Single center, open-label, non-randomized, non-placebo-controlled study to investigate the pharmacokinetics, metabolic disposition and mass balance after single administration of 25 mg [14C]BAY 2433334 (oral solution) in healthy male participants.

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

Summary

ID

NL-OMON50127

Source
ToetsingOnline

Brief title
Human Mass Balance Study

Condition

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

Synonym
blood clots, stroke

Research involving
Human

Sponsors and support

Primary sponsor: Bayer AG
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: BAY 2433334, mass balance, open-label, pharmacokinetics

Outcome measures

Primary outcome

%AE,ur and %AE,fec (and amount in vomit as a percent of the dose, if

applicable) of BAY 2433334 and its metabolites based on radioactivity excreted

in urine and feces as a percent of the dose to assess mass balance of total

radioactivity

- AUC*, Cmax of total radioactivity in plasma and whole blood

- AUC*, Cmax of BAY 2433334 and BAY 2826102 (and metabolites, if applicable) in

plasma

Secondary outcome

Frequency of participants with treatment emergent adverse events

Study description

Background summary

BAY 2433334 is a compound that may potentially be used for the treatment or prevention of blood clots in the heart, in blood vessels or in the brain as it can happen after heart attacks, with an irregular heart rhythm or due other

reasons. Worldwide, disease of the heart or blood vessels is the leading cause of death in adults with an estimated 17.7 million deaths in 2015. BAY 2433334 is a blood thinner (an *anti-coagulant*) which can prevent the formation of blood clots in blood vessels (so-called *thrombo-embolic* disorders). These blood clots can travel through the bloodstream and block arteries which prevents blood from delivering oxygen and nutrients to the organs. When that happens in the heart, it is called a heart attack and when in the brain it is called a stroke. All these conditions may ultimately result in death or permanent disability. BAY 2433334 aims to prevent the formation of the blood clot (anticoagulation). It works by blocking a *blood clotting* protein (FXIa) from performing its function.

Study objective

The objective of this study is to determine the mass balance and routes of excretion of total radioactivity after a single oral 25 mg dose of [14C]BAY 2433334 given as solution. For further clinical development, human mass balance data are required to elucidate the absorption, distribution, metabolism, and excretion (ADME) of BAY 2433334.
To quantify total radioactivity in plasma and whole blood.
To quantify BAY 2433334 and BAY 2826102 (M-10 metabolite) concentrations in plasma.
Evaluate the safety and tolerability of 25 mg BAY 2433334 administered as an oral solution in healthy male participant.

Study design

The study will consist of 1 period during which the subjects will stay in the research center for 16 days (15 nights). Day 1 is the day of administration of the study compound. The subjects are expected at the research center at 11:00 AM in the morning prior to the day of administration of the study compound. They will leave the research center on Day 15 of the study, or earlier from Day 11 onwards. They will also have to consider 4 additional 24-hour visits for the collection of urine and feces and to take blood samples. The subject is asked to collect a feces sample from within 48 hours prior to entry in the clinic.

Intervention

BAY 2433334 will be given as an oral solution of 6.25 milliliters (mL). Immediately after administration of the study compound the participant will receive a glass with 240 mL of water, which they will have to drink completely. All volunteers will receive the same treatment.
The participant will receive 25 mg BAY 2433334 containing 3.7 Mega Becquerel (MBq) of radioactivity.

Study burden and risks

BAY 2433334 has been administered to in total 172 healthy men before in 4 previous clinical studies. These studies found no relevant effects of BAY 2433334 on several health parameters, including heart tracings (ECGs), blood pressure, and heart rate. Side effects that were reported include:
• Nausea
• Headcache
• Dizziness
• Dry mouth
• Bitter taste sensation
• Fast or irregular heartbeat
• Tingling or pricking sensation(paresthesia) in hands and fingertips
• Sensation of cold in feet
• Sensation of *lump in the throat*

In previous clinical trials, single doses of 5 mg up to 150 mg have been administered and were considered safe and well tolerated in healthy male volunteers. Therefore, the dose that will be used in this study (25 mg 14C-labeled BAY 2433334) is also expected to be safe and well tolerated.
BAY 2433334 has been studied extensively in the laboratory and in animals. Studies in animals showed effects of BAY 2433334 on pancreas, liver and thyroid. Therefore, intensive monitoring is used in the human studies to make sure human volunteers do not develop similar signs or symptoms. In all the previous studies in humans, no changes in the function of pancreas, liver, and thyroid was found after administration of BAY 2433334.
The mode of action of BAY 2433334 is to slow down the clotting of blood. A risk of compounds that have a similar working mechanism as BAY 2433334 is that they can result in bleeding. So far, bleedings have not been reported in previous studies of BAY 2433334 in humans.

An allergic reaction is always possible with a drug that a volunteer has not taken before. Unexpected serious allergic reactions can be life-threatening. Some things that may happen during an allergic reaction to any type of medication include rash, breathing difficulty, sudden drop in blood pressure, swelling of mouth/throat/eyes, fast pulse and/or sweating.
The study compound may also have side effects that are still unknown.

Drawing blood and/or insertion of the indwelling cannula (tube in an arm vein) may be painful or cause some bruising. On the day of administration of the study compound, blood will be sampled very frequently to determine the course of the concentration of BAY 2433334 in the blood over time.
To make a heart tracing, electrodes (small, plastic patches) will be pasted at specific locations on your arms, chest and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

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 white male
Between 18 and 55 years of age.
BMI is between 18 and 29.9 kilograms/meter2

Exclusion criteria

1. A history of relevant diseases of vital organs, of the central nervous system or other organs.
2. Medical disorder, condition or history of such that would impair the participant's ability to participate or complete this study in the opinion of the investigator.

3. Incompletely cured pre-existing diseases for which it can be assumed that the absorption, distribution, metabolism, elimination and effects of the study intervention will not be normal.
4. Known hypersensitivity to the study interventions (active substance or excipients of the preparation).
5. Known severe allergies e.g. allergies to more than 3 allergens, allergies affecting the lower respiratory tract - allergic asthma, allergies requiring therapy with corticosteroids, urticaria or significant non-allergic drug reactions.

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):	28-01-2020
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	12-12-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-01-2020
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	EUCTR2019-002766-13-NL
CCMO	NL72254.056.19