

# Study to evaluate the safety, tolerability, and effect of the body and food on RO7308480 following oral administration in healthy participants

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<b>Registration date</b> 11/02/2022	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 10/02/2022	<b>Condition category</b> Other	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

This is the first study where the drug RO7308480 will be given to humans. The aims of this study are to test the safety of RO7308480 at different dose levels, determine how well it is tolerated by the participants; measure how the body absorbs, distributes, and gets rid of it (this is called pharmacokinetics); and to determine the effect that food can have on its pharmacokinetics. The study results will be used to support further clinical development of RO7308480.

### Who can participate?

Healthy volunteers between 18 to 55 years of age

### What does the study involve?

This study consists of two parts, Part 1, and Part 2. Participants will be assigned to either Part 1 or Part 2.

#### Part 1

Participants may be asked to be in the study for about 8 weeks in Part 1. This includes:

1. A screening visit within 28 days before treatment administration where tests will be done to check if the participants are eligible to take part in the study
2. An inpatient stay at the clinic for 8 days and 7 nights (from 2 days before until 6 days after treatment)
3. Six walk-in visits on Days 7, 8, 10, 12, 14, and 28 after treatment.

Part 1 or the "single-ascending dose" stage will evaluate the safety, tolerability, and pharmacokinetics of RO7308480. Participants will be divided into seven different groups, with each group receiving a higher dose level than the preceding group. A higher dose level will only be administered in participants after the lower dose levels have been shown to be safe and well-tolerated in previous participants. Each group will have a maximum of 12 participants of which 9 will receive RO7308480 and 3 will receive a placebo (a drug without the active substance).

Each of the seven dose levels will be split into two groups. Two participants will be dosed on Day 1 (one participant will receive RO7308480 and one participant will receive a placebo). The rest of the group (a minimum of five participants on active treatment and a minimum of one participant on placebo) will be dosed no earlier than 24 hours later.

Participants will be given RO7308480 or matching placebo capsules to be swallowed whole with about 240 ml water at room temperature on the morning of Day 1 after an overnight fast of at least 10 hours.

## Part 2

Participants may be asked to be in the study for about 14 weeks in Part 2. This includes:

1. A screening visit within 28 days before treatment administration where tests will be done to check if the participants are eligible to take part in the study
2. An inpatient stay at the clinic twice – each time for 7 days and 6 nights (from 1 day before each of the treatments until 6 days after each treatment)
3. A period in between the two treatment administrations of 14 to 28 days where the drug is expected to be eliminated after the first administration (wash-out)
4. Six ambulatory visits on Days 7, 8, 10, 12, 14, and 28 after the second treatment.

Part 2 or the “food effect” (FE) assessment will evaluate the effect of food on the levels of RO7308480 in the body, whether and how food affects the speed and extent with which the body absorbs, distributes, and gets rid of RO7308480. A maximum of 12 participants will be enrolled in Part 2.

There will be two study periods in Part 2. In the first period, six participants will receive RO7308480 under fasted conditions (overnight fasting) and the remaining six will receive the same dose of the drug under fed conditions (after breakfast). In the second period, participants will receive the same dose of RO7308480 under the other condition. In other words, if the first study drug administration was done under fasted conditions, the second one will be done in the fed condition, and vice-versa. There will be an interval of about 14 to 28 days between both periods (wash-out period).

What are the possible benefits and risks of participating?

Participants will not receive any benefit from participating in this study, but the information that is learned may help further the clinical development of RO7308480.

Participants may experience side effects from the treatments or procedures in this study. Side effects can vary from mild to very serious and may be different from person to person.

RO7308480 has not yet been tested in humans, and the side effects of this drug are not known at this time. Based on laboratory studies and knowledge of other drugs, the potential risks listed below may occur.

1. Allergic reactions such as itching, difficulty breathing, a rash, and/or a drop in blood pressure
2. Central nervous system related effects
3. Slurred speech (e.g., mumbling)
4. Mental disturbances such as mood disorders, prolonged periods of extreme sadness, agitation, and irritability
5. Symptoms of overdose may include sedation, unconscious state, and slow or ineffective breathing

There may be a risk in exposing an unborn child to the study treatment, and not all potential consequences are known at this time. Women and men must take precautions to avoid exposing an unborn child or a breastfed baby to the study treatment. Participants who are pregnant, become pregnant, or are currently breastfeeding cannot take part in this study.

Where is the study run from?

F. Hoffmann-La Roche Ltd (USA)

When is the study starting and how long is it expected to run for?

November 2021 to July 2022

Who is funding the study?

F. Hoffmann-La Roche Ltd (USA)

Who is the main contact?

global-roche-genentech-trials@gene.com

## Contact information

### Type(s)

Public

### Contact name

Dr Clinical Trials

### Contact details

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United States of America

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## Additional identifiers

### EudraCT/CTIS number

2021-004128-13

### IRAS number

### ClinicalTrials.gov number

Nil known

### Secondary identifying numbers

BP43318

## Study information

### Scientific Title

A Phase I randomized, investigator/participant-blind, adaptive, single ascending dose, placebo-controlled study to investigate the safety, tolerability, pharmacokinetics, and food effects of RO7308480 following oral administration in healthy participants

### Study objectives

The purpose of this study is to assess the safety, tolerability, pharmacokinetics (PK), and food effects (FE) of single-ascending oral doses of RO7308480 in healthy participants.

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

Approved 11/01/2022, Committee for the Protection of Persons South-East IV (Centre Léon Bérard 28 rue Laennec - 69373 Lyon Cedex 08; +33 (0)4 78 78 27 61; cppse4@lyon.unicancer.fr), ref: 21.04076.000032

## **Study design**

Phase I randomized two-part study:

Part 1: adaptive investigator/participant-blind single-ascending dose (SAD) placebo-controlled parallel design

Part 2: open-label single-dose two-period two-sequence two-treatment ("fed-fasted", "fasted-fed") crossover design

## **Primary study design**

Interventional

## **Secondary study design**

Randomised parallel trial

## **Study setting(s)**

Other

## **Study type(s)**

Treatment

## **Participant information sheet**

Not applicable

## **Health condition(s) or problem(s) studied**

Safety, tolerability, pharmacokinetics, and food effects of single-ascending oral doses of RO7308480 in healthy participants

## **Interventions**

Part 1: RO7308480-SAD Cohorts: Participants will receive a single dose of RO7308480 capsule, orally, under fasted conditions on Day 1 in cohort 1. The dose will be escalated in subsequent cohorts in six steps as per the Sponsor's clinical pharmacologist and Principal Investigator's judgment

Part 1: Placebo-SAD Cohorts: Participants will receive a single dose of RO7308480 matching placebo capsule, orally, under fasted conditions on Day 1 of the SAD stage

Part 2: Food Effect Assessment (FE)-Fasted Period: Participants will receive a single dose of RO7308480 capsule, orally, under fasted conditions on Day 1 of the FEC-fasted period

Part 2: FE-Fed Period: Participants will receive a single dose of RO7308480 capsule, orally, 30 minutes after a standardized high fat, high-calorie breakfast on Day 1 of the FE-fed period

This study consists of two parts, Part 1, and Part 2. Participants will be assigned to either Part 1 or Part 2.

## Part 1

Participants may be asked to be in the study for about 8 weeks in Part 1. This includes:

1. A screening visit within 28 days before treatment administration where tests will be done to check if the participants are eligible to take part in the study
2. An inpatient stay at the clinic for 8 days and 7 nights (from 2 days before until 6 days after treatment)
3. Six walk-in visits on Days 7, 8, 10, 12, 14, and 28 after treatment.

Part 1 or the “single-ascending dose” stage will evaluate the safety, tolerability, and pharmacokinetics of RO7308480. Participants will be divided into seven different groups, with each group receiving a higher dose level than the preceding group. A higher dose level will only be administered in participants after the lower dose levels have been shown to be safe and well-tolerated in previous participants. Each group will have a maximum of 12 participants of which 9 will receive RO7308480 and 3 will receive a placebo (a drug without the active substance).

Each of the seven dose levels will be split into two groups. Two participants will be dosed on Day 1 (one participant will receive RO7308480 and one participant will receive a placebo). The rest of the group (a minimum of five participants on active treatment and a minimum of one participant on placebo) will be dosed no earlier than 24 hours later.

Participants will be given RO7308480 or matching placebo capsules to be swallowed whole with about 240 ml water at room temperature on the morning of Day 1 after an overnight fast of at least 10 hours.

## Part 2

Participants may be asked to be in the study for about 14 weeks in Part 2. This includes:

1. A screening visit within 28 days before treatment administration where tests will be done to check if the participants are eligible to take part in the study
2. An inpatient stay at the clinic twice – each time for 7 days and 6 nights (from 1 day before each of the treatments until 6 days after each treatment)
3. A period in between the two treatment administrations of 14 to 28 days where the drug is expected to be eliminated after the first administration (wash-out)
4. Six ambulatory visits on Days 7, 8, 10, 12, 14, and 28 after the second treatment.

Part 2 or the “food effect” (FE) assessment will evaluate the effect of food on the levels of RO7308480 in the body, whether and how food affects the speed and extent with which the body absorbs, distributes, and gets rid of RO7308480. A maximum of 12 participants will be enrolled in Part 2. There will be two study periods in Part 2. In the first period, six participants will receive RO7308480 under fasted conditions (overnight fasting) and the remaining six will receive the same dose of the drug under fed conditions (after breakfast). In the second period, participants will receive the same dose of RO7308480 under the other condition. In other words, if the first study drug administration was done under fasted conditions, the second one will be done in the fed condition, and vice-versa. There will be an interval of about 14 to 28 days between both periods (wash-out period).

## Intervention Type

Drug

## Phase

Phase I

## Drug/device/biological/vaccine name(s)

RO7308480

## Primary outcome measure

1. Part 1 and 2: Percentage of participants with adverse event (AEs), recorded by non-leading verbal questioning of the participant, from screening up to Day 14 and 28 days after study drug administration (up to approximately 6 months) in single-ascending dose (SAD) and food effect assessment (FE) stages, respectively
2. Part 1 and 2: Percentage of participants with the severity of AEs as assessed by the investigator (mild, moderate, or severe) from screening up to Day 14 and 28 days after study drug administration (up to approximately 6 months) in SAD and FE stages, respectively
3. Part 1 and 2: Percentage of participants with clinically significant changes in vital signs values measured using body temperature (tympanic), pulse rate, respiratory rate, and blood pressure from screening up to Day 14 and 28 days after study drug administration (up to approximately 6 months) in SAD and FE stages, respectively
4. Part 1 and 2: Percentage of participants with clinically significant changes in physical findings measured by assessment of cardiovascular, respiratory, gastrointestinal, dermatological, neurological, and musculoskeletal systems in addition to head, eyes, ears, nose, throat, neck, and lymph nodes from screening up to Day 14 and 28 days after study drug administration (up to approximately 6 months) in SAD and FE stages, respectively
5. Part 1 and 2: Percentage of participants with clinically significant changes in neurological findings assessed using measurement of motor and sensory skills, functioning of cranial nerves (including pupillary responses), coordination, gait, reflexes, and mental status from screening up to Day 14 and 28 days after study drug administration (up to approximately 6 months) in SAD and FE stages, respectively
6. Part 1 and 2: Percentage of participants with clinically significant changes in electrocardiogram (ECG) parameters measured using 12-lead ECG and Holter ECG (only in Part 1) from screening up to Day 14 and 28 days after study drug administration (up to approximately 6 months) in SAD and FE stages, respectively
7. Part 1 and 2: Percentage of participants with significant changes in clinical laboratory results measured using blood or urine samples collected from screening up to Day 14 and 28 days after study drug administration (up to approximately 6 months) in SAD and FE stages, respectively

## Secondary outcome measures

Measured from blood samples using a specific and validated liquid chromatography-mass spectrometry/mass spectrometry (LC-MS/MS) method:

1. Part 1: Maximum observed plasma concentration (C<sub>max</sub>) of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 hours (h) thereafter up to Day 14 in SAD stage
2. Part 1: Time to maximum observed concentration (T<sub>max</sub>) of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in SAD stage
3. Part 1: Area under the plasma concentration-time curve from time zero up to the last measurable concentration (AUC<sub>last</sub>) of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in SAD stage
4. Part 1: Area under the plasma concentration-time curve from time zero up to 24 h (AUC<sub>0-24h</sub>) of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in SAD stage
5. Part 1: Area under the plasma concentration-time curve from time zero extrapolated to infinity (AUC<sub>inf</sub>) of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in SAD stage
6. Part 1: Area under the plasma concentration-time curve from zero up to a given time (AUC<sub>0-t</sub>)

of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in SAD stage

7. Part 1: Terminal rate constant ( $\lambda_z$ ) calculated by linear regression of the log-transformed terminal part of the concentration-time curve of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in SAD stage

8. Part 1: Apparent terminal half-life ( $t_{1/2}$ ), computed as  $\log(2)$  per  $\lambda_z$  ( $\ln(2)/\lambda_z$ ) of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in SAD stage

9. Part 1: Apparent clearance (CL/F) calculated from Dose/AUC<sub>inf</sub> of RO7308480 measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in SAD stage

10. Part 1: Cumulative amount excreted (A<sub>e</sub>) unchanged into urine of RO7308480 and its metabolites, as appropriate, measured using urine samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 6 in Part 1 (SAD) only

11. Part 1: Fraction of dose excreted (F<sub>e</sub>) unchanged in urine of RO7308480 and its metabolites, as appropriate, measured using urine samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 6 in Part 1 (SAD) only

12. Part 1: Calculated renal clearance (CLR), computed as A<sub>e</sub>/AUC of RO7308480 measured using urine samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 6 in Part 1 (SAD) only

13. Part 2: Maximum observed plasma concentration (C<sub>max</sub>) of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in FE (fed and fasted state) stage

14. Part 2: Time to maximum observed concentration (T<sub>max</sub>) of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in FE (fed and fasted state) stage

15. Part 2: Area under the plasma concentration-time curve from time zero up to the last measurable concentration (AUC<sub>last</sub>) of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in FE (fed and fasted state) stage

16. Part 2: Area under the plasma concentration-time curve from time zero up to 24 h (AUC<sub>0-24h</sub>) of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in FE (fed and fasted state) stage

17. Part 2: Area under the plasma concentration-time curve from time zero extrapolated to infinity (AUC<sub>inf</sub>) of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in FE (fed and fasted state) stage

18. Part 2: Area under the plasma concentration-time curve from zero up to a given time (AUC<sub>0-t</sub>) of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in FE (fed and fasted state) stage

19. Part 2: Terminal rate constant ( $\lambda_z$ ) calculated by linear regression of the log-transformed terminal part of the concentration-time curve of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in FE (fed and fasted state) stage

20. Part 2: Apparent terminal half-life ( $t_{1/2}$ ), computed as  $\log(2)$  per  $\lambda_z$  ( $\ln(2)/\lambda_z$ ) of RO7308480 and its metabolites, as appropriate, measured using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 in FE (fed and fasted state) stage

21. Part 2: Apparent clearance (CL/F) calculated from Dose/AUC<sub>inf</sub> of RO7308480 measured

using blood samples at pre-dose and multiple time-points post-dose on Day 1 and every 12 h thereafter up to Day 14 FE (fed and fasted state) stage

**Overall study start date**

02/11/2021

**Completion date**

19/07/2022

## **Eligibility**

**Key inclusion criteria**

1. 18 to 55 years of age inclusive, at the time of signing the informed consent
2. Male and female participants who are overtly healthy (defined by the absence of evidence of any active or chronic disease) as determined by medical evaluation
3. Participants able to communicate with the study staff
4. Body mass index (BMI) of 18 to 30 kg/m<sup>2</sup> inclusive

**Participant type(s)**

Healthy volunteer

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

96

**Key exclusion criteria**

1. Any condition or disease detected during the medical interview/physical examination that could relapse during or immediately after the study
2. Use of any psychoactive medication, or medications known to have effects on central nervous system (CNS) or blood flow taken within 4 weeks prior to first dosing
3. History of convulsions (other than benign febrile convulsions of childhood) including epilepsy, or personal history of significant cerebral trauma or CNS infections (e.g., meningitis)
4. Any major illness within one month before the screening examination (e.g., COVID-19 infection) or any febrile illness within 1 week prior to screening and up to first study drug administration
5. Clinically significant abnormalities in laboratory test results
6. Current or chronic history of liver disease, or known hepatic or biliary abnormalities
7. Participants who, in the Investigator's judgment, pose a suicidal or homicidal risk, or any participant with a history of suicidal or homicidal attempts
8. Participants likely to need concomitant medication during the study period
9. Use of isotretinoin within 2 years prior to screening
10. Incomplete SARS-CoV-2/COVID-19 vaccinations scheme 2 weeks prior to administration of



the first dose

11. Participation in an investigational drug or device study within 90 days prior to screening, as calculated from the day of follow-up from the previous study, or more than four times a year

12. Show evidence of human immunodeficiency virus (HIV) infection and/or positive human HIV antibodies

13. Positive result on hepatitis B virus (HBV) or hepatitis C virus (HCV) at screening or within 3 months prior to starting study treatment

14. Any suspicion or history of alcohol abuse

15. Sensitivity to any of the study treatments, or components thereof, or drug or other allergy that contraindicates the participation in the study

16. Participants who regularly smoke more than 5 cigarettes daily or equivalent amount of tobacco and nicotine substitutes as determined by history, and unable or unwilling not to smoke during the in-house period

#### **Date of first enrolment**

15/02/2022

#### **Date of final enrolment**

20/06/2022

## **Locations**

#### **Countries of recruitment**

France

#### **Study participating centre**

##### **Biotrial**

7-9 Rue Jean-Louis Bertrand

Rennes

France

35000

## **Sponsor information**

#### **Organisation**

F. Hoffmann-La Roche Ltd

#### **Sponsor details**

1 DNA Way

South San Francisco

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94080

+1 (0)888 662 6728

global-roche-genentech-trials@gene.com

#### **Sponsor type**

Industry

**Website**

[https://www.roche.com/about\\_roche/roche\\_worldwide.htm](https://www.roche.com/about_roche/roche_worldwide.htm)

## **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**

19/07/2023

**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