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A study to evaluate the effect of various degrees of reduced liver function on the processing of fenebrutinib in the body

Submission date 05/10/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 10/10/2023	**Overall study status** Completed	
Last Edited 13/05/2024	**Condition category** Other	

Plain English summary of protocol

Background and study aims
A disease of the brain and spinal cord (central nervous system) called multiple sclerosis (MS), is a long-lasting (chronic) disease in which the body attacks the protective covering around nerves and damages the nerves. Fenebrutinib is an experimental drug being developed for the treatment of MS. Health authorities have not yet approved fenebrutinib for the treatment of MS.

The main aim of the study is to find out how mild or moderate liver damage (mild or moderate hepatic impairment) will affect the breakdown and removal of the study drug (fenebrutinib) from the body (this is called pharmacokinetics [PK]).

Who can participate?
People between 18 and 75 years of age with normal liver function or with mild or moderate liver damage (mild or moderate hepatic impairment) can participate in this study.

What does the study involve?
Participants will need to be a part of the study for about 5 weeks including the screening period. The study will include the following parts:
1. A screening period of up to 28 days to check the eligibility of participants to take part in the study.
2. A dosing/treatment period: Participants with normal liver function and mild or moderate liver damage will receive a single dose of fenebrutinib, by mouth (orally) on Day 1. Participants will have to get admitted to the clinic 1 day before receiving the treatment (Day -1) and stay in the clinic until Day 5.
3. A follow-up phone call to check on the participant will be made 7 days after the study drug administration to check on their well-being.

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, but the information learned from this study may be useful to treat future patients of multiple sclerosis. Participants may receive monetary compensation for taking part in the study.

Participants may have side effects due to fenebrutinib or procedures used in this study. Side effects can be mild to severe and even life-threatening or fatal, and they can vary from person to person. 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. 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. Blood samples will be collected during the study. Collection of these samples can cause pain, bruising, or infection where the needle is inserted. Electrocardiograms (ECGs) will be taken in this study. ECG patches may cause a skin reaction such as redness or itching, or localized skin discomforts and/or hair loss associated with the placement of ECG leads.

There may be a risk in exposing an unborn child to the study drug, and all risks are not 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 this study.

Where is the study run from?
Genentech Inc. (Switzerland)

When is the study starting and how long is it expected to run for?
July 2023 to January 2025

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

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

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Dr Clinical Trials

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Building 1, Grenzacherstrasse 124
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
GP44943

Study information

Scientific Title
A phase I, open-Label, single-Dose study to evaluate the effect of mild or moderate hepatic impairment on the pharmacokinetics of fenebrutinib

Study objectives
The main aim of this study is to determine the pharmacokinetics (PK) of a single oral dose of fenebrutinib in participants with mild or moderate hepatic impairment compared to demographically matched healthy participants with normal hepatic function.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 16/08/2023, Salus IRB (2111 West Braker Lane, Suite 100, Austin, Texas, 78758, United States of America; +1 512-380-1244; salus@salusirb.com), ref: None provided

Study design
Phase I multicenter non-randomized open-label parallel-group single-dose study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Multiple sclerosis (MS) (study conducted in volunteers with normal hepatic function or mild /moderate hepatic impairment)

Interventions
Cohort 1: Participants with normal hepatic function will receive a single dose of fenebrutinib, 200 milligrams (mg), orally, on Day 1.

Cohort 2: Participants with mild hepatic impairment will receive a single dose of fenebrutinib, 200 mg, orally, on Day 1.

Cohort 3: Participants with moderate hepatic impairment will receive a single dose of fenebrutinib, 200 mg, orally, on Day 1.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)
1. Area under the concentration-time curve from hour 0 to the last measurable concentration (AUC0-t) of fenebrutinib measured using a validated liquid chromatography with tandem mass spectrometry (LC-MS/MS) assay from the blood samples collected at multiple time points from Day 1 to Day 5
2. AUC extrapolated to infinity (AUC0-∞) of fenebrutinib measured using a validated LC-MS/MS assay from the blood samples collected at multiple time points from Day 1 to Day 5
3. Maximum observed concentration (Cmax) of fenebrutinib measured using a validated LC-MS /MS assay from the blood samples collected at multiple time points from Day 1 to Day 5

Key secondary outcome(s))
1. Number of participants with adverse events (AEs) and severity of AEs graded as per National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0 (NCI CTCAE; v5.0) from screening up to 14 days after the dose of study drug (approximately 6 weeks)

Completion date
14/01/2025

Eligibility

Key inclusion criteria
1. Male and female participants between 18 to 75 years of age, inclusive, at screening
2. Body weight ≥45 kilograms (kg) and within body mass index (BMI) range 18.0 to 42.0 kilograms per square meter (kg/m2), inclusive

Additional inclusion criteria for participants with normal hepatic function (Cohort 1) only:
1. In reasonably good health for their age
2. Matched to participants with mild or moderate hepatic impairment in sex, age (±10 years), and body weight (±15%)
3. Negative hepatitis panel
4. Normal hepatic function and no history of clinically significant hepatic dysfunction
5. Estimated glomerular filtration rate ≥80 millilitre per minute (mL/min) at screening, as calculated by the Chronic Kidney Disease Epidemiology Collaboration equation.

Additional inclusion criteria for participants with hepatic impairment (Cohorts 2 and 3) only:
1. Chronic (>6 months), stable (no acute episodes of illness within the previous 1 month prior to Screening due to deterioration in hepatic function) hepatic insufficiency with features of cirrhosis due to any etiology. Participants must also remain stable throughout the Screening period.
2. Considered to have mild or moderate hepatic impairment and has been clinically stable for at least 1 month prior to Screening. To be classified as having hepatic impairment, participants

must have a Child-Pugh score of 5 to 6 (inclusive; mild) or 7 to 9 (inclusive; moderate) with known medical history of liver disease and unambiguous medical history.
3. Negative hepatitis B virus core antibody and HbsAg screens and negative hepatitis C viral load.
4. Estimated glomerular filtration rate ≥60 mL/min at screening, as calculated by the Chronic Kidney Disease Epidemiology Collaboration equation.

Other protocol defined inclusion criteria could apply.

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
75 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 dose of study drug.
2. History of surgical or artificial shunts (i.e., transjugular intrahepatic portosystemic procedure).
3. History of malignancy within 5 years prior to screening, except for completely excised basal cell carcinoma or squamous cell carcinoma of the skin or cervical carcinoma in situ.
4. Significant illness, including infections, surgery, or hospitalization within the 2 weeks prior to dosing.
5. History of stomach or intestinal surgery or resection that would potentially alter absorption and/or excretion of orally administered drugs, except that uncomplicated hernia repair, appendectomy, and/or cholecystectomy will be allowed.
6. Malabsorption syndrome or other condition that would interfere with enteral absorption.

Additional exclusion criteria for participants with hepatic impairment (Cohorts 2 and 3) only:
1. Evidence of progressive liver disease that has worsened or is worsening within 1 month prior to Screening.
2. Evidence of hepatorenal syndrome
3. Ascites requiring paracentesis within 3 months prior to Check-in (Day -1) or other intervention, with the exception of diuretics.
4. Required treatment for gastrointestinal bleeding within 12 months prior to Check-in (Day -1)
5. Receipt of a liver transplant
6. Required additional medication for hepatic encephalopathy within 12 months prior to check-in (Day -1), unless deemed acceptable by the investigator.
7. One or more of the following laboratory results:
• Alkaline phosphatase >10 × upper limit of normal (ULN).

• Alanine aminotransferase or aspartate aminotransferase >5 × ULN.
• Bilirubin >3 × ULN in the absence of Gilbert’s Syndrome or hemolysis.

Other protocol defined exclusion criteria could apply.

Date of first enrolment
18/10/2023

Date of final enrolment
07/01/2025

Locations

Countries of recruitment
Canada

New Zealand

Study participating centre
Altasciences Montreal
1200 Beaumont Avenue
Montréal
Canada
H3P 3P1

Study participating centre
NZCR - Auckland
Ferncroft St
Grafton, Auckland
New Zealand
1010

Sponsor information

Organisation
Genentech Inc.

Funder(s)

Funder type
Industry

Funder Name
Genentech Inc.

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes