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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	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 10/03/2021	**Overall study status** Completed	
Last Edited 08/04/2024	**Condition category** Circulatory System	

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
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South San Francisco
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Additional identifiers

Protocol serial number
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 multipleascending 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

Primary study design
Interventional

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

Study type(s)
Treatment

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:
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Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
RO7440688

Primary outcome(s)
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)

Key secondary outcome(s)
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 (AUC0-last), AUC from time 0 to infinity (AUC0-inf), percentage of AUC extrapolated (AUC%extrap), Cmax, tmax, apparent clearance (CL/F), apparent volume of distribution during elimination phase (Vz/F), elimination rate constant (λZ), and apparent half-life (t1/2)
1.2. MAD stage: AUC0-tau, Cmax, tmax, Ctrough, average concentration at steady state (Cave,ss), peak/trough fluctuation at steady state, accumulation ratios (ARs) for Cmax and AUC0-tau on the last versus first day of dosing, CL/F, Vz/F, apparent steady-state volume of distribution (Vss /F), λZ, and t1/2
1.3. Food effect stage: AUC0-24, AUC0-last, AUC0-inf, AUC%extrap, Cmax, tmax, CL/F, Vz/F, λZ, t1

/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)
1.4 Drug-Drug Interaction stage: plasma pharmacokinetics of midazolam and its metabolite 1-hydroxy midazolam including, but not limited to AUC0-t, AUC0-inf, Cmax, tmax, CL/F, t1/2

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 (AUC0-last), AUC from time 0 to infinity (AUC0-inf), percentage of AUC extrapolated (AUC%extrap), Cmax, tmax, apparent clearance (CL/F), apparent volume of distribution during elimination phase (Vz/F), elimination rate constant (λZ), and apparent half-life (t1/2)
1.2. MAD stage: AUC0-tau, Cmax, tmax, Ctrough, average concentration at steady state (Cave,ss), peak/trough fluctuation at steady state, accumulation ratios (ARs) for Cmax and AUC0-tau on the last versus first day of dosing, CL/F, Vz/F, apparent steady-state volume of distribution (Vss /F), λZ, and t1/2
1.3. Food effect stage: AUC0-24, AUC0-last, AUC0-inf, AUC%extrap, Cmax, tmax, CL/F, Vz/F, λZ, t1 /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.

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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

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
65 Years

Sex
All

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

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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

Funder(s)

Funder type
Industry

Funder Name
Genentech

Results and Publications

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