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A study to find out the safety, tolerability and interaction of RO7268489 with body (including the effect of itraconazole on RO7268489) and also what the body does to RO7268489 after oral intake by healthy participants

Submission date 09/05/2024	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 10/05/2024	**Overall study status** Completed	
Last Edited 05/06/2024	**Condition category** Other	

Plain English summary of protocol

Background and study aims

New types of drugs are often given to healthy people - to see what the body does to the drugs and what the drugs do to the body - before they are given to people with a medical condition as a possible new treatment.

A study to see how safe RO7268489 is at different doses, how it gets to different parts of the body and how the body gets rid of it (and also to check how RO7268489 works and the effects it has) in healthy participants. Researchers also want to understand how several doses of itraconazole influence the uptake, breakdown, distribution and elimination of RO7268489 in the body

RO7268489 is an experimental medicine. This means health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) have not approved RO7268489 in combination with itraconazole.

Who can participate?

Healthy participants (males / females) of 18 - 64 years of age can take part in the study.

People may not be able to take part in this study if they have:

a. Any long-term or 'active' disease/s or infections, including those affecting any organs, mental health, allergies or cancer

b. A body mass index (BMI) of under 18.5 kilograms per square meter (kg/m^2) (underweight) or over 30 kg/m^2 (overweight)

c. Participants who are pregnant, or currently breastfeeding cannot take part in the study.

d. Participants planning to conceive during or shortly after the study (within 70 days after the final dose of RO7268489).

e. Men must also not donate/store sperm during this time.

What does the study involve?
The study consists of two parts (Part 1 and Part 2). Participants who take part in this clinical study will only be allowed to join one part of the study.

Participants will be screened to check if they are able to participate in the study. The screening period will take place from 8 and 4 weeks before the start of treatment for Part 1 and Part 2, respectively.

Part 1 is called “multiple-ascending dose (MAD)”: The purpose of this part is to evaluate the safety, tolerability, and drug levels in the body after multiple administration of the study drug. In this Part, 3 dose levels (also called dose groups) of RO7268489 or placebo are planned to be tested. A placebo is a substance that looks like a study drug but contains no active medication. If needed, there can be additional dose-level groups. Everyone in Part 1 will be randomly assigned to one of the following treatment groups: RO7268489 or placebo. This means that participants are put into a group by chance (like tossing a coin or rolling a dice). This is a double-blinded part. Neither the participants in the study nor the team running it will know which treatment is being given until the study is over. This is done to make sure that the results of the treatment are not affected by what participants expected from the received treatment. However, the study doctor can find out which group the participant is in, if the participants' safety is at risk. Participants will receive either RO7268489 or placebo once daily for 14 or 28 days, as an oral solution in the morning 30 minutes after the start of a standard breakfast.

Part 2 is called “drug-drug Interaction (DDI)”. The purpose of this part is to evaluate the effect of several doses of itraconazole on RO7268489 uptake, breakdown, distribution, and elimination and how safe and well tolerated it is when taken in combination with itraconazole. Everyone in Part 2 will be given a RO7268489 as an oral solution once daily for 18 days. From Day 11, itraconazole will be administered twice daily as an oral capsule for 8 days. This is an open-label part. This means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.

Participants will need to stay in the clinic for around 33 days (first group) and 19 days (second and third group) in Part 1 and for around 21 days in Part 2 for each treatment dose. Participants will be regularly seen by the clinical study doctor. The doctor will check how the body processes the treatment, and for any adverse effects participants may have. Total time of participation in the study will be approximately 20-22 weeks in Part 1 and 17 weeks in Part 2 of the study. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so.

What are the possible benefits and risks of participating?
RO7268489 is an experimental drug and is being given purely for research purposes, it is not intended that participants will receive any benefit from this study. But the information learned from this study may be useful to treat future patients.
It may not be fully known at the time of the study how safe and how well the study treatment works. The study involves some risks to the participant. But these risks are generally not greater than those related to routine medical care or the natural progression of the health condition. Participants interested in taking part will be informed about the risks and benefits, as well as any additional procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible effects and other options of treatment.

Risks associated with the study drugs or procedures
Participants may have unwanted effects of the RO7268489 used in this study. These unwanted

effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants will have regular check-ups to see if there are any unwanted effects.

RO7268489
Participants will be told about the known unwanted effects of RO7268489 and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Side effects can vary from mild to very serious and may be different from person to person. RO7268489 has had limited testing in humans, there may potentially also be side effects that are not known at this time. The known side effects of this drug, as well as potential side effects are listed below.
Allergic reactions on treatment with RO7268489, which can be in the form of itching, difficulty breathing, a rash, and/or drop in blood pressure.

RO7268489 will be given orally (by mouth) - participants will be told about any known side effects of this.
There may be a risk in exposing an unborn child to study the drug, and all risks are not known at this time. Women who are pregnant, become pregnant, or who are currently breastfeeding, cannot participate in this study.

Where is the study run from?
F. Hoffmann-La Roche Ltd (Switzerland)

When is the study starting and how long is it expected to run for?
February 2024 to March 2025

Who is funding the study?
F. Hoffmann-La Roche Ltd (Switzerland)

Who is the main contact?
global.trial_information@roche.com

Study website
http://www.marlinstudy.com/

Contact information

Type(s)
Public, Scientific, Principal Investigator

Contact name
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Additional identifiers

EudraCT/CTIS number
2024-510606-85-00

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
BP45248

Study information

Scientific Title
A randomized, investigator and participant-blind, adaptive, multiple ascending dose, placebo-controlled, parallel phase I study to investigate the safety, tolerability, pharmacokinetics (including the effect of itraconazole on RO7268489 pharmacokinetics), and pharmacodynamics of RO7268489 following oral administration in healthy participants

Study objectives
The main purpose of this study is to evaluate the safety and tolerability of multiple oral doses of RO7268489 and the effect of multiple oral doses of itraconazole on pharmacokinetic (PK) effect of multiple oral doses of RO7268489 in healthy participants.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 03/05/2024, Stichting Beoordeling Ethiek Biomedisch Onderzoek (Weiersstraat 1c 9401 ET Assen, Assen, 9401 ET, Netherlands; +31 59 2405871; info@stbebo.nl), ref: Nil known

Study design
Single center 2 part study
Part 1 is a randomized double-blind placebo-controlled parallel arm study
Part 2 is a non-randomized open-label single sequence study

Primary study design
Interventional

Secondary study design
Part 1: Randomised placebo-controlled trial; Part 2: Non- randomised open label study

Study setting(s)
Hospital

Study type(s)
Treatment, Safety

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Healthy volunteers

Interventions
Participants will receive the treatments in 2 parts
Part 1 (RO7268489): Participants will receive RO7268489 once-daily (QD), orally, for up to 28 days.
Part 1 (Placebo): Participants will receive RO7268489 matching placebo, QD, orally, for up to 28 days.
Part 2 (RO7268489+Itraconazole): Participants will receive RO7268489, QD, orally, for up to 18 days. Participants will also concomitantly receive itraconazole 200 milligrams (mg), orally, twice daily (BID), from Day 11 to Day 18.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Safety

Phase
Phase I

Drug/device/biological/vaccine name(s)
RO7268489, itraconazole

Primary outcome measure
Part 1: Number of participants with adverse events (AEs) and severity of AEs assessed using data from electronic case reported forms (eCRF) from screening up to Day 99
Part 2: PK parameters of RO7268489 and its metabolites, measured using standard non-compartmental method from the plasma samples collected at multiple timepoints up to Day 89

Secondary outcome measures
1. Part 1: PK parameters of RO7268489 and its metabolites, measured using standard non-compartmental methods from the plasma samples collected at multiple timepoints up to Day 99
2. Part 1: PK parameters of RO7268489 and its metabolites, measured using standard non-compartmental methods from the urine samples collected at multiple timepoints up to Day 30
3. Part 1: Concentration of RO7268489 and its metabolites in cerebrospinal fluid (CSF) measured using standard non-compartmental methods from samples collected at pre-dose and multiple timepoints post-dose up to Day 27
4. Part 1: Time course of 2-AG levels in CSF and serum measured using validated LC-MS/MS method from samples collected at pre-dose and multiple time-points post-dose up to Day 32
5. Part 1: Change from Baseline in 2- arachidonoylglycerol (2-AG) levels in CSF and serum measured using validated liquid chromatography coupled to tandem mass spectrometry (LC-MS /MS) method from samples collected at pre-dose and multiple timepoints post-dose up to Day 32
6. Part 1 and 2: Change in neuropsychiatric symptom scores using the Brief Psychiatric Rating Scale (BPRS) from baseline up to follow-up (Part 1: up to Day 99, Part 2: up to Day 89)
7. Part 1 and 2: Change in suicide risk the using Columbia-Suicide Severity Rating Scale (C-SSRS) from baseline up to follow-up (Part 1: up to Day 99, Part 2: up to Day 89)

8. Part 1 and 2: Assessment of withdrawal symptoms using the Cannabis Withdrawal Scale from baseline up to Day 54 and Day 34, respectively
9. Part 1: Change in cognition using a Neurocognitive Test Battery from screening up to follow-up (up to Day 99)
10. Part 2: Number of participants with AEs and severity of AEs determined according to data collected on eCRF from screening up to follow-up (up to Day 89)
11. Part 2: RO7268489 related change in 2-AG levels in the serum measured using validated LC-MS/MS method from samples collected at pre-dose and multiple time-points post-dose up to Day 89
12. Part 2: PK parameters of Itraconazole and its Metabolites, measured using standard non-compartmental methods from the plasma samples collected at multiple timepoints, from Day 11 to Day 34

Overall study start date
20/02/2024

Completion date
19/03/2025

Eligibility

Key inclusion criteria
1. Male or female participants aged 18 - 64 years, who are overtly healthy (defined by absence of evidence of any active or chronic disease)
2. BMI within the range of 18.5 to 30 kg/m² (inclusive)

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
64 Years

Sex
Both

Target number of participants
68

Key exclusion criteria
1. History of malignancy in the past 5 years.
2. History of any clinically significant psychiatric disorder.
3. History of severe unpleasant experience following the use of cannabis-containing products
4. History or evidence of any medical condition potentially altering the absorption, metabolism, or elimination of drugs.

5. Any contraindications for magnetic resonance imaging (MRI) scans or any brain/head abnormalities restricting MRI eligibility (Part 1 only).
6. Vaccination within 2 weeks prior to Day 1 including influenza and/or SARS-CoV-2/ COVID-19 vaccination

Date of first enrolment
10/06/2024

Date of final enrolment
08/01/2025

Locations

Countries of recruitment
Netherlands

Study participating centre
ICON
Van Swietenlaan 6,
Groningen
Netherlands
9728 NZ

Sponsor information

Organisation
F. Hoffmann-La Roche Ltd

Sponsor details
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Sponsor type
Industry

Website
www.roche.com/about/

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
19/03/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to participant-level data not being a regulatory requirement.

IPD sharing plan summary
Not expected to be made available