest dose tested to date in the first-in-human study (15 mg), 3 volunteers developed orthostatic reactions, i.e., the development of symptoms upon upright standing after lying down. The symptoms reported included orthostatic hypotension and fainting. All of these abnormalities recovered within several days. Because of the development of orthostatic reactions, the 15 mg dose will not be further evaluated. The dose planned to be administered in this study is 5 mg BAY 1021189.

In this study radiolabeled BAY 1021189 will be used. The amount of radioactivity in this dose will be 3.7 MBq (MBq = megaBecquerel, this is a unit to express the amount of radioactivity in the study medication). The average environmental background radiation burden in The Netherlands is approximately 2 mSv per year (mSv = milliSievert, this is the unit which indicates the burden on the human body; thus the effect on the human body of the amount of radioactivity administered). The additional radiation burden in this study due to the administration of 3.7 MBq 14C-labeled BAY 1021189 is calculated to be 0.96 mSv. This is approximately 48% of the average annual radiation burden.

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 subjects
45-65 yrs, inclusive
BMI: 18.0-30.0 kg/m2, inclusive

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 60 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):	23-04-2014
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	01-04-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-04-2014
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	EUCTR2013-005115-27-NL
CCMO	NL48530.056.14