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A study in healthy volunteers to investigate how different recipes and the particle size of an ingredient in the test medicine affects how the test medicine behaves

Submission date
17/06/2022

Recruitment status
No longer recruiting

Registration date
10/08/2022

Overall study status
Completed

Last Edited
11/08/2022

Condition category
Nervous System Diseases

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

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 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)

When is the study starting and how long is it expected to run for?
June 2022 to September 2023

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

Contact information

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Additional identifiers

EudraCT/CTIS number
2022-000888-42

IRAS number
1005691

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
GP43970, IRAS 1005691

Study information

Scientific Title

A Phase I, 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

Acronym
QSC206109

Study objectives
Primary objectives:
1. To determine the relative bioavailability, under fasted conditions, of two oral fenebrutinib immediate release tablets (test) with respect to the current Phase III tablet formulation of fenebrutinib (reference)
2. To characterize the pharmacokinetics (what the body does to the drug, PK) of fenebrutinib under fasted conditions under fasted conditions following administration of two oral fenebrutinib immediate release tablets and the current Phase III tablet formulation

Secondary objectives:
1. To assess the safety and tolerability of single oral doses of fenebrutinib in healthy subjects

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/08/2022, Fast Track REC (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, UK), ref: 22/FT/0080

Study design
Open randomized cross over trial

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Multiple sclerosis (MS) (study conducted in healthy volunteers)

Interventions
Computer-generated randomisation schedules will be used.

Part 1:
Participants will be randomly allocated to receive a single oral dose of each of the following across three periods:
1. Reference film-coated fenebrutinib tablets in the fasted state
2. Fenebrutinib Immediate Release Tablet 1 in the fasted state
3. Fenebrutinib Immediate Release Tablet 3 in the fed state

Part 2:
Participants will be randomly allocated to receive a single oral dose of each of the following across three periods:
1. Reference film-coated fenebrutinib tablets in the fasted state
2. Fenebrutinib Immediate Release Tablet 1 or 3 in the fasted state
3. Fenebrutinib Immediate Release Tablet 4 in the fasted state

Optional Part 3:
Participants will be randomly allocated to receive a single oral dose of each of the following across two periods:
1. Reference film-coated fenebrutinib tablets in the fasted state
2. Fenebrutinib Immediate Release Tablet 2 or fenebrutinib granules in the fasted state

Intervention Type
Drug

Phase
Phase I

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

Primary outcome measure
1. Relative bioavailability as assessed based on the PK parameter maximum observed concentration (Cmax) of fenebrutinib measured using blood samples
2. Relative bioavailability as assessed based on the PK parameter area under the curve (AUC) from time 0 to the time of last measurable concentration (AUC0-t) measured using blood samples
3. Relative bioavailability as assessed based on the PK parameter, AUC from time 0 extrapolated to infinity (AUC0-inf) for fenebrutinib measured using blood samples

Part 1 & 2:
Blood samples collected from Day 1 (period 1) to Day 3 of period 3, 48 hours post-final dose

Part 3:
Blood samples collected from Day 1 (period 1) to Day 3 of period 2, 48 hours post-final dose

Secondary outcome measures
1. Percentage of participants with adverse events (AEs) and serious adverse events (SAEs) assessed as per National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) grading scale from signing the informed consent form until the follow-up phone call (approximately 7 weeks for Parts 1 and 2, 6 weeks for Part 3)
2. Percentage of participants with clinically significant changes in laboratory safety tests measured using blood samples at screening, and at intervals from admission until final discharge

(approximately 7 weeks for Parts 1 and 2, 6 weeks for Part 3)
3. Percentage of participants with clinically significant changes in ECG parameters measured using 12-lead electrocardiograms (ECGs) at screening, and at intervals from admission until final discharge (approximately 7 weeks for Parts 1 and 2, 6 weeks for Part 3)
4. Percentage of participants with clinically significant changes in vital sign measurements, blood pressure, pulse rate, oral temperature and respiratory rate at screening, and at intervals from admission until final discharge (approximately 7 weeks for Parts 1 and 2, 6 weeks for Part 3)
5. Percentage of participants with clinically significant changes in physical examination parameters following evaluation of the head, eyes, ears, nose, and throat, and the cardiovascular, dermatologic, musculoskeletal, respiratory, GI, genitourinary, and neurologic systems at screening, and at intervals from admission until final discharge (approximately 7 weeks for Parts 1 and 2, 6 weeks for Part 3)

Overall study start date
15/06/2022

Completion date
10/09/2023

Eligibility

Key inclusion criteria
1. Aged 18 to 60 years, inclusive, at the time of signing the Informed Consent Form (ICF)
2. Healthy male subjects or healthy non-pregnant, non-lactating female subjects of non-childbearing potential. Female subjects must be either postmenopausal or surgically sterile
3. A body mass index (BMI) between 18.0 and 32.0 kg/m², inclusive, at screening
4. A body weight >50 kg at screening and admission (Day -1 of Period 1)
5. 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.
6. 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):
6.1. 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.
6.2. 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.
6.3. All male subjects:
6.3.1. 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.
6.3.2. Male subjects should not donate sperm for the duration of the study and for 28 days after the last study drug administration

6.4. Female subjects of non-childbearing potential:
6.4.1. Female subjects who are not of childbearing potential do not need to use any methods of contraception
6.4.2. 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

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
Both

Target number of participants
46

Key exclusion criteria
1. History of serious adverse reaction or serious hypersensitivity to any drug, or sensitivity or intolerance to any ingredient (including excipients) of the fenebrutinib formulations
2. Personal or family history of congenital long QT syndrome or family history of sudden death
3. 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.
4. History or evidence of active or latent mycobacterium tuberculosis (TB) infection, regardless of treatment history
5. 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
6. Presence or history of any condition that could possibly affect oral drug absorption
7. History of pancreatitis, cholecystectomy or gallstones, or clinically significant GI ulcer or bleeding
8. Presence or history of bleeding diathesis
9. Presence or history of hepatic diseases or Gilbert’s Syndrome
10. 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
11. Symptoms of COVID-19 or any other respiratory disease within the 2 weeks prior to admission to the CRU
12. Part 3 only: Subject has a medical condition that may adversely affect taste or smell activity

13. 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
14. Clinically significant abnormal clinical chemistry, hematology, coagulation, or urinalysis result as judged by the Investigator
15. Subjects with significantly impaired bone marrow function or significant anemia, leukopenia, neutropenia or thrombocytopenia as determined by the Investigator
16. 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
17. 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
18. Evidence of renal impairment at screening, as indicated by an estimated creatinine clearance (CLcr) of <70 ml/min using the Cockcroft-Gault equation

Please see the clinical protocol for the full list of exclusion criteria.

Date of first enrolment
22/08/2022

Date of final enrolment
10/09/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Quotient Sciences Limited
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Sponsor information

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Genentech, Inc. c/o F. Hoffmann-La Roche Ltd

Results and Publications

Publication and dissemination plan
1. Internal report
2. Submission to regulatory authorities
3. The findings of this Phase I study will be shared with the Sponsor, Genentech, Inc., only. As these findings are confidential due to commercial sensitivity, it is not appropriate to share the results of this study with other researchers at this time.

Intention to publish date
02/09/2024

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No