

A study to evaluate the safety, tolerability and processing by the body of RO7440688 in healthy volunteers

Submission date 05/02/2021	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 10/03/2021	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 08/04/2024	Condition category Circulatory System	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Current plain English summary as of 05/11/2021:

Background and study aims

The aim of this study is to test a new drug RO744068 compared with placebo at different doses, to find out if it is safe and to understand the way people process the drug. A placebo looks like a drug but has no active ingredient.

Who can participate?

Healthy male and female volunteers aged 18 to 65 years, inclusive

What does the study involve?

Participants are randomly assigned to receive either RO744068 or placebo as a single dose or multiple doses to determine the safety and the way people process the drug. The total maximum study duration for participants is about 50 days.

What are the possible benefits and risks of participating?

Participants are not expected to receive any direct benefits from the study, but the information that is learned may help other people in the future. RO744068 has not yet been tested in humans. This is the first trial of RO744068 in humans. For this reason, the side effects of this drug are not known at this time.

Where is the study run from?

Christchurch Clinical Studies Trust (New Zealand)

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

March 2021 to March 2022

Who is funding the study?

Genentech, Inc. (USA)

Who is the main contact?
global-roche-genentech-trials@gene.com

Previous plain English summary:

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Who is the main contact?

global-roche-genentech-trials@gene.com

Contact information

Type(s)

Scientific

Contact name

Dr Clinical Trials

Contact details

1 DNA Way

South San Francisco

United States of America

94080

+1 888-662-6728

global-roche-genentech-trials@gene.com

Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

GC42880

Study information

Scientific Title

A phase I, randomized, double-blind, placebo-controlled, dose-escalation study to evaluate the safety, tolerability, and pharmacokinetics of single and multiple ascending oral doses of RO7440688, the effect of food on the pharmacokinetics of RO7440688, and the effects of RO7440688 on midazolam pharmacokinetics in healthy volunteers

Study objectives

Current study hypothesis as of 05/11/2021:

To assess safety, tolerability, and pharmacokinetics of RO7440688 when administered to healthy volunteers.

Previous study hypothesis:

To assess safety, tolerability, and pharmacokinetics of RO7440688 when administered to healthy volunteers in single or multiple doses

Ethics approval required

Old ethics approval format

Ethics approval(s)

Not provided at time of registration

Study design

Single-centre Phase I trial including a randomized single ascending dose, food effect, and multiple ascending dose study, and a non-randomized drug-drug interaction study

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details to request a patient information sheet.

Health condition(s) or problem(s) studied

Cardiovascular disease

Interventions

Current intervention as of 05/11/2021:

Participants will be randomized to the treatment arms via a blinded Randomization List. In the single-ascending dose (SAD) study, each cohort will evaluate oral administration of RO7440688. The initial dose of RO7440688 will be 150 mg and subsequent doses will be determined based on review of safety and PK data. In SAD and Food Effect stages, all participants will reside at the clinical research unit for 72 hours after dosing and return for a scheduled non-residential follow-up visit. MAD participants will reside at the clinical research unit through the completion of the 7 day dosing period through 72 hours after last dose and complete non-residential follow-up visits through Day 35. The drug-drug interaction cohort is not randomized. Participants will be administered midazolam and multiple doses of RO7440688 (these dose levels will be determined by MAD) and will remain in the clinical research unit through completion of the dosing period up through 24 hours after the last dose and complete residential follow-up visits through Day 38.

Previous intervention:

Participants will be randomized to the treatment arms via a blinded Randomization List. In the single-ascending dose (SAD) study, each cohort will evaluate oral administration of RO7440688. The initial dose of RO7440688 will be 150 mg and subsequent doses will be determined based on review of safety and PK data. In SAD and Food Effect stages, all participants will reside at the clinical research unit for 72 hours after dosing and return for a scheduled non-residential follow-up visit. MAD participants will reside at the clinical research unit through the completion of the 7 day dosing period through 72 hours after last dose and complete non-residential follow-up visits through Day 35.

Intervention Type

Drug

Phase

Phase I

Drug/device/biological/vaccine name(s)

RO7440688

Primary outcome measure

1. Incidence of adverse events (DAIDS toxicity grading scale) throughout the study
2. Vital signs (respiratory rate, pulse rate, and systolic and diastolic blood pressure, and temperature) measured at baseline and daily post-dose (Day 1-15 in the SAD and Food Effect cohorts, and Day 1- 35 in the MAD cohorts)
3. Clinical laboratory test results, including chemistry panel, hematology panel, lipid panel, coagulation panel, methemoglobin level and urinalysis measured at baseline and post dose (Day 1-15 in SAD and Food Effect cohorts, and Day 1-35 in the MAD cohorts)

4. ECG abnormalities as measured by 12-lead ECG throughout the course of the study (Day 1-15 in the SAD and Food Effect cohorts, and Day 1- 35 in the MAD cohorts)

Secondary outcome measures

Current secondary outcome measures as of 05/11/2021:

1. Pharmacokinetics (PK) of RO7440688 following a single and multiple doses, and the effect of food on the PK of RO7440688 following a single dose, on the basis of plasma concentrations of RO7440688 measured at specified timepoints. The following PK parameters will be calculated if data allow:

1.1. SAD stage: AUC₀₋₂₄, AUC from time 0 to last quantifiable concentration (AUC_{0-last}), AUC from time 0 to infinity (AUC_{0-inf}), percentage of AUC extrapolated (AUC%extrap), C_{max}, t_{max}, apparent clearance (CL/F), apparent volume of distribution during elimination phase (V_z/F), elimination rate constant (λ Z), and apparent half-life (t_{1/2})

1.2. MAD stage: AUC_{0-tau}, C_{max}, t_{max}, C_{trough}, average concentration at steady state (C_{ave,ss}), peak/trough fluctuation at steady state, accumulation ratios (ARs) for C_{max} and AUC_{0-tau} on the last versus first day of dosing, CL/F, V_z/F, apparent steady-state volume of distribution (V_{ss}/F), λ Z, and t_{1/2}

1.3. Food effect stage: AUC₀₋₂₄, AUC_{0-last}, AUC_{0-inf}, AUC%extrap, C_{max}, t_{max}, CL/F, V_z/F, λ Z, t_{1/2}, relative bioavailability of RO7440688 following a high-fat breakfast versus fasted based on AUC and C_{max}, and relative bioavailability of RO7440688 following a low-fat breakfast versus fasted based on AUC and C_{max} (if appropriate)

1.4 Drug-Drug Interaction stage: plasma pharmacokinetics of midazolam and its metabolite 1-hydroxy midazolam including, but not limited to AUC_{0-t}, AUC_{0-inf}, C_{max}, t_{max}, CL/F, t_{1/2}

For SAD/food effect cohorts, PK will be collected on Day 1 (predose, 15min, 30min, 1h, 2h, 4h, 6h, 8h, 12h post-dose), Day 2 (24h post-dose), Day 3 (48h post-dose), Day 4 (72 post-dose), and anytime during clinic visit on Day 15.

For MAD cohorts, PK will be collected on Day 1 (predose, 15min, 30min, 1h, 2h, 4h, 6h, 8h, 12h post-dose), Day 2 (pre-dose), Day 3 (pre-dose), Day 5 (pre-dose), Day 7 (predose, 15min, 30min, 1h, 2h, 4h, 6h, 8h, 12h post-dose), Day 8 (24h after final dose), Day 9 (48h after final dose), Day 10 (72h after final dose), and anytime during clinic visit on Day 14.

For DDI cohorts, PK will be collected on Day 1 (predose, 30 m, 1, 2, 3, 4, 6, 8, 12, 16, 20 hpost-dose), Day 2 (24 h post-Day 1 dose), Day 7-9 (predose), Day 10 (same as Day 1), Day 11 (24 h post-final dose)

Previous secondary outcome measures:

1. Pharmacokinetics (PK) of RO7440688 following a single and multiple doses, and the effect of food on the PK of RO7440688 following a single dose, on the basis of plasma concentrations of RO7440688 measured at specified timepoints. The following PK parameters will be calculated if data allow:

1.1. SAD stage: AUC₀₋₂₄, AUC from time 0 to last quantifiable concentration (AUC_{0-last}), AUC from time 0 to infinity (AUC_{0-inf}), percentage of AUC extrapolated (AUC%extrap), C_{max}, t_{max}, apparent clearance (CL/F), apparent volume of distribution during elimination phase (V_z/F), elimination rate constant (λ Z), and apparent half-life (t_{1/2})

1.2. MAD stage: AUC_{0-tau}, C_{max}, t_{max}, C_{trough}, average concentration at steady state (C_{ave,ss}), peak/trough fluctuation at steady state, accumulation ratios (ARs) for C_{max} and AUC_{0-tau} on the last versus first day of dosing, CL/F, V_z/F, apparent steady-state volume of distribution (V_{ss}/F), λ Z, and t_{1/2}

1.3. Food effect stage: AUC₀₋₂₄, AUC_{0-last}, AUC_{0-inf}, AUC%extrap, C_{max}, t_{max}, CL/F, V_z/F, λ Z, t_{1/2}, relative bioavailability of RO7440688 following a high-fat breakfast versus fasted based on

AUC and Cmax, and relative bioavailability of RO7440688 following a low-fat breakfast versus fasted based on AUC and Cmax (if appropriate)

For SAD/food effect cohorts, PK will be collected on Day 1 (predose, 15min, 30min, 1h, 2h, 4h, 6h, 8h, 12h post-dose), Day 2 (24h post-dose), Day 3 (48h post-dose), Day 4 (72 post-dose), and anytime during clinic visit on Day 15.

For MAD cohorts, PK will be collected on Day 1 (predose, 15min, 30min, 1h, 2h, 4h, 6h, 8h, 12h post-dose), Day 2 (pre-dose), Day 3 (pre-dose), Day 5 (pre-dose), Day 7 (predose, 15min, 30min, 1h, 2h, 4h, 6h, 8h, 12h post-dose), Day 8 (24h after final dose), Day 9 (48h after final dose), Day 10 (72h after final dose), and anytime during clinic visit on Day 14.

Overall study start date

04/02/2021

Completion date

21/03/2022

Eligibility

Key inclusion criteria

1. Age ≥ 18 years and ≤ 65 years
2. Ability to comply with the study protocol, in the investigator's judgment
3. Use of contraceptive measures

Participant type(s)

Healthy volunteer

Age group

Mixed

Lower age limit

18 Years

Upper age limit

65 Years

Sex

Both

Target number of participants

116

Total final enrolment

67

Key exclusion criteria

Current participant exclusion criteria as of 05/11/2021:

1. Pregnant or breastfeeding, or intending to become pregnant during the study or within 14 days of last study drug dose for subjects in the SAD and food effect stages and 28 days for

subjects in the MAD and DDI stages

2. No comorbid conditions that may interfere with the evaluation of an investigational medical product
3. No history or evidence of substance abuse that would pose a risk to participants safety, interfere with the conduct of the study, or have an impact on the study results
4. History of severe allergic or anaphylactic reactions to human, humanized, or Current treatment with medications that are well known to prolong the QT

Previous participant exclusion criteria:

1. Pregnant or breastfeeding, or intending to become pregnant during the study or within 14 days of last study drug dose for subjects in the SAD and food effect stages and 28 days for subjects in the MAD stage
2. No comorbid conditions that may interfere with the evaluation of an investigational medical product
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4. History of severe allergic or anaphylactic reactions to human, humanized, or Current treatment with medications that are well known to prolong the QT

Date of first enrolment

20/04/2021

Date of final enrolment

11/12/2021

Locations

Countries of recruitment

New Zealand

Study participating centre

Christchurch Clinical Studies Trust

Level 4 - 264 Antigua St.

Christchurch

New Zealand

8011

Sponsor information

Organisation

Genentech, Inc

Sponsor details

1 DNA Way

South San Francisco

United States of America

94080
+1 888 662 6728
global.clinical_trial_registry@roche.com

Sponsor type
Industry

Website
http://www.roche.com/about_roche/roche_worldwide.htm

Funder(s)

Funder type
Industry

Funder Name
Genentech

Results and Publications

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

Intention to publish date
31/05/2023

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 confidentiality.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		23/07/2023	08/04/2024	Yes	No