A single-center, two-part, randomized, open-label, parallel-group, four-sequence, four-treatment, four-period crossover study to investigate the bioequivalence and the effect of food on the pharmacokinetics and safety of single oral doses of two different formulations of RO6868847 in healthy participants

Published: 05-07-2022
Last updated: 18-01-2025

In Part 1 we will investigate and compare to what extent RO6868847 is absorbed, distributed, metabolized, and eliminated from the body of 2 different types of tablet composition. This is done to see if both tablet compositions deliver the study...

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

Summary

ID

NL-OMON51381

Source
ToetsingOnline

Brief title
A bioequivalence and food effect study of two RO6868847 tablet formulations

Condition

- Diabetic complications

Synonym
non-proliferate diabetic retinopathy (NPDR)

Research involving
Human

Sponsors and support

Primary sponsor: Hoffmann-La Roche
Source(s) of monetary or material Support: pharmaceutical industry

Intervention

Keyword: bioequivalence, food effect, PK, RO6868847

Outcome measures

Primary outcome

Part 1 (Bioequivalence)

RO6868847 plasma concentrations and derived pharmacokinetic (PK) parameters.

Part 2 (Food Effect)

RO6868847 plasma concentrations and derived pharmacokinetic (PK) parameters.

Secondary outcome

Part 1 and Part 2

Incidence and severity of adverse events (AEs).

Changes in vital signs, physical findings, electrocardiogram (ECG) parameters,

and clinical laboratory test results.

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. 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 two other studies. In total, 128 healthy male and female subjects have received RO6868847 to date.

Study objective

In Part 1 we will investigate and compare to what extent RO6868847 is absorbed, distributed, metabolized, and eliminated from the body of 2 different types of tablet composition. This is done to see if both tablet compositions deliver the study compound (RO6868847) in the same manner into the body.

In Part 2 we will investigate how food effects the absorption, distribution, metabolization, and elimination of the study compound (RO6868847) from the body. For this the study compound will be given once on a full stomach and once on an empty stomach to see if this changes the uptake of the study compound.

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

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

Study design

The study will take about 12 weeks from the first visit (screening) until the last visit (follow-up visit).

For the study it is necessary that the volunteer stays in the research center

for 4 periods of 5 days (4 nights). This will be followed by 1 short visit to the research center per period.

The volunteer will be given 30 mg and 200 mg RO6868847 as oral tablets with 240 milliliters (mL) of (tap) water. In Part 1 the volunteer will receive RO6868847 four times in total with two different tablet compositions.

All subjects in Part 2 will receive the study compound two times with a breakfast and two times without breakfast on Day 1.

Intervention

All doses are administered on Day 1 as a single dose as follows:

Part 1 (fasted condition)
A: 30 mg RO6868847 Type 1/2
B: 30 mg RO6868847 Type 3
C: 200 mg RO6868847 Type 1/2
D: 200 mg RO6868847 Type 3

Part 2
A: 30 mg RO6868847 fasted Type 3
B: 30 mg RO6868847 fed Type 3
C: 200 mg RO6868847 fasted Type 3
D: 200 mg RO6868847 fed Type 3

Study burden and risks

Possible side effects:
The study compound may cause side effects.

RO6868847 has been tested in 128 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.

There were no important changes in laboratory tests, urine, blood pressure, or pulse rate or ECG, physical and neurological examination, and questionnaires monitoring suicidal thoughts, mood and perception. One participants who received multiple doses of 300 mg of RO6868847 for 11 days showed an increase in pulse rate with ECG changes that did not cause any symptoms. When the subject stopped taking RO6868847, the ECG changes returned to normal within a

few days.

To minimize potential risks, heart and vessels will be closely monitored at screening and during the course this study.

Laboratory experiments have suggested that RO6868847 may interact with certain other medications. The responsible doctor can inform you of what these other medications are. You should not take any other medication, unless agreed by the responsible doctor.

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.

Possible Discomforts:
Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, sweating, low pulse rate, or drop in blood pressure with dizziness or fainting.

Heart tracing
To make a heart tracing, electrodes will be placed on the volunteers arms, chest and legs. Prolonged use of these electrodes can cause skin irritation.

Meals
The high-fat breakfast is a big breakfast containing e.g., 2 fried eggs, fried potatoes and bacon (Part 2 only).

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 throat may cause one to gag. When the sample is taken from the back of the nose, a stinging sensation may be experienced and the eyes may become watery.

Contacts

Public
Hoffmann-La Roche

Grenzacherstrasse 124
Basel CH-4070
CH
Scientific
Hoffmann-La Roche

Grenzacherstrasse 124
Basel CH-4070
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Willing to participate and able to give written informed consent and to comply with the study restrictions according to International Council for Harmonisation (ICH) and local regulations.
2. Male or female, between 18 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 ECG, hematology, blood chemistry, serology, coagulation, and urinalysis.
4. Participants must weigh at least 50.0 kg and must have a body mass index (BMI) within the range of 18.0 to 32.0 kg/m2, inclusive.
5. Male and female: The contraception and abstinence requirements are intended to prevent exposure of an embryo to the study treatment. The reliability of sexual abstinence for enrollment eligibility needs to be evaluated in relation to the duration of the clinical study and the preferred and usual lifestyle of the participant. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or post-ovulation methods) and withdrawal are not acceptable methods of preventing fetal/embryonic drug exposure.
a) Female:
A female participant is eligible to participate if she is not pregnant, not

breastfeeding, and at least one of the following conditions applies:
• Woman of non-childbearing potential (WONCBP).
• Woman of childbearing potential (WOCBP), who:
- Agrees to remain abstinent (refrain from heterosexual intercourse) or use a condom plus an additional highly effective contraceptive method that results in a failure rate of <1% per year during the treatment period and for at least 90 days after the last dose of study treatment. Examples of contraceptive methods with a failure rate of <1% per year include bilateral tubal occlusion, intercourse with a sterilized male, established proper use of hormonal contraceptives that inhibit ovulation, hormone-releasing intrauterine devices, and copper intrauterine devices.
- Has a negative pregnancy test at screening and Day -1.
b) Male:
During the treatment period and for at least 90 days after the last dose of study treatment, agree to:
• Remain abstinent (refrain from heterosexual intercourse) or use a condom plus an additional highly effective contraceptive method that results in a failure rate of <1% per year as described above, with a partner who is a WOCBP.
• With pregnant female partner, remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures such as a condom to avoid exposing the embryo.
• 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, or cirrhosis.
2. Concomitant disease or condition that could interfere with, or treatment of which might interfere with, the conduct of the study, or that 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 4 weeks before the screening examination or any febrile illness within 1 week prior to screening and up to first study treatment 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 triplicate ECG recordings (e.g., PQ/PR interval >210 ms, QTcF >450 ms for males and QTcF >470 ms for females) 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 in the past 5 years.

Further criteria apply

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	01-08-2022
Enrollment:	48
Type:	Actual

Ethics review

Approved WMO Date:	05-07-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-07-2022
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	EUCTR2022-001575-13-NL
CCMO	NL81676.056.22

Study results

Date completed: 07-12-2022

Results posted: 06-12-2023

First publication
25-08-2023