

Healthy Volunteers

A study medicine (fenebrutinib) manufactured in different ways – how do different fenebrutinib formulations move through the body

A phase 1, single center, randomized, open-label study investigating the effect of formulation, and active pharmaceutical ingredient particle size on the pharmacokinetics of fenebrutinib in healthy subjects

Trial Status
Completed

Trial Runs In
1 Country

Trial Identifier
ISRCTN17780768 GP43970

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 1, single center, randomized, open-label study investigating the effect of formulation, and active pharmaceutical ingredient particle size on the pharmacokinetics of fenebrutinib in healthy subjects

Trial Summary:

This clinical trial tested a new medicine called “fenebrutinib” to understand how different manufacturing processes affect the behavior of different formulations in the body. The study took place at one study site in the United Kingdom. The trial was designed as a phase 1, randomized, open-label study, meaning that participants were randomly assigned to different treatment groups and both the researchers and participants knew which treatment was being administered.

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

Phase 1
Phase

ISRCTN17780768 GP43970
Trial Identifiers

Eligibility Criteria:

Gender
Male and female

Age
18 to 60 years old

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Yes

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Background and study aims The sponsor is developing the test medicine fenebrutinib for the potential treatment of multiple sclerosis (MS). MS is a condition that can affect the brain and spinal cord, causing a wide range of potential symptoms, including problems with vision, arm or leg movement, sensation or balance, and affects about 2.3 million people worldwide. There are medical procedures available that may involve piercing or cutting into the body or inserting instruments (invasive treatments) that target a type of white blood cells called B-cells have been shown to be an effective treatment of MS, however, the Sponsor is developing a medicine that can be taken orally (by mouth) which would provide a less invasive therapeutic option for patients with MS. This three-part healthy volunteer trial will try to identify how new recipes (formulations) of the test medicine are taken up by the body (pharmacokinetics), the level of test medicine in the blood following oral dosing (relative bioavailability) and try to provide additional safety and tolerability information for the test medicine.

Who can participate? Male and female volunteers of non-childbearing potential, aged between 18 and 60 years.

What does the study involve? In Part 1 and Part 2, up to 15 volunteers will receive single oral doses of different recipes of the test medicine across three periods. Part 3 is optional, and if utilized, up to 16 volunteers will receive single doses of different recipes of the test medicine across two periods. In each part, volunteers will be discharged on Day 3 of the final period and will receive a follow-up phone call 7 – 10 days after the final dose. Volunteers' blood will be taken throughout the study for analysis of the test medicine and for their safety. Volunteers are expected to be involved in this study for 7 weeks for Part 1 and Part 2, and 6 weeks for Part 3, from screening to the follow-up call.

What are the possible benefits and risks of participating? This is a healthy volunteer study. Participants will be administered fenebrutinib only for research purposes and it is not intended that the participants will receive any benefit from it. However, the information learned in this study may help future patients. Participants will be compensated for taking part in this research study with an inconvenience allowance. It is considered that the risk/benefit evaluation in this study supports the use of healthy volunteers. As MS affects both men and women, both healthy male volunteers and healthy female volunteers of non-childbearing potential will be enrolled in this study. There is always a risk that the stipend in healthy volunteer studies could represent coercion. The time spent in the clinic, travel, inconvenience and other expenses factor in calculating the stipend. Perception of risk is not considered in this calculation. Volunteers may experience side effects from the test medicine. Full information on possible side effects is provided to volunteers in the Participant Information Sheet and Informed Consent Form. When investigating new medicines there is also a risk of unexpected side effects and occasionally allergic reactions. All volunteers will be closely monitored during the study and safety assessments will be performed at regular intervals. Risks are further mitigated by ensuring that only volunteers who meet all inclusion/exclusion criteria are included and that if the safety of any volunteer represents a concern they will be withdrawn. There will be an extended

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period of fasting for the volunteers taking part in this study. To ensure an adequate fluid intake, the volunteers will be allowed fluids up to 1 hour before dosing and from 1 hour after dosing, will be provided with 240 ml of water at dosing, and will be monitored for signs of dehydration and fatigue. Blood samples will be collected during the study. Collection of these samples can cause soreness and bruising of the arms but these problems usually clear up within a few days to a few weeks. ECG stickers on volunteers' chests and limbs may cause some local irritation and may be uncomfortable to remove but volunteers will be closely monitored to ensure any local irritation does not persist.

Where is the study run from? Genentech, Inc. c/o F. Hoffmann-La Roche Ltd (Switzerland)

Who is funding the study? Genentech, Inc. c/o F. Hoffmann-La Roche Ltd (Switzerland)

Who is the main contact? Trial Information Support Line (TISL), global-roche-genentech-trials@gene.com

Inclusion Criteria:

- Aged 18 to 60 years, inclusive, at the time of signing the Informed Consent Form (ICF)
- Healthy male subjects or healthy non-pregnant, non-lactating female subjects of non-childbearing potential. Female subjects must be either postmenopausal or surgically sterile
- A body mass index (BMI) between 18.0 and 32.0 kg/m², inclusive, at screening
- A body weight >50 kg at screening and admission (Day -1 of Period 1)
- Subjects must be fully vaccinated (i.e., have received the full first/second dose[s], as applicable for the vaccine type, plus any recommended booster doses, per current UK guidance) against COVID-19 virus infection at least 12 weeks prior to the admission visit.
- Must agree to adhere to the following required contraception requirements (which are considered to be more conservative than the guidance issued by the Heads of Medicines Agency: Clinical Trials Facilitation Group):
 - Male subjects with partners of childbearing potential: male subjects who are sexually active with a partner of childbearing potential must use, with their partner, a condom plus an approved method of highly effective contraception from the time of informed consent until 28 days after last study drug administration. This is longer than 5 half-lives of fenebrutinib (which has been calculated as 3 days) and is in line with contraception requirements in other ongoing fenebrutinib studies.
 - Male subjects with partners of non-childbearing potential: There is a significant risk of drug exposure through the ejaculate (which also applies to vasectomized males) that might be harmful to sexual partners. Therefore, even if a male is sexually active with a partner of non-childbearing potential, they will be required to use a condom from first administration of IMP until the follow-up phone call.
 - All male subjects:
 - Alternatively, sexual abstinence is considered a highly effective method of contraception only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the subject.

- Male subjects should not donate sperm for the duration of the study and for 28 days after the last study drug administration
- Female subjects of non-childbearing potential:
 - Female subjects who are not of childbearing potential do not need to use any methods of contraception
 - Female subjects should not participate in egg donation from dosing, for the duration of the study and for at least 28 days after the last study drug administration

Exclusion Criteria:

- History of serious adverse reaction or serious hypersensitivity to any drug, or sensitivity or intolerance to any ingredient (including excipients) of the fenebrutinib formulations
- Personal or family history of congenital long QT syndrome or family history of sudden death
- Evidence of active infection (with the exception of fungal nail infections or oral herpes) or any major episode of infection requiring hospitalization or treatment with IV antimicrobials within 8 weeks prior to and during screening or treatment with oral antimicrobials within 2 weeks prior to and during screening. 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.
- History or evidence of active or latent mycobacterium tuberculosis (TB) infection, regardless of treatment history
- History of stomach or intestinal surgery or resection that could potentially alter absorption and/or excretion of orally administered drugs, except that appendectomy, and/or hernia repair will be allowed
- Presence or history of any condition that could possibly affect oral drug absorption
- History of pancreatitis, cholecystectomy or gallstones, or clinically significant GI ulcer or bleeding
- Presence or history of bleeding diathesis
- Presence or history of hepatic diseases or Gilbert's Syndrome
- History of cancer, including hematologic malignancy and solid tumors, except for appropriately treated carcinoma in situ of the cervix or non-melanoma skin carcinoma with 3-year disease-free follow-up
- Symptoms of COVID-19 or any other respiratory disease within the 2 weeks prior to admission to the CRU
- Part 3 only: Subject has a medical condition that may adversely affect taste or smell activity
- Evidence of current SARS-CoV-2 (i.e., the virus that causes COVID-19) infection. SARS-CoV-2 antigen testing may be performed based on current infection rates and availability of tests
- Clinically significant abnormal clinical chemistry, hematology, coagulation, or urinalysis result as judged by the Investigator
- Subjects with significantly impaired bone marrow function or significant anemia, leukopenia, neutropenia or thrombocytopenia as determined by the Investigator
- Abnormalities in hepatic synthetic function tests (e.g., prothrombin time [PT], international normalized ratio [INR], activated partial thromboplastin time [APTT]) judged by the Investigator to be clinically significant
- Positive for hepatitis C virus (HCV) antibody, hepatitis B surface antigen (HBsAg), hepatitis B core antibody [total HBcAb] with detectable hepatitis B virus (HBV) DNA or human immunodeficiency virus (HIV) 1 & 2 antibodies at screening
- Evidence of renal impairment at screening, as indicated by an estimated creatinine clearance (CL_{Cr}) of <70 ml/min using the Cockcroft-Gault equation