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A study to evaluate the safety, tolerability, processing by the body and mechanism of action of RO7486967 in participants with ulcerative colitis

Submission date
01/11/2021

Recruitment status
No longer recruiting

Registration date
04/11/2021

Overall study status
Completed

Last Edited
16/11/2023

Condition category
Digestive System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The purpose of this study is to test the safety of RO7486967 and to find out what effects, good or bad, RO7486967 has on participants. RO7486967 is a small chemical molecule that can inhibit the formation of a protein complex known as “inflammasome,” which could worsen the inflammation of participant’s intestine.
RO7486967 is an experimental drug, which means Health Authorities have not approved RO7486967 for the treatment of any diseases.

Who can participate?
People aged between 18 to 75 years with moderate to severe active ulcerative colitis.

What does the study involve?
Participants will be randomly assigned by a computer program to one group (drug or placebo), i. e. randomized. This means that participants are put into a group by chance (like tossing a coin). Neither a participant nor the study doctor may choose the group to be in. RO7486967 or placebo is provided in gelatin capsules which the participant needs to swallow with a bit of water. A participant will take 3 capsules each day for 7 days consecutively. The total length of time in the study, including the screening, dosing period(s), and follow-up periods, will be approximately 6 weeks. First part involves the study screening which includes discussion of the study, medical history check, physical examination, vital signs check, blood and urine sample collection, measurement of the electrical activity of the heart and pregnancy testing (if female). Then, RO7486967 or placebo is provided in gelatin capsules which one needs to swallow with a bit of water.

What are the possible benefits and risks of participating?
RO7486967 is being given to participants purely for research purposes; it is not intended that one will receive any benefit from it, as the treatment duration of 7 days is too short. New, more effective, and convenient medicines can only be developed by performing research studies such

as this one. Information from this study may help doctors learn more about RO7486967 and the treatment of UC. Ultimately, it is the future patients who will hopefully benefit from the results of this study.
Participants may have side effects from the medications or procedures used in this study. However, Roche, the study doctor, and other doctors do not know all of the side effects that could occur. Side effects can vary from mild to very serious and may vary from person to person. Many side effects go away soon after participants stop what is causing them. In some cases, side effects can be serious (in very rare cases may be fatal) and may be longlasting or may never go away. Participants should talk to the study doctor about any side effects that one has have while taking part in the study. Everyone taking part in the study will be watched carefully for any side effects and cared for as appropriate. The study doctors may give medications to help lessen side effects.

Where is the study run from?
Charité Research Organisation GmbH

When is the study starting and how long is it expected to run for?
December 2020 to June 2022

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

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

Contact information

Type(s)
Public

Contact name
Dr Clinical Trials

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Additional identifiers

Protocol serial number
BP43099

Study information

Scientific Title

Randomized, double-blind, sponsor-open, phase 1b study to assess the safety, pharmacokinetics and to explore the pharmacodynamics of RO7486967 in patients with moderate to severe active ulcerative colitis

Study objectives
To assess safety, tolerability and pharmacokinetics while exploring the pharmacodynamics of RO7486967 when administered to participants with ulcerative colitis

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/10/2021, Landesamt für Gesundheit und Soziales, Geschäftsstelle der Ethik-Kommission des Landes Berlin (Turmstr. 21, Haus A, Berlin, 10559, Germany; +49 (0)228 99 307 4318; ct@bfarm.de), ref: 61-3910-4044959

Primary study design
Interventional

Study design
Phase 1 single-centre randomized placebo-controlled double-blind study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Ulcerative colitis

Interventions
Participants will be randomized to receive either RO7486967 or a placebo orally via a randomization list provided from the sponsor to the site. The treatment duration will be 7 days and a follow up of 7 days after the last study drug is administered.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
RO7486967

Primary outcome(s)
1. Percentage of participants with adverse events, with severity determined according to National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0 (NCI CTCAE v5.0), measured throughout the study.
2. Pharmacokinetic (PK) parameters of RO7486967 using blood samples at predose, 30 min., 1, 2, 4, 6 and 10 h on days 1 and 5; predose on days 2, 3, 4, 6 and 7; early withdrawal and follow up visit.
The following PK parameters will be calculated if data allows:
Time to maximum observed concentration (Tmax), maximum concentration (Cmax),

concentration measured at the end of the dosing interval prior to the next drug administration (Ctrough), area under the concentration-time curve extrapolated to infinity (AUC0-inf) and over the dosing interval (AUCtau), apparent clearance after the first dose administration (CL/F = dose /AUCinf) as well as at steady-state (CLss/F = dose/AUCtau), apparent volume of distribution (V /F), and estimates of T1/2.

Key secondary outcome(s)
1. Changes in c-reactive protein (CRP) in blood and calprotectin in stool at check-in, on days 1, 2, 5 and 6 at 6 h, early withdrawal and follow up visit.

Completion date
30/06/2022

Eligibility

Key inclusion criteria
1. Between the ages of 18 to 75 years (inclusive)
2. Diagnosis of UC at least 12 weeks prior to screening.
3. Participants with active moderate to severe ulcerative colitis as measured by partial >= MCS 3, with stool frequency subscore >=1, rectal bleeding subscore >=1, and fecal calprotectin >=150 mcg/g.
4. Most recent colonoscopy within the preceding 3 years at the time of screening.
5. Body mass index (BMI) within the range of 18-35 kg/m² (inclusive).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
75 Years

Sex
All

Total final enrolment
19

Key exclusion criteria
1. Diagnosis of fulminant UC, Crohn’s disease or indeterminate colitis, microscopic colitis, segmental colitis associated with diverticulosis, ischemic colitis, or radiation-induced colitis based on medical history, endoscopy, and/or histological findings.
2. Active infections requiring systemic therapy with antibiotic, antiviral, or antifungal medication

or febrile illness within 7 days before Day 1.
3. History of primary or acquired immunodeficiency.
4. History of chronic pulmonary disease with resultant clinically significant abnormal pulmonary function.
5. History of clinically significant cardiac or cardiovascular disease or uncontrolled hypertension.
6. Presence of chronic liver disease.
7. Evidence of colonic dysplasia that cannot be completely removed.
8. History of tuberculosis or a positive Quantiferon® Gold test.
9. History of clinically significant severe drug allergies, multiple drug allergies, or allergy to any constituent of the investigational medicinal product (IMP).
10. Lymphoma, leukemia, or any malignancy within the past 10 years, except for basal cell or squamous epithelial carcinomas of the skin that have been resected with no evidence of metastatic disease for 3 years and in situ carcinoma of the cervix that was completely removed surgically.
11. History or presence of clinically significant ECG abnormalities before study drug administration (e.g., PQ/PR interval >=220 ms, QT corrected for heart rate using Fridericia's correction factor (QTcF),<350 or >=450 ms) or clinically significant cardiovascular disease (e.g., cardiac insufficiency, coronary artery disease, cardiomyopathy, congestive heart failure, family history of congenital long QT interval syndrome, family history of sudden death).
12. Fecal microbiota transplant, defined as receipt of any product derived from the feces of another human and administered per oral, per nasogastric or nasoduodenal, or per rectum within the last 6 months.
13. Bowel surgery within 12 months prior to study start.
14. History of colectomy or partial colectomy.
15. History of known bleeding disorder or diseases with an increased risk of bleeding tendency.

Date of first enrolment
25/11/2021

Date of final enrolment
09/06/2022

Locations

Countries of recruitment
Germany

Study participating centre
Charité Research Organisation GmbH
Germany
10117

Sponsor information

Organisation
Roche (Switzerland)

ROR
https://ror.org/00by1q217

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 are not expected to be made available due to there being no regulatory requirement to do so.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		14/11/2023	16/11/2023	Yes	No