ForPatients
by Roche

Multiple Sclerosis (MS)

A study in healthy people to compare two different formulations of a study medicine (fenebrutinib) and look at how its absorption is affected by food and by lowering stomach acid production

Trial Status	Trial Runs In	Trial Identifier
Completed	1 Country	ISRCTN23183841 GP44941

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official 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.

Trial Summary:

Scientists developed a new, single-tablet version of a medicine called fenebrutinib. The first goal was to check that the new single tablet worked exactly the same way in the body as the older two-tablet version. They also wanted to find out if eating a high-fat meal or taking a stomach acid-reducing medicine—changed how well the body absorbed fenebrutinib. Healthy volunteers between the ages of 18 and 60 could join, as long as they met all the rules and didn't have any health conditions that would prevent their participation. Researchers took blood samples both before and several times after people took the medicine, to measure how much fenebrutinib was in the blood and how fast the body absorbed it. Participants were observed for any unwanted side effects. Since only healthy people were in the trial, no one received direct health benefits. The great benefit was that they helped advance medical research. The risks came from the mild side effects of the medicine, which had already been tested on many people before this study began.

Genentech, Inc. (A part of F. Hoffmann-La Roche Ltd., Switzerland)	**Phase I**
Sponsor	Phase

ISRCTN23183841 GP44941
Trial Identifiers

Eligibility Criteria:

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Gender	Age	Healthy Volunteers
Both	18 to 60 years old	Yes

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)

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

Who is the main contact? global.trial_information@roche.com

Inclusion Criteria:

- Males or females, between 18 and 60 years of age, inclusive.
- Body weight #45 kilograms (kg) and within body mass index (BMI) range of 18 to 32 kilogram per meter square (kg/m²), inclusive.
- In good health, determined by no clinically significant findings from medical history, physical examination, 12-lead electrocardiogram (ECG), and vital signs.
- 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.
- Negative test for selected drugs of abuse at Screening (does not include alcohol) and at Check-in (Day -1; does include alcohol).
- 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.
- 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.
- 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.

- 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.
- For Part 2: able to complete a standard high-fat meal within 30 minutes.
- Able to comprehend and willing to sign an informed consent form (ICF).

Exclusion Criteria:

- 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)
- 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
- 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
- History of significant hypersensitivity, intolerance, or allergy to any drug compound, food, or other substance, unless approved by the investigator
- 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.
- 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)
- 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
- 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)
- 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
- 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
- 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
- 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)
- History of pancreatitis, cholecystectomy or gallstones, or clinically significant GI ulcer or bleeding
- 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
- 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
- Use of alcohol- or caffeine-containing foods or beverages within 48 hours prior to Check-in (Day -1), unless deemed acceptable by the investigator