Open-label, non-randomized study investigating the excretion balance, Pharmacokinetics, and metabolism of a single oral dose of [14c]-labeled ro6868847 in healthy male participants

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Ethical review	Approved WMO
Status	Completed
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON51247

Source
ToetsingOnline

Brief title
Excretion balance, PK, and metabolism of [14C]-labeled RO6868847

Condition

- Diabetic complications

Synonym
Diabetes, Diabetic retinopathy

Research involving
Human

Sponsors and support

Primary sponsor: F. Hoffmann-La Roche Ltd
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Excretion balance, Healthy male participants, Pharmacokinetics, Ro6868847

Outcome measures

Primary outcome

To characterize mass balance, rates and routes of elimination of [14C]-labeled RO6868847, using conventional analytical methods (and accelerator mass spectrometry [AMS] if necessary).

To assess the pharmacokinetics (PK) of total drug-related [14C]-radioactivity, [12C] RO6868847 and its metabolite(s), as appropriate, using conventional analytical methods (and AMS if necessary).

Secondary outcome

To identify and quantify the metabolic profiles of RO6868847 in plasma, blood pellet (if appropriate), urine and feces, based on [14C]-radioactive metabolic profiling, and characterize any major metabolite(s), using conventional analytical methods (and AMS if necessary).

To assess the safety and tolerability of a single oral dose of [14C/12C] RO6868847 in healthy participants.

Study description

Background summary

RO6868847 is being developed for the possible treatment of diabetic retinopathy. Diabetic retinopathy is a complication of diabetes, caused by high blood sugar levels damaging the back of the eye, which can seriously affect vision. RO6868847 is a study compound to be taken as a drink. It has been generated to bind to a structure known as the CB2 (cannabinoid 2) receptor, which is found in many different tissues throughout the body, including the retina (tissue at the back of the eye). In experiments with animals and tests with human cells, it was shown that RO6868847 has anti-inflammatory effects. As diabetic retinopathy involves inflammation, RO6868847 may have beneficial effects on diabetic retinopathy.

RO6868847 is an experimental study compound, which means Health Authorities have not approved it for the treatment of any disease.

RO6868847 has been previously given to humans in three other studies. In total, 122 healthy male and female participants have received RO6868847 to date. This will be the first time that the radiolabeled form of RO6868847 will be given to humans.

Study objective

The purpose of this study is to investigate how quickly and to what extent RO6868847 is absorbed, distributed, metabolized (broken down), and eliminated from the body (this is called pharmacokinetics). A very small part of the study compound RO 6868847 to be administered has been labeled with 14-Carbon (14C) and therefore is radioactive. This enables the investigator to trace the study compound in blood, urine, and feces.

We also look at the effect of the volunteers genetic information on his body*s response to RO6868847. This part of the study is mandatory.

We will also investigate how safe the new compound RO6868847 is and how well it is tolerated when it is used by healthy male participants.

Study design

The study will be divided as follows:
• 1 screening visit to see if the volunteer is eligible for the study: Up to 4 weeks prior to receiving the study compound.
• 1 in-house period of 15 or 22 nights where the volunteer stays in the research center from Day -1 (the day before receiving RO6868847) until either

Day 15 or Day 22 (the length of his stay will depend on the amount of radioactivity the volunteer have passed in his urine and feces up to Day 15).
• Up to 7 visits to the research center between Day 24 to Day 36 to bring the urine and feces the volunteer collected at home and for further checks and assessments (if required; the need for these visits will depend on the amount of radioactivity you have passed in your urine and feces. You may also be asked to come for additional visits after Day 36 if the responsible doctor thinks this is necessary).
• 1 follow-up visit: 5 to 9 days after the volunteers last urine and feces samples have been taken.

The volunteer will be given one dose of 300 mg RO6868847 as a drink on Day 1 after having fasted overnight for at least 10 hours. The volunteer will be given 50 milliliter (mL) of RO6868847 to swallow, followed by 170 mL of water. After this, the vial that the volunteer were given the study compound in will be rinsed twice with 10 mL of water, which the volunteer will also be required to drink. Thus, the total volume will be 240 mL (study compound drink + water + rinses).

Intervention

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Study burden and risks

Side effects:
The study compound may cause side effects.
RO6868847 has been tested in 122 healthy volunteers in two studies. In those studies, RO6868847 was well tolerated and safe across all doses tested. Side effects were mild and did not increase with increasing doses of RO6868847. The most frequently reported side effects were: redness of skin where blood was drawn (11 events), complications with blood draws (4 events), headache (3 events) and constipation (2 events). In a study where a single dose of RO6868847 was administered, no constipation was observed. Each of these side effects is *common* and may affect between 1 in 10 and 1 in 100 people.

The study compound may also have (serious) side effects that are still unknown. In addition to unknown side effects, there is a (small) chance that an allergic reaction will occur. This can be caused by the study compound or other ingredients that are used to prepare the formulation. Allergic reactions can

occur with any drug and this can be in the form of itching, difficulty breathing, and a skin rash and/or drop in blood pressure. In very rare cases, the volunteer could suffer a life-threatening allergic reaction.

Possible discomforts:
Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling canula (a tube in a vein in the arm) can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment (bruising) of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, seating, low heart rate, or drop in blood pressure with dizziness or fainting.
In total, we will take about 460 milliliters (mL) of blood from the volunteer. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time. If the investigator thinks it is necessary for the safety of a participant, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn will be more than the amount indicated above.

Heart tracing (ECG)
The volunteer will have small, soft patches (electrodes), stuck temporarily on different parts of his body. There is no pain or discomfort during an ECG; however, the area of skin in which the ECG pads will be stuck may need to be shaved, and the pads may cause a skin reaction such as redness or itching. Taking the pads off may cause localized irritation to the skin and/or hair loss, similar to having a plaster taken off.

Coronavirus test
Samples for the coronavirus test will be taken from the back of the volunteers nose and throat using swabs. Taking the samples only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the volunteers throat may cause him to gag. When the sample is taken from the back of the volunteers nose, he may experience a stinging sensation and his eyes may become watery.

Radiation load

Contacts

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Basel 4070

CH
Scientific
F. Hoffmann-La Roche Ltd

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CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Able and willing to provide written informed consent and to comply with the study protocol according to ICH and local regulations.
2. Male participants aged 35 to 64 years of age (inclusive), at screening.
3. Healthy participants. Health status is defined by absence of evidence of any active or chronic disease following a detailed medical and surgical history, a complete physical examination including vital signs, 12-lead electrocardiogram (ECG), hematology, clinical chemistry, serology, coagulation, and urinalysis.
4. Body weight > 50 kg and body mass index within the range 18 to 30 kg/m2 (inclusive), at screening.
5. Male participants who, for 3 months after the dosing of [14C/12C] RO6868847, agree to:
- Remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures such as a condom plus an additional contraceptive method that together result in a failure rate of < 1% per year, with a partner who is a woman of childbearing potential
- With a pregnant female partner, remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures such as a condom to avoid exposing the embryo to RO6868847
- Refrain from donating sperm.

Exclusion criteria

1. History of any clinically significant gastrointestinal, renal, hepatic, broncho pulmonary, neurological, psychiatric, cardiovascular, endocrinological, hematological, or allergic disease, metabolic disorder, cancer, or cirrhosis.
2. Concomitant disease or condition that could interfere with, or treatment of which might interfere with, the conduct of the study, or would, in the opinion of the Investigator, pose an unacceptable risk to the participant in this study, including but not limited to any major illness within 1 month prior to screening or any febrile illness within 1 week prior to screening and up to study drug administration.
3. History or evidence of any medical condition potentially altering the absorption, metabolism, or elimination of drugs. Surgical history of the gastrointestinal tract affecting gastric motility or altering the gastrointestinal tract (with the exception of uncomplicated appendectomy and hernia repair).
4. History or presence of clinically significant ECG abnormalities based on the average of the triplicate ECG recordings (e.g., PQ/PR interval > 210 ms, QTcF > 450 ms) or cardiovascular disease (e.g., cardiac insufficiency, coronary artery disease, cardiomyopathy, congestive heart failure, family history of congenital long QT syndrome, family history of sudden death).
5. History of malignancy.

Further criteria apply

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	19-03-2021
Enrollment:	10

Type:	Actual

Ethics review

Approved WMO Date:	15-02-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-03-2021
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	EUCTR2020-005922-27-NL
CCMO	NL76662.056.21

Study results

Date completed:	07-05-2021
Results posted:	05-04-2022

First publication
10-03-2022