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A study to compare low-volume blood sampling techniques versus conventional blood collection from veins to evaluate drug concentration profiles after administration of a single dose of various study drugs in healthy subjects

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Registration date 12/01/2022	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 10/01/2022	**Condition category** Other	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims

The aim of this study is to test and compare different methods of collecting blood to see how the methods differ with regard to determining how a participant's body processes a single dose of study drug (how the study drug is absorbed, distributed, broken down, and removed by one's body). The following collection methods will be studied:

1. Venipuncture: blood is drawn through a needle inserted into the participant's arm (the current standard for blood sampling).
2. TASSO OnDemand: this device sticks to the skin with a light adhesive. When the button is pressed, a vacuum forms and a lancet pricks the surface of the skin. The vacuum draws blood out of participants' capillaries (blood-containing structures) and into a tube attached to the bottom of the device.
3. Neoteryx Mitra: this device collects a very small amount of blood on two sponge tips after a separate skin prick using a lancet.

Who can participate?

People aged between 18 to 65 years who are healthy

What does the study involve?

This study has three parts:

1. Screening (to see if people are eligible for the study)
2. Check-in and treatment
3. Follow-up (to check after treatment is finished)

The study screening period will be from Days –35 to –2. If participants are eligible and agree to take part in this study, participants will check into the study site, where they will be required to

remain for 2 days during this study. On Day 1, participants will receive a single dose of one of the study drugs given as an infusion (into the vein) and will undergo blood sampling. There will be also standard tests and evaluations for participants' safety.
During this study, there will be up to nine visits. The first visit may last 3 days and later visits may last 3 hours. The total time in the study will be up to about 4.5 months.

What are the possible benefits and risks of participating?
Participants will not receive any benefit from participating in this study but the information that is learned may help patients with certain diseases or conditions in clinical trials in the future. There may be side effects from the drug or procedures used in this study, which can be mild to severe and even life-threatening, and they can vary from person to person. The study doctor will assess right away if participants have any of the following during the study:
1. Symptoms that are new or have worsened
2. Changes in prescribed or over-the-counter medications (including herbal therapies)
3. Visits to the doctor or hospital, including urgent care or emergency room visits
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. If participants are pregnant, become pregnant, or are currently breastfeeding, one cannot take part in this study. As is true for any experimental drug, there may be unknown and potentially serious or life-threatening side effects, infusion-related injuries or death. These adverse events (side effects) listed in the table below were reported in previous studies from patients who received more than one dose of the study drug.

Crenezumab is an experimental drug that is being studied as a potential treatment for patients with Alzheimer's disease, a brain disease that causes problems with memory, behavior, and thinking ability. Subjects may experience side effects from the drug or procedures in this study. Side effects can vary from mild to very serious and may be different from person to person. The majority of side effects identified in studies are from observations following dosing over an extended period and are not likely to occur with administration of only one dose of crenezumab. Risks associated with crenezumab include allergic reactions such as itching, difficulty breathing, rash and/or drop in blood pressure; pneumonia, local reactions at site of infusion/injection. There is also a rare risk of death.

Giredestrant is still being studied, and the side effect profile is not completely known. So far, the known side effects appear to be mild to moderate in severity with no known serious risks. The vast majority of these side effects resolved without the need for treatment or interruption of giredestrant. It is also possible that subjects might experience side effects that are unknown at this time. As is true for any experimental drug, there may be unknown and potentially serious or life-threatening side effects, including death, that could occur with giredestrant. However, the majority of side effects identified in studies are from observations following dosing over an extended period and are not likely to occur with only one dose of giredestrant. Common side effects observed with giredestrant include joint pain, diarrhea, dizziness, fatigue, muscle and/or bone pain, nausea, hot flushes and vomiting.

Etrolizumab is still being studied, and the side effect profile is not completely known. The majority of side effects identified in studies are from observations following dosing over an extended period and are not likely to occur with only one dose of etrolizumab. The very common side effects include joint ache, fatigue, rash, common cold and uncommon side effects are skin inflammation, rash with the presence of flat discolored area, appendicitis.

Hydroxychloroquine has well-established safety profiles, as it has been marketed for over 60 years for the treatment of malaria, rheumatoid arthritis, and systemic lupus erythematosus.

While most of the side effects reported are for more than one dose of hydroxychloroquine, as a healthy volunteer who is receiving a single dose of the drug, patients may or may not experience some of these common side effects: Nausea, vomiting, stomach pain or cramps, loss of appetite, weight loss, diarrhea, dizziness, spinning sensation, headaches, ringing in the ears, mood changes, nervousness, irritability, skin rash, itching, hair loss and blurred vision.

Where is the study run from?
F. Hoffmann-La Roche Ltd (USA)

When is the study starting and how long is it expected to run for?
June 2021 to May 2022

Who is funding the study?
F. Hoffmann-La Roche Ltd (USA)

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

Contact information

Type(s)
Public

Contact name
Dr Trial Information Support Line (TISL)

Contact details
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Additional identifiers

Protocol serial number
GE43429

Study information

Scientific Title
An open-label, parallel-group study to compare low-volume blood sampling techniques versus conventional venipuncture for the assessment of pharmacokinetic profiles of a single dose of various study drugs in healthy subjects

Study objectives

To determine whether low-volume sampling can be used as an alternative method of sample collection for drug concentration evaluation of small molecules and monoclonal antibodies (MAbs) compared with samples from venipuncture.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/09/2021, Salus IRB (2111 West Braker Lane Suite 100, Austin, TX 78758, USA; +1 (0) 512 380 1244; salus@salusirb.com), ref: GE43429

Primary study design
Interventional

Study design
Open-label non-randomized parallel-group study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Blood sampling techniques

Interventions
Crenezumab
Subjects in the crenezumab treatment group will receive a single intravenous dose of 15 mg/kg crenezumab.

Etrolizumab
Subjects in the etrolizumab treatment group will receive a 210 mg dose via subcutaneous (SC) injection.

Giredestrant
Subjects in the giredestrant group will receive a single oral dose of a 30-mg giredestrant capsule.

Hydroxychloroquine
Subjects in the hydroxychloroquine group will receive a single oral dose of a 200-mg hydroxychloroquine tablet.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Crenezumab, etrolizumab, giredestrant, hydroxychloroquine

Primary outcome(s)

1. Drug concentrations collected using venipuncture versus low-volume sampling performed by trained site staff and evaluated using the bioanalytical method comparability criteria on Days 1, 2, 4, 8, 15, 29, 43, 57, 85 for crenezumab and etrolizumab; Days 1, 2, 3, 5, 6, 7 and 8 for giredestrant and Days 1, 2, 3, 4, 6, 8, 15, 29, 43, 57 and 85 for hydroxychloroquine
2. Evaluation of bias and impact to interchangeability (i.e., no trend over the range of concentrations) using 90% confidence intervals at Days 1, 2, 4, 8, 15, 29, 43, 57, 85 for crenezumab and etrolizumab; Days 1, 2, 3, 5, 6, 7 and 8 for giredestrant and Days 1, 2, 3, 4, 6, 8, 15, 29, 43, 57 and 85 for hydroxychloroquine
3. Determination of equivalent operational performance for venipuncture and low-volume sampling techniques on the basis of the number of failed samples and the number of outliers assessed at Days 1, 2, 4, 8, 15, 29, 43, 57, 85 for crenezumab and etrolizumab; Days 1, 2, 3, 5, 6, 7 and 8 for Giredestrant and Days 1, 2, 3, 4, 6, 8, 15, 29, 43, 57 and 85 for hydroxychloroquine
4. PK parameters from samples obtained using venipuncture, Neoteryx Mitra (whole blood), and TASSO-Plus (serum for monoclonal therapeutics or plasma for small molecules) collected by trained site staff at Days 1, 2, 4, 8, 15, 29, 43, 57, 85 for crenezumab and etrolizumab; Days 1, 2, 3, 5, 6, 7 and 8 for giredestrant and Days 1, 2, 3, 4, 6, 8, 15, 29, 43, 57 and 85 for hydroxychloroquine

Key secondary outcome(s)
1. Safety evaluated on the basis of the incidence and severity of adverse events, with severity determined according to NCI CTCAE v5.0, change from baseline in targeted vital signs, and change from baseline in targeted clinical laboratory test results at Check-In, Days 1, 2, 4, 8, 15, 29, 43, 57, 85 for crenezumab and etrolizumab; Check-In, Days 1, 2, 3, 5, 6, 7 and 8 for giredestrant and Check-In, Days 1, 2, 3, 4, 6, 8, 15, 29, 43, 57 and 85 for hydroxychloroquine
2. Incurred sample reanalysis feasibility on samples collected from Mitra tips assessed using evaluation of frozen whole blood extracts to freeze thaw at Days 1, 2, 4, 8, 15, 29, 43, 57, 85 for crenezumab and etrolizumab; Days 1, 2, 3, 5, 6, 7 and 8 for giredestrant and Days 1, 2, 3, 4, 6, 8, 15, 29, 43, 57 and 85 for hydroxychloroquine
3. Subject experience with low-volume sampling techniques compared with venepuncture assessed using patient satisfaction survey at Days 15, 85 for crenezumab and etrolizumab; day 8 for giredestrant and Days 2, 15 and 85 for hydroxychloroquine

Completion date
19/05/2022

Eligibility

Key inclusion criteria
1. Body mass index 18–32 kg/m2
2. Body weight 45–120 kg
3. Good health, as demonstrated by no clinically significant findings from medical history, physical examination, 12-lead ECG, and vital signs
4. Clinical laboratory evaluations (including chemistry panel [fasted at least 8 hours], CBC, coagulation testing [PT, INR, aPTT, and fibrinogen], and urinalysis [see Appendix 5]) within the reference range for the respective test laboratory, unless deemed not clinically significant by the investigator
5. Negative test for selected drugs of abuse at screening (does not include alcohol) and at check-in (Day –1) (does include alcohol)
6. Negative hepatitis panel (including hepatitis B surface antigen, hepatitis B virus core antibody, and hepatitis C virus antibody) and negative human immunodeficiency virus (HIV) antibody

screens
7. Negative screening test for latent mycobacterium tuberculosis (TB) infection by QuantiFERON® TB Gold
Indeterminate results may be confirmed by repeat test or by a purified protein derivative (PPD) skin test
8. Agreement to refrain from strenuous exercise from 48 hours prior to check-in (Day –1) and during the study duration
9. For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception, and agreement to refrain from donating eggs
10. For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use a condom, and agreement to refrain from donating sperm

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Pregnancy or breastfeeding, or intention to become pregnant during the study or within the following time windows after the dose of study treatment:
1.1. 8 weeks after the dose of crenezumab
1.2. 24 weeks after the dose of etrolizumab
1.3. 9 days after the dose of giredestrant
1.4. 29 weeks after the dose of hydroxychloroquine
2. Significant history or clinical manifestation of any metabolic, immunologic, allergic, dermatological, hepatic, renal, hematological, pulmonary, respiratory, cardiovascular, gastrointestinal, neurological, or psychiatric disorder, acute infection, or other unstable medical disease (as determined by the Investigator)
3. History of significant hypersensitivity, intolerance, or allergy to any drug compound, food, or other substance, unless approved by the Investigator
4. History or presence of an abnormal ECG that, in the Investigator’s opinion, is clinically significant
5. QTcF interval of > 450 ms for males or > 470 ms for females; PR interval of > 210 ms; or QRS complex of >120 ms
6. History of alcoholism or drug addiction within 6 months prior to check-in (Day –1) that, in the judgment of the Investigator, may put the subject at risk for being unable to participate for the full duration of the study
7. History of malignancy, except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, Stage I uterine cancer, or completely excised basal cell or squamous cell carcinoma of the skin
8. History of active or latent TB, regardless of treatment history

9. Participation in any other investigational study drug trial in which receipt of an investigational study drug occurred within 5 half-lives or 30 days (whichever is longer) prior to check-in (Day –1)
10. Receipt of any prescription medications/products within 14 days prior to check-in (Day –1), unless deemed acceptable by the investigator
11. Receipt of any new over-the-counter (OTC), non-prescription preparations (including vitamins; minerals; and phytotherapeutic-, herbal-, and plant-derived preparations) within 7 days prior to check-in (Day –1), unless deemed acceptable by the Investigator
12. Consumption of alcohol-containing foods or beverages within 72 hours prior to check-in (Day –1), unless deemed acceptable by the Investigator
13. Use of tobacco- or nicotine-containing products (including, but not limited to, cigarettes, e-cigarettes, pipes, cigars, chewing tobacco, nicotine patches, nicotine lozenges, or nicotine gum) within 6 months prior to check-in (Day –1)
14. Donation of blood within 30 days prior to screening or plasma within 2 weeks prior to screening
15. Receipt of blood products within 2 months prior to check-in (Day –1)
16. Poor peripheral venous access
17. Any acute or chronic condition that, in the investigator's judgment, would limit the subject's ability to complete and/or participate in this clinical study

Date of first enrolment
10/11/2021

Date of final enrolment
22/02/2022

Locations

Countries of recruitment
United States of America

Study participating centre
WCCT Global, Inc
United States of America
90630

Sponsor information

Organisation
Roche (United States)

ROR
https://ror.org/011qkaj49

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

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 for Phase I studies

IPD sharing plan summary
Not expected to be made available