ISRCTN41455091 https://doi.org/10.1186/ISRCTN41455091

A study to evaluate the effect of highly reduced kidney 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 severe kidney damage (severe renal 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 to 75 years of age with normal kidney function or severe kidney damage (severe renal impairment) can participate in this study.

What does the study involve?
Participants will be part of this study for approximately 5 weeks. The study will be conducted in 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 during which participants with normal kidney function and severe kidney 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 4.
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 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.

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 December 2024

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

Contact details
Building 1, Grenzacherstrasse 124
Basel
Switzerland
CH-4070
+41 616878333
global.trial_information@roche.com

Additional identifiers

Protocol serial number
GP44942

Study information

Scientific Title
A phase I, open-label, single-dose study to evaluate the effect of severe renal impairment on the pharmacokinetics of fenebrutinib

Study objectives
The main purpose of this study is to determine the pharmacokinetics (PK) of a single oral dose of fenebrutinib in participants with severe renal impairment compared with demographically matched healthy participants with normal kidney function.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 25/08/2023, 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

Primary study design
Interventional

Study design
Phase 1 multicenter non-randomized open-label single-dose parallel-group study

Study type(s)
Other

Health condition(s) or problem(s) studied
Multiple sclerosis (MS) (study conducted in volunteers with normal renal function or severe renal impairment)

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

Cohort 2: Participants with severe renal 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 (AUC) from hour zero 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 plasma samples collected at multiple time points, from Day 1 to Day 4
2. AUC extrapolated to infinity (AUC 0-∞) of fenebrutinib measured using a validated LC-MS/MS assay from the plasma samples collected at multiple time points, from Day 1 to Day 4
3. Maximum observed concentration (Cmax) of fenebrutinib measured using a validated LC-MS /MS assay from the plasma samples collected at multiple time points, from Day 1 to Day 4

Key secondary outcome(s)
1. Number of participants with adverse events (AEs), and severity of AEs assessed according to 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
25/12/2024

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 renal function (Cohort 1) only:
1.In reasonably good health for their age
2. Estimated glomerular filtration rate (eGFR) determined using the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation ≥ 90 millilitres per minute (mL/min)
3. Matched to participants with severe renal impairment in sex, age (±10 years), and body weight (±15%)
Additional inclusion criteria for participants with severe renal impairment (Cohort 2) only:
Participants must have eGFR <30 mL/min and not be on dialysis and have stable renal function.

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. Clinically significant liver disease, e.g., hepatitis, cirrhosis, and/or confirmed liver enzyme elevations (aspartate aminotransferase [AST], alanine aminotransferase [ALT], or gamma-glutamyl transferase >1.5 × upper limits of normal [ULN], or bilirubin >1.5 × ULN)
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 conditions that would interfere with enteral absorption.

Additional exclusion criteria for participants with normal renal function (Cohort 1) only:
Significant history or clinical manifestation of renal injury or disease

Additional exclusion criteria for participants with severe renal impairment (Cohort 2) only:
1. Functioning renal transplant or who are active on the transplant waiting list.
2. Renal impairment due to hepatic disease (hepatorenal syndrome).
3. Blood potassium concentration <3 millimoles per litre (mmol/L) or >6 mmol/L at Screening.
4. Hemoglobin concentration <8.5 grams per decilitre (g/dL) at Screening.

Other protocol defined exclusion criteria could apply.

Date of first enrolment
06/06/2024

Date of final enrolment
18/12/2024

Locations

Countries of recruitment
New Zealand

Study participating centre
NZCR Christchurch
264 Antigua Street
Christchurch
New Zealand
8011

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