ForPatients
by Roche

Multiple Sclerosis (MS)Relapsing Multiple Sclerosis (RMS)

Testing different doses of a new medicine (fenebrutinib) and its effect on heart rhythm (QT interval) in healthy people

Trial Status	Trial Runs In	Trial Identifier
Completed	1 Country	ISRCTN26497758 GP42654

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 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)

Trial Summary:

This clinical trial was done in healthy people to test a new medicine called, “fenebrutinib,” being developed for the treatment of multiple sclerosis or MS. This study was done to find out if fenebrutinib had any effect on the “QT interval,” a measure of a part of the heart’s electrical signal. Doctors need to know which medicines increase the QT interval so that patients can be monitored for an increased risk for heart-related side effects. This was a randomized, double-blind, placebo-controlled, single ascending dose, Phase 1 study, to test the safety, tolerability, and pharmacokinetics of fenebrutinib in healthy people.

Genentech, Inc. (A part of F. Hoffmann-La Roche Ltd., Switzerland)	Phase 1
Sponsor	Phase

ISRCTN26497758 GP42654
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	18 to 60 years	Yes

Background and study aims

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Healthy volunteers were enrolled at one study center in the USA to evaluate the safety, tolerability, and pharmacokinetics of fenebrutinib which is being developed for the treatment of multiple sclerosis. Sixteen people joined Part A to look at safety and pharmacokinetics. Eighty-five people joined Part B to look at the effect on QT interval. Results showed fenebrutinib to be safe and tolerable at the doses tested while some non-serious side effects occurred. Fenebrutinib did not increase the QT interval in any significant manner.

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)

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

Inclusion Criteria:

- Males or females of non-childbearing potential, between 18 and 60 years of age, inclusive;
- Within body mass index (BMI) range 18 to 31 kg/m², inclusive, with a bodyweight >45 kg;
- In good health, determined by no clinically significant findings from medical history, 12-lead ECG, and vital signs;
- 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;
- 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);
- 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;
- 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).
- 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;
- 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.

Exclusion Criteria:

- 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)
- 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
- History of significant hypersensitivity, intolerance, or allergy to any drug compound, food, or other substance, unless approved by the investigator
- 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

- Family history of intracranial bleed (berry aneurysm, hemorrhagic stroke) or recent personal history of head trauma
- History of vasculitis
- Having one or more of the following clinical laboratory evaluations at Screening:
    - Estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² 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 m²
    - 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
- 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
- Sustained (i.e., confirmed upon repeat) pulse >100 or <45 beats per minute at Screening
- Personal or family history of congenital long QT syndrome or family history of sudden death
- 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
- Short QTc (mean QTcF <300 msec) at Screening or Check-in (Day -1 for Part A, Period 1 Day -1 for Part B)
- 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, H2 blockers, antacids)
- 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
- 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)
- History of tuberculosis (TB) or treatment with TB prophylaxis within 12 months prior to study enrollment
- Use of oral antibiotics within 4 weeks or IV antibiotics within 8 weeks prior to the Screening evaluation
- Any vaccination within 6 weeks prior to dosing
- 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)
- 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)
- 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
- Use of acetaminophen within 24 hours prior to Check-in (Day -1 for Part A, Period 1 Day -1 for Part B)
- 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
- 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)
- 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
- Strenuous exercise from 7 days prior to Check-in (Day -1 Part A, Period 1 Day -1 for Part B)
- 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
- Poor peripheral venous access

- 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
- 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
- Receipt of blood products within 2 months prior to Check-in (Day -1 for Part A, Period 1 Day -1 for Part B)
- 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.