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A study to evaluate the safety, tolerability, and processing by the body of single-ascending doses of RO7490677 in healthy participants

Submission date 04/07/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 07/07/2022	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 18/07/2022	**Condition category** Digestive System	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aim:
Inflammatory bowel disease (IBD) is a type of inherited disorder that causes frequent pain and swelling (inflammation) of the intestines. The cause of IBD remains unknown, however environmental factors may trigger inflammation. IBD includes two related diseases, Ulcerative Colitis (UC) and Crohn's Disease (CD). Fibrostenotic Crohn's disease (FCD) is a subtype of CD in which chronic or long-term inflammation of the digestive tract (gastrointestinal tract; GI) is observed.

Zinpentraxin alfa (also called RO7490677) increases the regulatory capacity of a protein called pentraxin-2 (PTX-2) thus promoting healing and reducing scarring (fibrosis). It is an experimental drug, which means health authorities have not approved RO7490677 for the treatment of any disease. It has previously been tested in healthy volunteers and in participants with disease-causing scar tissue built up in the lungs (idiopathic pulmonary fibrosis) and an uncommon type of bone marrow cancer (myelofibrosis). The sponsor is developing the test medicine, to potentially treat diseases such as FCD.

The main purpose of this study is to test the drug at different doses to find out if it is safe and to understand the way the body processes the drug.

Who can participate?
Healthy volunteers aged between 18 and 65 years.
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What does the study involve?
The maximum length of participation in the study, once enrolled, will be up to 1 month. The study involves three parts:
1. Screening (to see if the participants are eligible for the study): The participants will be asked to complete some procedures and tests, including blood and urine tests, to check their eligibility. They might be asked to come back for further visits for confirmation.
2. Residential Phase (where the participants will receive treatment and stay in the clinic, for assessments): The participants will receive one infusion into the vein (intravenous) of either

zinpentraxin alfa or medicine that looks like a drug but has no active medicinal ingredients (placebo) the day after they check-in at the study site. The treatment (RO7490677 or placebo) will be decided by chance (like tossing a coin). The participant will have a one in four chance of getting placebo. Neither participant nor the study doctor can choose or know the group the participant is in. The infusion will take about an hour. The participants will be required to check in to the study site 1 day before they receive the study drug, and the stay at the clinic will be for about 9 nights.
3. Follow-up (to check on the participant after treatment is finished): The participants will return to the study site for a follow-up visit (lasting about 2 hours) about 20 days after they check out.

What are the possible benefits and risks of participating?
Participants will not receive any direct medical benefit from participating in this study, but the information will help other people with diseases such as fibrostenotic Crohn's disease in the future. Participants will also receive a compensation of up to $5030 depending upon clinic visits and follow-up visits. Participants may have side effects from the drugs or procedures used in this study that are mild to severe and even life-threatening, and they can vary from person to person. zinpentraxin alfa (RO7490677) has had limited testing in humans. The potential side effects based on human and laboratory studies or knowledge of similar drugs, are listed below.
1. Fever
2. Chills
3. Dizziness
4. Rash
5. Headache
6. Nausea (feeling of sickness in your stomach)
7. Vomiting
8. Anaphylaxis or hypersensitivity (allergic reaction): Anaphylaxis is a serious, potentially life-threatening allergic reaction requiring immediate medical treatment by your doctor. The reaction may cause hives on the skin, itchiness of the skin, extremely low blood pressure, swelling of the throat, difficulty breathing, and loss of consciousness
9. Immune system might develop special proteins in the body that respond to a substance that is foreign to the body (antibodies) to RO7490677 (the study drug)
10. Tiredness (fatigue)
11. Cough
12. Common cold (nasopharyngitis)
13. Worsening of idiopathic pulmonary fibrosis
14. Loose, watery, and more frequent bowel movements (diarrhoea)
15. Inflammation of the airways (bronchitis)
16. Joint stiffness (arthralgia)
17. Abdominal pain
There may be side effects that are not known at this time.

There may be some risks associated with the procedures performed during the study, as drawing blood can cause pain, bruising, or infection where the needle is inserted. Some people experience dizziness, fainting, or upset stomach when their blood is drawn.

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

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?
From October 2021 to November 2023

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

Who is the main contact?
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Contact information

Type(s)
Public

Contact name
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Additional identifiers

Protocol serial number
GP44089

Study information

Scientific Title
A Phase Ia, Randomized, Investigator- and Subject-Blinded, Placebo-Controlled Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of Single-Ascending Doses of RO7490677 in Healthy Volunteers

Study objectives
To assess the safety, tolerability, and pharmacokinetics (PK) of zinpentraxin alfa (RO7490677) compared with placebo in healthy participants.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/05/2022, Salus IRB (2111 W. Braker Lane, Suite 100, Austin, Texas, 78758; +1-512-380-1244; salus@salusirb.com), ref: not applicable

Primary study design

Interventional

Study design
Phase 1, randomized, placebo controlled, single-centre, single-ascending dose (SAD) study

Study type(s)
Other

Health condition(s) or problem(s) studied
Fibrostenotic Crohn’s disease (FCD)

Interventions
RO7490677: Participants will receive zinpentraxin alfa (RO7490677) as single intravenous (IV) infusion on Day 1 delivered over 70-80 min. Dose escalation in additional cohorts, if required, will be made based on available safety data, and when applicable, PK, and anti-drug antibody (ADA) data from the previous cohorts.

Placebo: Participants will receive zinpentraxin alfa matching placebo as single IV infusion on Day 1 delivered over 70-80 min.

In each cohort, a sentinel group of 2 participants will be randomized in a 1:1 ratio and dosed first with study drug: 1 participant with RO7490677 and the other with placebo. The remaining participants in the same cohort will be randomized in a 5:1 ratio to receive RO7490677 or placebo.

The study site will obtain the participant's identification number and treatment assignment from a randomization list provided by a contract research organization (CRO) biostatistician.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
zinpentraxin alfa (RO7490677)

Primary outcome(s)
1. Safety measured using the incidence of Adverse Events (AEs) between screening and the end of study treatment, or early discontinuation (approximately up to 64 days)
2. Safety measured using the severity of AEs per National Cancer Institute-Common Terminology Criteria for Adverse Events version 5.0 (NCI CTCAE v5.0) grading scale between screening and the end of study treatment, or early discontinuation (approximately up to 64 days)
3. Number of participants with a clinically significant change from baseline in vital signs measured using respiratory rate, pulse rate, systolic and diastolic blood pressure, and temperature at screening, check-in (Day -1), and at multiple timepoints until the end of study treatment, or early discontinuation (approximately up to 64 days)
4. Number of participants with a clinically significant change from baseline in clinical laboratory tests assessed using blood and urine samples collected at screening, check-in (Day -1), and at multiple timepoints until the end of study treatment, or early discontinuation (approximately up to 64 days)

5. Number of participants with a clinically significant change from baseline in 12-Lead ECG parameters at screening, check-in (Day -1), and at multiple timepoints until the end of study treatment, or early discontinuation (approximately up to 64 days)

Key secondary outcome(s)
1. Plasma concentration of RO7490677 measured using plasma samples collected at predose and at multiple timepoints post-dose until the end of study treatment, or early discontinuation (approximately up to Day 29)
2. Area under the concentration-time curve (AUC) of RO7490677 measured using plasma samples collected at predose and at multiple timepoints post-dose until the end of study treatment, or early discontinuation (approximately up to Day 29)
3. Maximum observed concentration (Cmax) of RO7490677 measured using plasma samples collected at predose and at multiple timepoints post-dose until the end of study treatment, or early discontinuation (approximately up to Day 29)
4. Total clearance (CL) of RO7490677 measured using plasma samples collected at predose and at multiple timepoints post-dose until the end of study treatment, or early discontinuation (approximately up to Day 29)
5. Volume of distribution of RO7490677 measured using plasma samples collected at predose and at multiple timepoints post-dose until the end of study treatment, or early discontinuation (approximately up to Day 29)
6. Terminal drug-elimination half-life (t1/2) of RO7490677 measured using plasma samples collected at predose and at multiple timepoints post-dose until the end of study treatment, or early discontinuation (approximately up to Day 29)
7. Number of participants with anti-drug antibodies (ADA) to RO7490677 measured using plasma samples collected at predose and at multiple timepoints post-dose until the end of study treatment, or early discontinuation (approximately up to Day 29)

Completion date
03/11/2023

Eligibility

Key inclusion criteria
1. Aged ≥18 and ≤65 years at the time of signing the Informed Consent Form (ICF)
2. Body mass index (BMI) ≥18 and ≤32 kg/m² at screening
3. Weight ≥45 and ≤100 kg at screening
4. Clinical laboratory evaluations (not including lymphocyte subsets) at screening and on Day -1 within the reference range for the test laboratory unless deemed not clinically significant by the investigator
5. Ability to restrict alcohol intake (≤2 servings of alcohol per day, where: one serving is 12 ounces of beer, 5 ounces of wine, 1.5 ounces of spirits, or equivalent), to refrain from the use of tobacco or nicotine products (smoking/vaping), and to refrain from illicit drug use during the study
6. For female participants of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception
7. For male participants: agreement to remain abstinent (refrain from heterosexual intercourse) or use a condom and agree to refrain from donating sperm

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
All

Key exclusion criteria
1. Pregnancy or breastfeeding, or intention of becoming pregnant during the study or within 8 weeks after the final dose of the study drug
2. Major surgery within 8 weeks prior to screening, or planned major surgery during the study or planned within 3 months after the dose of study drug
3. History or clinical manifestations of significant metabolic, hepatic, renal, pulmonary, cardiovascular, haematologic, gastrointestinal, urologic, neurologic, or psychiatric disorders, as determined by the investigator
4. History of serious or uncontrolled hypertension or treatment with antihypertensive medications
5. History of malignancy within 5 years prior to screening, except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, or Stage I uterine cancer
6. History of severe allergic or anaphylactic reactions to human, humanized, or murine monoclonal antibodies
7. Treatment with any immunosuppressive medication within 30 days or 5 drug-elimination half-lives, whichever is longer, prior to initiation of study drug
8. Donation of blood or plasma from 30 days prior to screening through study completion or end of treatment (ET), inclusive
9. Use of a non-biologic investigational drug or participation in an investigational study with a non-biologic drug within 30 days or 5 drug-elimination half-lives, whichever is longer, prior to initiation of study drug
10. Use of biologic investigational therapy or participation in an investigational study involving biologic therapy within 3 months or 5 drug-elimination half-lives, whichever is longer, prior to initiation of study drug
11. Use of tobacco or nicotine products including electronic cigarettes (i.e. vaping) within 3 months of screening, as indicated by medical history or urine cotinine levels
12. Positive for hepatitis C virus (HCV) antibody and RNA, hepatitis B surface antigen (HBsAg), or human immunodeficiency virus (HIV) antibody at screening
13. Positive for coronavirus (COVID-19) infection at screening and Day -1
14. Positive for tuberculosis (TB) during screening or within 3 months prior to screening
15. History of or currently active primary or secondary immunodeficiency

Date of first enrolment
07/07/2022

Date of final enrolment

08/11/2022

Locations

Countries of recruitment
United States of America

Study participating centre
Covance Research Unit
Daytona Beach
Daytona
United States of America
32117

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