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A study to compare two different formulations of fenebrutinib and to assess the effect of food and rabeprazole on the processing of fenebrutinib by the body in healthy participants

Submission date 07/05/2024	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 07/05/2024	**Overall study status** Completed	
Last Edited 11/09/2025	**Condition category** Other	

Plain English summary of protocol

Background and study aims
Multiple sclerosis is a health condition in which the body's natural defense (immune system) attacks the protective covering of nerve fibers in the brain and spinal cord. This leads to communication issues between the brain and the rest of the body.

This study is testing a medicine called fenebrutinib. It is being developed for the treatment of multiple sclerosis.

Fenebrutinib is an experimental medicine. This means health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) have not approved fenebrutinib for the treatment of multiple sclerosis.

This study aims to compare the two different types of fenebrutinib pills (reference and test tablets) to check if fenebrutinib is absorbed into the body at the same speed and to the same extent from both these pills (bioequivalence). This study will aim to test how fenebrutinib gets to different parts of the body, and how the body changes and gets rid of it when given along with food and a medicine called rabeprazole.

Who can participate?
Healthy people (males and females) of 18-60 years of age can take part in the study. People may not be able to take part in this study if they have a liver disease that has suddenly developed or has been developing slowly and may worsen over an extended period. People with a history of stomach or intestinal surgery may not be able to take part in this study.

People who are pregnant or are currently breastfeeding cannot take part in the study.

What does the study involve?
People will be screened to check if they can participate in the study. The screening period will take place approximately 28 days before the start of the treatment.

Everyone who joins this study will be split into 2 groups randomly (like flipping a coin) to receive fenebrutinib given as a pill by mouth.

In Group I there will be two sequences in which the medicine will be administered.
Sequence 1: Participants will receive two pills of fenebrutinib (reference pills), by mouth followed by one pill of fenebrutinib (test pill) on an empty stomach by mouth, after a period of 3 days. After 3 days from the second dose, the participants will again receive fenebrutinib in the same sequence as described above.
Sequence 2: Participants will receive a single test pill of fenebrutinib, by mouth followed by 2 reference pills of fenebrutinib by mouth on an empty stomach, after a period of 3 days. After 3 days from the second dose, the participants will again receive fenebrutinib in the same sequence as described above.

In Group 2 there will be four sequences in which the medicine will be administered:
Sequence 1: Participants will receive a single test pill of fenebrutinib, by mouth on an empty stomach. After a period of 3 days, a single test pill of fenebrutinib will be given after a high-fat meal. After 3 days from the second dose, participants will receive rabeprazole by mouth, two times a day, for 3 days followed by fenebrutinib and rabeprazole given together on the fourth day on an empty stomach.
Sequence 2: Participants will receive a single test pill of fenebrutinib, by mouth on an empty stomach. After a period of 3 days, a single test pill of fenebrutinib will be given after a high-fat meal. After 3 days from the second dose, participants will receive rabeprazole by mouth, two times a day, for 3 days followed by fenebrutinib and rabeprazole given together on the fourth day after a high-fat meal.
Sequence 3: Participants will receive a single test pill of fenebrutinib, by mouth after a high-fat meal. After a period of 3 days, a single test pill of fenebrutinib will be given on an empty stomach. After 3 days from the second dose, participants will receive rabeprazole by mouth, two times a day for 3 days followed by fenebrutinib and rabeprazole given together on the fourth day on an empty stomach.
Sequence 4: Participants will receive a single test pill of fenebrutinib, by mouth after a high-fat meal. After a period of 3 days, a single test pill of fenebrutinib will be given on an empty stomach. After 3 days from the second dose, participants will receive rabeprazole by mouth, two times a day, for 3 days followed by fenebrutinib and rabeprazole given together on the fourth day after a high-fat meal.

This is an open-label study. This means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.

During this study, the participants will be required to stay at the clinic for 13 days and will be seen by the study doctor every day. Study doctors will check on the participants to see if there are any unwanted effects. Participants will receive a follow-up phone call 7 to 10 days after completing the study treatment during which the study doctor will check on the participant’s well-being. Total time of participation in the study will be about 7 weeks, including screening for both Groups 1 and 2. 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?
Taking part in the study will not provide any therapeutic benefit to healthy participants.

However, the information collected in the study can help other people with health conditions in the future.

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 participants. People 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 side effects.

Risks associated with the study drug
Participants may have unwanted effects of the drug 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.

Fenebrutinib
Participants will be told about the known unwanted effects of fenebrutinib and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects include hepatic transaminase elevation, possible unwanted effects hepatotoxicity, infections, bleeding, cytopenia, gastrointestinal effects, and malignancy.

The study medicine(s) may be harmful to an unborn baby. Women and men must take precautions to avoid exposing an unborn baby to the study treatment.

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?
September 2023 to October 2024

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

Who is the main contact?
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Contact information

Type(s)
Public, Scientific, Principal investigator

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Integrated Research Application System (IRAS)
1009864

Protocol serial number
GP44941

Study information

Scientific Title
A phase I, open-label, randomized, 2-part study to evaluate the bioequivalence of single oral doses of 2 different formulations of fenebrutinib and the effect of food and rabeprazole on the pharmacokinetics of fenebrutinib in healthy subjects

Study objectives
The main purpose of this study is to assess the bioequivalence of fenebrutinib to-be-marketed tablet (test) compared to two fenebrutinib 100 mg film-coated tablets used as reference. The study also aims to assess the effect of food and rabeprazole on the pharmacokinetics (PK) of to-be-marketed tablets of fenebrutinib.

Ethics approval required
Ethics approval required

Ethics approval(s)
Submitted 10/04/2024, Surrey Borders Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, United Kingdom; +44 207 104 8057; surreyborders.rec@hra.nhs.uk), ref: 24/LO/0228

Primary study design
Interventional

Study design
Phase I open-label single-dose randomized 2-part study

Study type(s)
Other

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

Interventions
Part 1, Sequence ABAB: Participants will first receive a single oral dose of reference fenebrutinib, 200 milligrams (mg) film-coated tablets (treatment A), under fasted conditions on Day 1 of Period 1. Participants will then receive a single oral dose of the to-be-marketed (test) fenebrutinib tablet (treatment B), under fasted conditions on Day 1 of Period 2. This will be followed by treatment A on Day 1 of Period 3 and then treatment B on Day 1 of Period 4.

There will be a 3-day washout between each drug administration.

Part 1 - Sequence BABA: Participants will first receive a single oral dose of test fenebrutinib tablet (treatment B), under fasted conditions on Day 1 of Period 1. Participants will then receive a single oral dose of reference fenebrutinib, 200 mg film-coated tablet (treatment A), under fasted conditions on Day 1 of Period 2. This will be followed by treatment B on Day 1 of Period 3 and then treatment A on Day 1 of Period 4

There will be a 3-day washout between each drug administration.

Part 2 - Sequence CDE: Participants will receive a single oral dose of test fenebrutinib tablet (treatment C), under fasted conditions on Day 1 of Period 1. On Day 1 of Period 2 participants will receive a single oral dose of test fenebrutinib tablet, after a high-fat meal (treatment D). This will be followed by oral administration of rabeprazole 20 mg, twice daily (BID) on Days 1 to 3 and co-administration of test fenebrutinib tablet with rabeprazole 20 mg under fasted condition (treatment E) in Period 3.

There will be a 3-day washout between each drug administration.

Part 2 - Sequence CDF: Participants will receive a single oral dose of test fenebrutinib tablet (treatment C), under fasted conditions on Day 1 of Period 1. On Day 1 of Period 2, participants will receive a single oral dose of test fenebrutinib tablet, after a high-fat meal (treatment D). This will be followed by oral administration of rabeprazole 20 mg, BID on Days 1 to 3 and co-administration of test fenebrutinib tablet with rabeprazole 20 mg on Day 4 after a high-fat meal (treatment F) in Period 3.

There will be a 3-day washout between each drug administration.

Part 2 - Sequence DCE: Participants will receive a single oral dose of test fenebrutinib tablet, after a high-fat meal on Day 1 of Period 1 (treatment D). On Day 1 of Period 2, participants will receive a single oral dose of test fenebrutinib tablet (treatment C), under fasted conditions. This will be followed by oral administration of rabeprazole 20 mg, BID on Days 1 to 3 and co-administration of test fenebrutinib tablet with rabeprazole 20 mg on Day 4 under fasted condition (treatment E) in Period 3.

There will be a 3-day washout between each drug administration.

Part 2 - Sequence DCF: Participants will receive a single oral dose of test fenebrutinib tablet, after a high-fat meal on Day 1 of Period 1 (treatment D). On Day 1 of Period 2, participants will receive a single oral dose of test fenebrutinib tablet, under fasted conditions (treatment C). This will be followed by oral administration of rabeprazole 20 mg, BID on Days 1 to 3 and co-administration of test fenebrutinib tablet with rabeprazole 20 mg on Day 4 after a high-fat meal (treatment E) in Period 3.

There will be a 3-day washout between each drug administration.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)

Part 1:
1. Maximum observed concentration (Cmax) of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 4
2. Area under the concentration-time curve from hour 0 to last measurable concentration (AUC 0-t) of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 4
3. Area under the concentration-time curve extrapolated to infinity (AUC 0-∞) of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 4

Part 2:
1. Cmax of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 2 and Days 4 to 6 of Period 3
2. Time to Observed Maximum Concentration (Tmax) of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 2 and Days 4 to 6 of Period 3
3. AUC 0-t of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 2 and Days 4 to 6 of Period 3
4. AUC 0-∞ of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 2 and Days 4 to 6 of Period 3
5. Apparent terminal elimination rate constant (λz) of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 2 and Days 4 to 6 of Period 3
6. Apparent terminal elimination half-life (t1/2) of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 2 and Days 4 to 6 of Period 3
7. Apparent systemic clearance (CL/F) of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 2 and Days 4 to 6 of Period 3
8. Apparent volume of distribution during the terminal elimination phase (Vz/F) of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 2 and Days 4 to 6 of Period 3
9. Relative bioavailability for Cmax (FrelCmax) of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 2 and Days 4 to 6 of Period 3
10. Relative bioavailability for AUC0-∞ (FrelAUC0-∞) of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 2 and Days 4 to 6 of Period 3

Key secondary outcome(s)

Part 1:
1. Tmax of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 4
2. λz of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 4

3. t1/2 of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 4
4. CL/F of fenebrutinib measured a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 4
5. Vz/F of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 4
6. FrelCmax of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 4
7. FrelAUC0-∞ of fenebrutinib measured using a model independent approach from blood samples collected at pre-dose and multiple timepoints post dose up to Day 3 of Periods 1 to 4
8. Number of participants with adverse events (AEs) and severity of AEs assessed as per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) (v5.0) from screening up to 10 days after the last dose (up to approximately 49 days)

Part 2:
1. Number of participants with AEs and severity of AEs assessed as per NCI CTCAE v5.0 from screening up to 10 days after last dose (up to approximately 49 days)

Completion date
23/10/2024

Eligibility

Key inclusion criteria
1. Males or females, between 18 and 60 years of age, inclusive.
2. Body weight ≥45 kilograms (kg) and within body mass index (BMI) range of 18 to 32 kilogram per meter square (kg/m^2), inclusive.
3. In good health, determined by no clinically significant findings from medical history, physical examination, 12-lead electrocardiogram (ECG), and vital signs.
4. Clinical laboratory evaluations (including chemistry panel [fasted at least 8 hours], complete blood count (CBC), and coagulation testing [prothrombin time (PT), international normalized ratio (INR), and activated partial thromboplastin time (aPTT)]) and urinalysis (UA) with complete microscopic analysis are within the reference range for the test laboratory, or clinically acceptable to the investigator if outside the normal range.
5. Negative test for selected drugs of abuse at Screening (does not include alcohol) and at Check-in (Day -1; does include alcohol).
6. Negative hepatitis panel (hepatitis B surface antigen [HBsAg], hepatitis B virus core antibody, hepatitis B surface antibody [unless consistent with vaccination or immunity due to natural infection], and hepatitis C virus antibody) and negative HIV antibody screens.
7. For females of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use highly effective contraception, and agreement to refrain from donating eggs, as defined in the protocol.
8. For males: agreement to remain abstinent (refrain from heterosexual intercourse) or use a condom with spermicide, and agreement to refrain from donating sperm, as defined in the protocol.
9. Any participant (male or female) who is abstinent or in a homosexual relationship at the time of signing ICF and becomes sexually active or in a heterosexual relationship during the above-defined period must agree to use a highly effective contraception as listed above.
10. For Part 2: able to complete a standard high-fat meal within 30 minutes.
11. Able to comprehend and willing to sign an informed consent form (ICF).

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
All

Key exclusion criteria
1. Participants who are pregnant or breastfeeding or intending to become pregnant during the study or within 28 days after the final dose of the study drug. Females must have a negative serum pregnancy test result at Screening and Check-in (Day -1)
2. Evidence of any infectious, metabolic, allergic, dermatological, hepatic (including Gilbert's syndrome), renal, hematological, pulmonary, cardiovascular, gastrointestinal (GI), neurological, or psychiatric disorder that, in the investigator's opinion, would preclude subject participation
3. Known or suspected active infection at Screening or baseline (excluding onychomycosis), or any major episode of infection requiring hospitalization or treatment with IV antimicrobials within 8 weeks prior to or during Screening or treatment with oral antimicrobials within 2 weeks prior to or during Screening
4. History of significant hypersensitivity, intolerance, or allergy to any drug compound, food, or other substance, unless approved by the investigator
5. History of stomach or intestinal surgery or resection that would potentially alter absorption and/or excretion of orally administered drugs except for appendectomy or hernia repair which will be allowed.
6. Participation in any other trial in which receipt of an investigational study drug occurred within 3 months or 5 half-lives, whichever is longer, prior to Check-in (Day -1)
7. History of any drug or alcohol abuse within 12 months prior to Screening and/or alcohol consumption of >2 units per day for males and >1 unit per day for females. One unit of alcohol equals 285 mL of beer or lager, 25 mL liquor, or 84 mL wine
8. 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)
9. Dyspepsia, gastroesophageal reflux disease (GERD), ulcer, or GI symptoms for which the subject has recently taken (within 14 days prior to Check-in [Day -1]) prescription or over-the-counter proton pump inhibitors (PPIs), H2 blockers, or antacids for the control of gastric acidity
10. Use of any prescription medications/products within 14 days or 5 half-lives, whichever is longer, prior to Check-in (Day -1), unless deemed acceptable by the investigator
11. Use of any over-the-counter, non-prescription preparations (including vitamins, minerals, and phytotherapeutic/herbal/plant-derived preparations) within 14 days or 5 half-lives, whichever is longer, prior to Check-in (Day -1), unless deemed acceptable by the investigator
12. Participants vaccinated with live, attenuated vaccines (e.g., the intranasal live attenuated influenza vaccines, Bacillus Calmette- Guérin virus, varicella) within 6 weeks prior to first dosing

(Day 1 of Period 1)
13. History of pancreatitis, cholecystectomy or gallstones, or clinically significant GI ulcer or bleeding
14. 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) and during the entire study
15. Use of furanocoumarin derivatives (e.g., grapefruit, Seville oranges, pomegranates, or star fruit) or poppy seed-containing foods or beverages within 7 days prior to Check-in (Day -1), unless deemed acceptable by the investigator
16. Use of alcohol- or caffeine-containing foods or beverages within 48 hours prior to Check-in (Day -1), unless deemed acceptable by the investigator

Date of first enrolment
22/07/2024

Date of final enrolment
26/08/2024

Locations

Countries of recruitment
United Kingdom

Study participating centre
TBD
United Kingdom
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Sponsor information

Organisation
F. Hoffmann-La Roche Ltd

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

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