ForPatients
by Roche

Multiple Sclerosis (MS)

How a new medicine called fenebrutinib behaves in the body when taken alone and when taken with other medicines

Trial Status	Trial Runs In	Trial Identifier
Completed	1 Country	GP45241 ISRCTN12005942

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, open-label, single-dose, fixed-sequence, two-part study to evaluate the effect of itraconazole and carbamazepine on fenebrutinib pharmacokinetics in healthy subjects

Trial Summary:

This study investigated how fenebrutinib, a study medicine being developed for multiple sclerosis, behaves in the body when taken alone and with other medicines. Researchers wanted to understand drug-drug interactions with itraconazole (a strong enzyme inhibitor) and with carbamazepine (a strong enzyme inducer). Healthy male and female volunteers, aged 18 to 60, could participate. This was a Phase 1, open-label, single-dose, fixed-sequence study. In two separate parts, participants first received fenebrutinib alone, followed by a washout period, and then received fenebrutinib co-administered with either itraconazole (Part 1) or carbamazepine (Part 2). Blood samples were routinely collected at various times after each dose to measure the levels of fenebrutinib in the body. The primary measurements focused on how much fenebrutinib entered the bloodstream, how quickly it reached its highest level, and how it was eliminated from the body – when taken alone and with itraconazole or carbamazepine. Strict safety monitoring and stopping rules were in place to ensure participant's safety.

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

GP45241 ISRCTN12005942
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers

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All	18 to 60 years	Yes

This Phase 1, open-label, two-part study, conducted at one center in the United Kingdom, involved 32 healthy volunteers. The primary objective was to determine how fenebrutinib, an investigational medicine for multiple sclerosis, behaved in the body when taken alone and with other medicines, specifically with itraconazole (a strong enzyme inhibitor) and carbamazepine (a strong enzyme inducer). The study found that itraconazole significantly increased fenebrutinib's overall and peak exposure in the body, while carbamazepine substantially decreased them. The findings from this study are supportive of fenebrutinib's continued clinical development.

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 problems between the brain and the rest of the body. This study is testing a medicine called fenebrutinib. It is being developed to treat multiple sclerosis. Fenebrutinib is an experimental medicine. This means health authorities (like the U.S. Food and Drug Administration, European Medicines Agency, and the United Kingdom Medicines and Healthcare products Regulatory Agency [MHRA]) have not approved fenebrutinib for the treatment of multiple sclerosis. This study aims to test the safety of fenebrutinib. Also, it aims to understand how fenebrutinib gets to different parts of the body, and how the body changes and gets rid of it when given along with medicines called itraconazole or carbamazepine.

Who can participate? Healthy people 18 to 60 years of age with multiple sclerosis can take part in the study. People with a history of stomach or intestinal surgery may not be able to take part in this study.

What does the study involve? Participants will be screened to check if they can participate in the study. The screening period will take place up to 28 days before the start of treatment. Everyone who joins this study will be either enrolled in Part 1 or Part 2 of the study. In both parts, participants will receive treatment in two periods (Periods 1 and 2).

In Part 1, participants will be given fenebrutinib, as a pill by mouth, on Day 1 of Period 1 and Day 8 of Period 2. Participants will also be given itraconazole, as a pill by mouth, from Days 4 to 10 during Period 2.

In Part 2, participants will be given fenebrutinib, as a pill by mouth, on Day 1 of Period 1 and Day 18 of Period 2. Participants will also be given multiple doses of carbamazepine, as a pill by mouth from Days 4 to 20 during Period 2.

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 doctor will see the participants regularly during their stays at the clinic (13 days in Part 1 and 22 days in Part 2). They will see how well the treatment is working and any unwanted effects participants may have. Participants will receive a follow-up telephone call from the study doctor to check on their well-being after 8-10 days of completing the study treatment. The total time of participation in the study will be about 7 weeks for Part 1 and 8 weeks for Part 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? Fenebrutinib is an experimental drug and is being given purely for research purposes, it is not intended that participants will receive any benefit from this study. However, the information collected in the study can help other people with multiple sclerosis in the future. 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.

Risks associated with the study Participants may have side effects of the medicines used in this study. These side effects can be mild to severe, even life-threatening, and vary from person to person. All volunteers will be closely monitored during the study and safety assessments will be performed at regular intervals.

Fenebrutinib
Full information on risks associated with fenebrutinib is provided to volunteers in the Informed Consent Form. When investigating new medicines there is also a risk of unexpected side effects and occasionally allergic reactions. Known unwanted effects include the risk of liver injury. Fenebrutinib may be harmful to an unborn baby, and not all potential risks are known at this time. Women and men must take precautions to avoid exposing an unborn child to the study drug. Participants who are pregnant, become pregnant or are currently breastfeeding cannot take part in the study.

Itraconazole Known unwanted effects include headache, dizziness, and runny nose.

Carbamazepine Known unwanted effects include increased thoughts of suicide, liver damage, dizziness, drowsiness, unsteadiness, nausea, vomiting, abdominal pain, and frequent watery stools.

Who is funding the study? Genentech Inc. (USA)

Who is the main contact? global-roche-genentech-trials@gene.com

Inclusion Criteria:

- Body weight #45 kilograms (kg), within the body mass index range of 18 to 32 kilograms per metre squared (kg/m2).
- Participants in good health, determined by no clinically significant findings from medical history, 12-lead electrocardiogram (ECG), and vital signs.

Exclusion Criteria:

- Part 2 only: Participants that test positive for human leukocyte antigen-B (HLA-B)*1502 allele and/or HLA-A 3101 allele
- 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
- Evidence of any infectious, metabolic (except well-controlled/stable hypothyroidism), allergic, dermatological, hepatic, renal, hematological, pulmonary, cardiovascular, gastrointestinal (GI), neurological, or psychiatric disorder that would preclude subject participation
- Any acute or chronic liver disease, e.g., hepatitis, cirrhosis (Child-Pugh Class A, B, or C), or Gilbert's Syndrome
- History of stomach or intestinal surgery or resection that would potentially alter absorption and/or excretion of orally administered drugs, except that appendectomy and hernia repair will be allowed
- History of pancreatitis, cholecystectomy or gallstones, or clinically significant GI ulcer or bleeding
- History of malignancy, except for appropriately treated carcinoma in situ of the cervix or non-melanoma skin carcinoma with 5-year disease-free follow-up
- Use of any moderate or strong CYP3A inhibitor or inducer within 30 days or 5 half-lives, whichever is longer, before Check-in (Period 1 Day -1)
- Participants vaccinated with live, attenuated vaccines within 6 weeks before first dosing (Period 1 Day 1)
- Dyspepsia, gastroesophageal reflux disease, ulcer, or GI symptoms for which the participant has recently taken (within 14 days before Check-in [Period 1 Day -1]) prescription or over-the-counter proton-pump inhibitors (PPIs), H2 blockers, or antacids for the control of gastric acidity