

# A two-part study to evaluate the safety, tolerability, and processing by the body (pharmacokinetics) of fenebrutinib (part A) and to evaluate the effect of fenebrutinib on the heartbeat (QT/QTc interval) (part B) in healthy subjects

<b>Submission date</b> 21/04/2021	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 29/05/2021	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 01/08/2022	<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 a two-part study of an investigational drug called fenebrutinib that will be performed in healthy volunteers. Part A will evaluate the safety and drug levels in the blood of single doses of fenebrutinib. This information will help with the selection of the doses to test in part B. Part B of the study will primarily evaluate whether fenebrutinib has any effect on the electrocardiogram, a measurement of the heart's electrical activity.

### Who can participate?

Healthy volunteers

### What does the study involve?

In part A of the study, a single dose of oral fenebrutinib or placebo will be given to volunteers to evaluate the safety and drug levels in the blood. This information will help with the selection of the doses to test in part B. In part B of the study, on different days volunteers will be given a single dose of fenebrutinib (at two different dose levels), moxifloxacin (an antibiotic), and placebo. The objective of part B is to evaluate whether fenebrutinib has any effect on the electrocardiogram, a measurement of the heart's electrical activity. Part B will also evaluate the safety and blood levels of fenebrutinib. Volunteers will participate in either part A or B, but not both.

### What are the possible benefits and risks of participating?

Study volunteers will not receive any medical benefit. They will be compensated for their time. One identified risk of fenebrutinib is potential increased blood level of liver enzymes. Other risks that have not been observed but are theoretically possible include infection, change in

levels of certain cells in the blood, liver injury, effect on vaccinations, bleeding, nausea, vomiting, diarrhea, abnormal heart rhythm, inflammation (swelling or redness) of blood vessels, ability to fight cancer, birth defects, or rash.

Where is the study run from?  
Genentech (USA)

When is the study starting and how long is it expected to run for?  
November 2020 to August 2022

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

Who is the main contact?  
global-roche-genentech-trials@gene.com, reference Protocol ID GP42654

## Contact information

### Type(s)

Public

### 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

GP42654

## Study information

### Scientific Title

A two-part, phase 1, randomized, double-blind, single ascending dose study to evaluate the safety, tolerability, and pharmacokinetics of fenebrutinib in healthy subjects (part A) and a

randomized, single-dose, placebo- and positive-controlled, crossover phase 1 study to evaluate the effect of fenebrutinib on the QT/QTc interval in healthy subjects (part B)

### **Study objectives**

To evaluate the safety, tolerability and clinical activity of fenebrutinib in healthy subjects

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approved 10/03/2021, Salus IRB (2111 West Braker Lane, Suite 100, Austin, TX, USA; +1 512-380-1244; salus@salusirb.com), ref: 8441772

### **Study design**

Single center phase I double-blinded two-part interventional study

### **Primary study design**

Interventional

### **Secondary study design**

Randomised controlled trial

### **Study setting(s)**

Hospital

### **Study type(s)**

Treatment

### **Participant information sheet**

No participant information sheet available

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

Safety, tolerability and clinical activity of fenebrutinib in healthy subjects

### **Interventions**

Part A: Single Ascending Dose Study

Participants will enroll in three sequential cohorts (A1, A2, and A3) that will test single ascending doses. In cohort A1, participants will receive a single dose of fenebrutinib or placebo, administered orally. Dosing of subsequent cohorts A2 and A3 will be contingent upon available preliminary fenebrutinib safety, tolerability, and PK data from the preceding dose. Participants in cohorts A2 and A3 will also receive a single dose of oral fenebrutinib or placebo; the dose will be determined based on analysis of the data from the prior cohort.

Duration: 1 day of treatment, 7 days of follow-up.

Part B: Thorough QT Interval Study

The fenebrutinib therapeutic dose and suprathreshold dose in Part B will be selected based on PK and safety data from Part A. Each participant will receive a single dose of the following treatments:

1. Fenebrutinib therapeutic dose
2. Fenebrutinib suprathreshold dose
3. Positive control, moxifloxacin 400-mg tablet

#### 4. Placebo

Duration: Approximately 24 days of treatment and 7 days of follow-up.

The randomization is done using a randomization list and unblinded pharmacist since there is only one site for this study. In Part A of the study participants are randomized 3:1 to active drug or placebo. In part B, participants are randomized 1:1:1:1 to one of four sequences of receiving the study drugs.

#### Intervention Type

Drug

#### Phase

Phase I

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

fenebrutinib, RO7010939

#### Primary outcome measure

Part A:

1. Incidence and severity of AEs and incidence of abnormalities measured using clinical laboratory evaluations, 12-lead ECGs, vital signs measurements, and physical examinations throughout the study

2. Pharmacokinetics measured using C<sub>max</sub>, t<sub>max</sub>, AUC<sub>0-∞</sub> and/or AUC<sub>0-t</sub>, and t<sub>1/2</sub> of fenebrutinib on days 1 and 2

Part B

1. Placebo-adjusted change from predose-averaged baseline QTcF ( $\Delta\Delta$ QTcF) of fenebrutinib measured using ECG on days 1 and 2

#### Secondary outcome measures

Part B:

1. Incidence and severity of AEs and incidence of abnormalities measured using clinical laboratory evaluations, 12-lead ECGs, vital signs measurements, and physical examinations throughout the study

2. Pharmacokinetics measured using C<sub>max</sub>, t<sub>max</sub>, AUC<sub>0-∞</sub> and/or AUC<sub>0-t</sub>, and t<sub>1/2</sub> of fenebrutinib and moxifloxacin on days 1 and 2

3. Absolute and change from baseline in heart rate and PR, RR, QRS, QT, and QTcB intervals; and change from baseline T-wave morphology and U-wave presence measured using ECG on days 1 and 2

4.  $\Delta\Delta$ QTcF of moxifloxacin measured using ... at 1, 1.5, 2, 3, and 4 hours postdose

5. Change from baseline QTcF ( $\Delta$ QTcF) at the individual t<sub>max</sub> for each treatment ( $\Delta$ QTcF, t<sub>max</sub>) measured using ECG

#### Overall study start date

23/11/2020

#### Completion date

21/08/2022

## Eligibility

#### Key inclusion criteria

1. Males or females of non-childbearing potential, between 18 and 60 years of age, inclusive;
2. Within body mass index (BMI) range 18 to 31 kg/m<sup>2</sup>, inclusive, with a bodyweight >45 kg;
3. In good health, determined by no clinically significant findings from medical history, 12-lead ECG, and vital signs;
4. Clinical laboratory evaluations (including chemistry panel [fasted at least 10 hours], complete blood count [CBC], coagulation [prothrombin time {PT}, international normalized ratio {INR}, and activated partial thromboplastin time {aPTT}], and urinalysis [UA] with complete microscopic analysis) within the reference range for the test laboratory, unless deemed not clinically significant by the investigator;
5. Negative test for selected drugs of abuse and cotinine at Screening (does not include alcohol) and at Check-in (Day -1 for Part A, Period 1 Day -1 for Part B; does include alcohol);
6. Negative hepatitis panel (hepatitis B virus core antibody, hepatitis B surface antigen, and hepatitis C virus antibody) and negative human immunodeficiency virus (HIV) antibody screens;
7. Females will not be pregnant or breastfeeding, and must be either postmenopausal (at least 12 months without a period [i.e., amenorrhea]; in a woman at least 50 years of age and documented by a serum follicle-stimulating hormone [FSH] level consistent with postmenopausal status [i.e., ≥40 IU/L] in the absence of a reversible medical iatrogenic cause) or surgically sterile (e.g., tubal ligation, bilateral salpingectomy, or hysterectomy) for at least 90 days. For all females, the pregnancy test result must be negative at Screening and Check-in (Day -1 for Part A, Period 1 Day -1 for Part B).
8. Males with partners of childbearing potential will either be sterile (confirmed by documentation in addition to agreeing to using a condom from Check-in [Day -1 for Part A, Period 1 Day -1 for Part B] until 90 days following study completion) or agree to use from Check-in (Day -1 for Part A, Period 1 Day -1 for Part B) until 90 days following study completion, one of the following approved methods of contraception: male condom with spermicide; sterile sexual partner; use by female sexual partner of an intrauterine device with spermicide; a female condom with spermicide; a contraceptive sponge with spermicide; an intravaginal system [e.g., NuvaRing®]; a diaphragm with spermicide; a cervical cap with spermicide; or oral, implantable, transdermal, or injectable contraceptives. Subjects will refrain from sperm donation from Check-in (Day -1 for Part A, Period 1 Day -1 for Part B) until 90 days or 5 half-lives plus 74 days (a spermatogenesis cycle), whichever is longer, following study completion. Male subjects (including men who have had vasectomies) whose partners are currently pregnant should use a barrier method for the duration of the study and for 90 days or 5 half-lives plus 74 days (a spermatogenesis cycle), whichever is longer, after the study completion. This is to ensure that the fetus is not exposed to the drug in the ejaculate;
9. Receive an explanation of the mandatory WGS component of the study;
10. Able to comprehend and willing to sign an Informed Consent Form (ICF);
11. Able to comply with the study restrictions.

**Participant type(s)**

Healthy volunteer

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

## Target number of participants

96

### Key exclusion criteria

1. Significant history or clinical manifestation of any metabolic, allergic, dermatological, hepatic, renal, hematological, pulmonary, cardiovascular, gastrointestinal (GI), neurological, or psychiatric disorder (as determined by the investigator)
2. Evidence of active infection (with the exception of fungal nail infections or oral herpes); history of recurrent bacterial, viral, mycobacterial, or fungal infections (defined as >2 similar episodes requiring anti-microbial treatment within the previous 12 months), with the exception of recurrent oral or genital herpes (herpes simplex virus 1/herpes simplex virus 2) or uncomplicated urinary tract infections in females; or history of infection requiring hospitalization within 8 weeks prior to Screening
3. History of significant hypersensitivity, intolerance, or allergy to any drug compound, food, or other substance, unless approved by the investigator
4. Any personal or family history of bleeding disorders and any personal use of drugs known to affect blood clotting within 30 days prior to dosing
5. Family history of intracranial bleed (berry aneurysm, hemorrhagic stroke) or recent personal history of head trauma
6. History of vasculitis
7. Having one or more of the following clinical laboratory evaluations at Screening:
  - Estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m<sup>2</sup> as calculated using the Cockcroft-Gault or Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (may be repeated if 45 to 59 mL/min/1.73 m<sup>2</sup>)
  - ALT or AST >2 × ULN (may be repeated if 2 to 3 × ULN)
  - Total bilirubin >1.5 × ULN (may be repeated if 1.6 to 3 × ULN)
  - Abnormalities in hepatic synthetic function tests (e.g., PT, INR, aPTT, albumin) judged by the investigator to be clinically significant
8. Sustained (i.e., three consecutive occasions of assessments) systolic blood pressure measurements <85 or >140 mmHg or diastolic blood pressure measurements <45 or >90 mmHg at Screening
9. Sustained (i.e., confirmed upon repeat) pulse >100 or <45 beats per minute at Screening
10. Personal or family history of congenital long QT syndrome or family history of sudden death
11. History or presence of an abnormal ECG (including marked mean QTcF prolongation ≥450 msec) at Screening or Check-in (Day -1 for Part A, Period 1 Day -1 for Part B) that, in the investigator's opinion, is clinically significant
12. Short QTc (mean QTcF <300 msec) at Screening or Check-in (Day -1 for Part A, Period 1 Day -1 for Part B)
13. Subject had dyspepsia for which he/she had recently taken (within 2 weeks prior to Check-in [Day -1 Part A, Period 1 Day -1 for Part B]) prescription and/or over-the-counter medicinal products for the control of gastric acidity (e.g., proton-pump inhibitors, H<sub>2</sub> blockers, antacids)
14. History of stomach or intestinal surgery or resection or any GI disorder that would potentially alter absorption and/or excretion of orally administered drugs, except that appendectomy, hernia repair, and/or cholecystectomy will be allowed
15. History of alcoholism or drug addiction within 1 year prior to Check-in (Day -1 for Part A, Period 1 Day -1 for Part B)
16. History of tuberculosis (TB) or treatment with TB prophylaxis within 12 months prior to study enrollment
17. Use of oral antibiotics within 4 weeks or IV antibiotics within 8 weeks prior to the Screening evaluation
18. Any vaccination within 6 weeks prior to dosing

19. Participation in any other investigational study drug trial in which receipt of an investigational study drug occurred within 30 days or 5 half-lives, whichever is longer, prior to Check-in (Day -1 for Part A, Period 1 Day -1 for Part B)
20. Use of any moderate or strong CYP3A inhibitor or inducer within 30 days or 5 half-lives, whichever is longer, prior to Check-in (Day -1 for Part A, Period 1 Day -1 for Part B)
21. Use of any prescription medications/products within 14 days or 5 half-lives, whichever is longer, prior to Check-in (Day -1 for Part A, Period 1 Day -1 for Part B), unless deemed acceptable by the investigator
22. Use of acetaminophen within 24 hours prior to Check-in (Day -1 for Part A, Period 1 Day -1 for Part B)
23. Use of any over-the-counter, non-prescription preparations (including vitamins; minerals; and phytotherapeutic-, herbal-, and plant-derived preparations) within 14 days or 5 half-lives, whichever is longer, prior to Check-in (Day -1 for Part A, Period 1 Day -1 for Part B), unless deemed acceptable by the investigator
24. Use of tobacco- or nicotine-containing products (including, but not limited to, cigarettes, e-cigarettes, pipes, cigars, chewing tobacco, nicotine patches, nicotine lozenges, or nicotine gum) within 6 months prior to Check-in (Day -1 for Part A, Period 1 Day -1 for Part B)
25. Use of grapefruit-containing foods or beverages within 7 days prior to Check-in (Day -1 for Part A, Period 1 Day -1 for Part B), unless deemed acceptable by the investigator
26. Strenuous exercise from 7 days prior to Check-in (Day -1 Part A, Period 1 Day -1 for Part B)
27. Use of alcohol- or caffeine-containing foods or beverages within 48 hours prior to Check-in (Day -1 for Part A, Period 1 Day -1 for Part B), unless deemed acceptable by the investigator
28. Poor peripheral venous access
29. History of malignancy, except for appropriately treated carcinoma in situ of the cervix or non-melanoma skin carcinoma with 3-year disease-free follow-up
30. Donation or loss of blood in excess of approximately 450 mL from 30 days prior to Screening through study completion, inclusive, or of plasma from 2 weeks prior to Screening through study completion, inclusive
31. Receipt of blood products within 2 months prior to Check-in (Day -1 for Part A, Period 1 Day -1 for Part B)
32. Any acute or chronic condition that, in the opinion of the investigator, would limit the subject's ability to complete and/or participate in this clinical study.

**Date of first enrolment**

27/04/2021

**Date of final enrolment**

18/07/2022

**Locations****Countries of recruitment**

United States of America

**Study participating centre**

**Covance Research Unit**

Dallas

United States of America

75247

# Sponsor information

## Organisation

Roche (United States)

## Sponsor details

Genentech  
1 DNA Way  
San Francisco  
United States of America  
94080  
+1 888-662-6728  
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)

## ROR

<https://ror.org/011qkaj49>

# Funder(s)

## Funder type

Industry

## Funder Name

Roche

## Alternative Name(s)

F. Hoffmann-La Roche Ltd, F. Hoffmann-La Roche & Co, F. Hoffmann-La Roche AG, Roche Holding AG, Roche Holding Ltd, Roche Holding, Roche Holding A.G., Roche Holding, Limited, F. Hoffmann-La Roche & Co., Roche Holdings, Inc.

## Funding Body Type

Government 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

20/10/2023

### 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 this not being a regulatory requirement.

### IPD sharing plan summary

Not expected to be made available