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A study to assess the safety, processing by the body, and effects on the body following 4 weeks of selnoflast dosing in participants with coronary artery disease

Submission date
23/06/2022

Recruitment status
No longer recruiting

Registration date
05/07/2022

Overall study status
Completed

Last Edited
30/06/2022

Condition category
Circulatory System

[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:
Coronary artery disease (CAD) is a form of heart (cardiovascular) disease that is caused by a buildup of plaque in the blood vessels (arteries) that provide blood to the heart and body. Research has suggested that swelling (inflammation) may play a role in CAD and that blocking the inflammation causing factors could be helpful. Selnoflast is an experimental drug and is not yet approved by the health authorities. It is a drug that is being developed to lower inflammation in patients with CAD.

Selnoflast will be tested in a parent study as well as a sub-study both enrolling different participants. The purpose of this study and sub-study is to compare the effects, good or bad, of selnoflast versus medication that looks like a drug but has no active ingredient (placebo) in participants with CAD and high levels of C reactive protein (CRP). Participants with alteration (mutation) of the diseased tet methylcytosine dioxygenase 2 (TET2) gene that causes an age-related blood cells disorder (clonal hematopoiesis of indeterminate potential [CHIP]), in addition to narrowing of the blood vessels of the heart (CAD) and elevated CRP, will be enrolled in the sub-study. CRP is a protein indicative of inflammation in the body, it can be measured in blood by a routine laboratory test.

Who can participate?
People who are 18 years and over, diagnosed with coronary artery disease

What does the study involve?
Participants will be a part of either the parent study or the sub-study for a total of three months respectively.
Both these studies will be conducted in three parts:
1. Screening Period: Participants will have to undergo a certain test to see if they are eligible to participate in the study. There will be two screening visits 4 weeks before the start of the study
2. Treatment Period: Participants will receive either selnoflast (study drug) or placebo once in

the morning and once in the evening during the treatment period. The two doses must be taken not more than 14 hours apart. The participants will have to visit the clinic on Days 1, 8, 15, 22 to receive the study drug. On Days 1 and 15, participants will have to fast for at least 2 hours before receiving the drug. Participants in the sub-study will not have the requirement to fast before receiving the study drug. Participants can also consent for a Day 2 clinic visit in the parent study. Sub-study participants will not have the optional Day 2 clinic visit. Each visit may last for 2 to 6 hours. During the rest of the days, participants will self-administer the drug at home and maintain a record of the at-home dosing times in a paper diary.
3. Follow-up Period: Participants will have to visit the clinic on Days 29, 35, 42, 49 and 56 for follow-up visits. These visits will be to check on the participant after completion of the study treatment.

The participants in the parent study and sub-study will be divided into two groups decided by chance. Participants will have a one in two chance of being placed in either group.

Group 1: Participants will receive selnoflast, given as pills to be taken by mouth twice a day for about 28 days
Group 2: Participants will receive a dummy pill (placebo), to be taken by mouth twice a day for about 28 days

What are the possible benefits and risks of participating?
Participants may or may not receive any benefit from the study drug, but the information that is learned may help other people who have a similar medical condition in the future. Participants might experience side effects that can be mild to severe and vary from person to person. Selnoflast is an experimental drug and has limited testing in humans there may be side effects that are not known or expected at this time. The known and potential side effects of this drug are listed below:
1. Allergic Reactions: Allergic reactions can happen with any drug. These can be in the form of itching, difficulty breathing, a rash, and/or a drop in blood pressure.
2. The most common side effects observed in the study conducted on healthy volunteers were mild headache and nausea
3. Infection: Selnoflast affects a protein that regulates the immune system. Inhibition of the immune system could result in an increased likelihood of getting an infection.
4. Liver Damage: There may be some mild increase in laboratory tests used to evaluate liver function. Participants who have an abnormal blood test of liver function, will not be included in this study.
5. Decrease in the effect of vaccines: A protein (NLRP3) is activated by many vaccines. NLRP3 makes sure that the immune system responds properly to the vaccination. Hence, if NLRP3 is blocked the response to a vaccination can be weakened. Therefore, it is possible that the participants' response to vaccination could be reduced when they are being treated with selnoflast.

There may be a risk in exposing an unborn child to the study drug, and all risks are not known at this time. Women who are pregnant, become pregnant, or are currently breastfeeding must take precautions to avoid exposing an unborn child to the study drug.

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?
April 2022 to July 2023

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

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

Contact information

Type(s)
Public

Contact name
Dr Clinical Trials

Contact details
1 DNA Way
South San Francisco
United States of America
94080
+1 888-662-6728
global-roche-genentech-trials@gene.com

Additional identifiers

Protocol serial number
GC43343

Study information

Scientific Title
A phase Ic multicenter, randomized, double-blind, placebo-controlled study to assess the safety, pharmacokinetics, and pharmacodynamics following 4 weeks of NLRP3 inhibition with selnoflast in participants with coronary artery disease

Study objectives
The main purpose of this parent study and sub-study is to evaluate the safety, pharmacokinetics (PK), and pharmacodynamics (PD) of selnoflast compared with placebo in participants with coronary artery disease (CAD) with elevated high-sensitivity C-reactive protein (hsCRP). The sub-study will evaluate participants with CAD, pathogenic tet methylcytosine dioxygenase 2 (TET2) mutation(s) leading to clonal hematopoiesis of indeterminate potential (CHIP) (TET2/CHIP participants), and elevated hsCRP

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, WCG IRB (1019 39th Avenue SE, Suite 120, Puyallup, Washington, WA 98374, USA;
+1 855-818-2289; clientservices@wcgirb.com)

Primary study design
Interventional

Study design
Phase Ic multicenter randomized double-blind placebo-controlled study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Coronary artery disease

Interventions
The participants in the parent study and sub-study will be divided in the following two treatment arms:
1. Selnoflast: Participants will receive selnoflast capsules, orally, twice daily (BID), from Day 1 to Day 28
2. Placebo: Participants will receive selnoflast matching placebo capsules, orally, BID, from Day 1 to Day 28

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)
1. Percentage of participants with adverse events (AEs) measured from screening up to 28 days after the final dose of study drug (up to day 56)
2. Percentage of participants with severity of AEs determined according to the National Cancer Institute common terminology criteria for adverse events version 5.0 (NCI CTCAE v5.0) grading scale measured from screening up to 28 days after the final dose of study drug (up to day 56)
3. Percentage of participants with clinically significant changes in vital sign values measured using respiratory rate, pulse rate, systolic and diastolic blood pressure and temperature measured from screening up to 28 days after the final dose of study drug (up to day 56)
4. Percentage of participants with clinically significant abnormalities in electrocardiogram (ECG) parameters Measured Using Single 12-Lead ECG from screening up to 28 days after the final dose of study drug (up to day 56)
5. Percentage of participants with clinically significant laboratory findings measured using blood and urine samples from screening up to 28 days after the final dose of study drug (up to day 56)

Key secondary outcome(s)
1. Plasma concentration of selnoflast and its metabolites, if applicable, measured using plasma samples collected at specified timepoints (pre-dose and post-dose) from day 1 to day 29
2. Change From baseline in hsCRP measured using blood samples collected at specified timepoints from screening up to 28 days after the final dose of study drug (up to day 56)

Completion date

28/07/2023

Eligibility

Key inclusion criteria
1. Aged 18 years and over at the time of signing Informed Consent Form
2. A diagnosis of stable CAD with a history of myocardial infarction (MI) (known or suspected to be atherothrombotic Type 1) at least 90 days prior to screening Visit 1. Sub-study participants may have coronary revascularization at least 90 days prior to screening visit 1 and within 10 years of screening visit 1
3. Elevated plasma hsCRP level of ≥ 2 mg/l at screening visit 1 and 2
4. QTcF ≤ 450 ms in men and ≤ 470 ms in women by a single 12-lead ECG recording
5. Participants with CAD, pathogenic TET2 mutation(s) indicating a variant allele frequency (VAF) > 2% indicative of CHIP, and elevated hsCRP will be enrolled in the sub-study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Individuals with Class III and IV heart failure According to New York Heart Association
2. Planned procedure or surgery during the study and any major surgery within 90 days prior to screening Visit 1
3. Treatment with a live, attenuated vaccine within 90 days prior to the randomization visit
4. Treatment with a COVID-19 vaccine (including boosters) or other non-live vaccines (e.g., flu) within 28 days prior to the randomization visit
5. Current treatment with medications that are well known to prolong the QT interval or a known history of long QT syndrome or torsade de pointes
6. Positive hepatitis C virus (HCV) antibody test and subsequent positive HCV RNA test at screening
7. Positive hepatitis B surface antigen (HBsAg) or hepatitis B core antibody (HBcAb) test at screening
8. Positive human immunodeficiency virus (HIV) tests (HIV-1 antibody, HIV-1/2 antibody, HIV-2 antibody) at screening
9. History of tuberculosis or a positive interferon-γ (IFN-γ) release test at screening
10. Uncontrolled hypertension, defined as an average systolic blood pressure > 160 mmHg or an average diastolic blood pressure > 100 mmHg at each screening visit
11. Prior malignancy other than basal cell skin carcinoma, fully excised squamous cell carcinoma, and cervical intraepithelial neoplasia
12. Poor peripheral venous access

13. Uncontrolled cardiac arrhythmia, defined as recurrent and highly symptomatic ventricular tachycardia, atrial fibrillation with rapid ventricular response, or supraventricular tachycardia that are not controlled by medications, within 90 days prior to randomization

Date of first enrolment
31/07/2022

Date of final enrolment
30/06/2023

Locations

Countries of recruitment
United States of America

Study participating centre
TBD
United States of America
TBD

Sponsor information

Organisation
F. Hoffmann-La Roche Ltd

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

IPD sharing plan summary
Not expected to be made available