A Randomized, Placebo-controlled, Single Ascending Dose Study to Investigate the Safety, Tolerability, and Pharmacokinetic Profile of REC-4881 in Healthy Volunteers

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON51761

Source
ToetsingOnline

Brief title
SAD and FE study to assess the safety, tolerability, PK and PD of REC-4881

Condition

- Other condition

Synonym
Colon cancer

Health condition

Colon cancer

Research involving

Human

Sponsors and support

Primary sponsor: Recursion Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Pharmaceutical Industry.

Intervention

Keyword: Inherited colon cancer, REC-4881

Outcome measures

Primary outcome

To evaluate the safety and tolerability of single ascending doses (SADs) of

orally administered REC-4881 in healthy adult volunteers.

Secondary outcome

To characterize the plasma pharmacokinetics (PK) of SADs of orally administered

REC-4881 and REC 1157786 (its enantiomer) in healthy

adult volunteers.

To evaluate the effect of food on the single-dose PK of REC-4881 and REC

1157786.

Study description

Background summary

REC-4881 is a new compound that may potentially be used for the treatment of inherited colon cancer. REC-4881 inhibits mitogen activated protein kinase (MEK), an enzyme involved in normal functioning of human cells. In a healthy individual MEK can regulate cell division at a normal rate. In tumors MEK is overactivated and causes excessive cell division and growth. From studies in animals it is known that REC-4881 can counter this process. REC-4881 can possibly be used in the future for the treatment of inherited colon cancer in patients.

Study objective

In this study we will investigate how safe the new compound REC-4881 is and how well it is tolerated when it is used by healthy participants.

We also investigate how quickly and to what extent REC-4881 is absorbed, transported, and eliminated from the body. In addition, we look at the effect of REC-4881 on a specific enzyme.

For Group 1: In addition, we will look at the effect of food on how the body handles REC-4881. To study this, the study compound will be given once with and once without food. Depending on these results, thereafter, a higher dose of REC 4881 will be given either with or without food.

We compare the effects of REC-4881 with the effects of a placebo. A placebo is a compound without any active ingredient. Please note that when the term *study compound* is used in this document, we mean REC-4881, placebo, or both.

REC-4881 has been used by humans before. In addition, it has been extensively tested in the laboratory and on animals. REC-4881 will be tested at various dose levels.

Study design

For Group 1, the study takes about 9 weeks from the inspection to leaving the research center. For Group 2, the study from the inspection up to and including leaving the research center takes a maximum of approximately 10 weeks.

For the study, it is necessary for Group 1 and Group 2 to stay in the study center for a period of 37 days (36 nights).

Day 1 is the first day of receiving the study drug. We expect the volunteer at the study center on the day prior to the first administration of the study drug. You must report to the research center between 9:30 a.m. and 2:00 p.m. One will leave the study center on Day 36 (Group 1) or Day 28 (Group 2) of the study.

Group 1 will receive three times REC-4881 or placebo as capsules by mouth containing 240 milliliters (mL) of (tap) water. REC-4881 is given twice as a 4 mg dose and once as a 8 mg dose.

Group 2 will receive REC-4881 or placebo three times as capsules by mouth containing 240 milliliters (mL) (tap) of water. REC-4881 is given once as a 4 mg dose, once a 8mg dose and once as a 12 mg dose.

Intervention

Group 1:
Treatment

4 mg REC-4881 once or placebo (with food or fasting) Days 1 and 15
8 mg REC-4881 once or placebo (with food or fasted) Day 29

Group 2:
Treatment

4 mg REC-4881 once or placebo (with food or fasting) Days 1
8 mg REC-4881 once or placebo (with food or fasting) Days 15
12 mg REC-4881 once or placebo (with food or fasting) Days 29

Study burden and risks

blood draw
Blood draws may hurt or cause bruising. Using an indwelling cannula can sometimes cause inflammation, swelling, hardening of the artery, or blood clotting and bleeding around the puncture site. In some individuals, a blood draw can sometimes cause paleness, nausea, sweating, slow heart rate, or drop in blood pressure with dizziness or fainting.

All in all, we take approximately 263 milliliters (ml) of blood from the examination until you leave the research center if you participate in both Group 1 and in Group 2. This amount is not a problem in adults. For comparison: at the blood bank 500 ml of blood is taken at once at a time. If the investigator deems this necessary to ensure the safety of the participant, additional samples may be taken for any additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

ECG
To make a heart film, electrodes are placed on the arms, chest and legs. To monitor the electrical activity of the heart over a longer period of time, electrodes are placed on the chest and abdomen. Prolonged use of these electrodes may cause skin irritation.

Meals/Fasting
The high-fat breakfast is a large breakfast, including 2 fried eggs, hash browns and bacon. One must eat this breakfast completely. Especially for small eaters, it can be difficult to eat this breakfast completely.

If one has to fast for a long time during the examination, this can lead to complaints such as dizziness, headache, stomach complaints or fainting.

Coronavirus test
Samples for the coronavirus test will be taken with cotton swabs at the back of the nose and throat. Collecting the samples only takes a few seconds, but can

cause discomfort and discomfort. Taking a sample from the back of the throat may result in gagging. When the sample is taken from the back of the nose, you may experience a stinging sensation and the eyes may water.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Male or female participant aged 18 to 50 years, inclusive.
2. Participant must provide written informed consent.
3. Participant's body mass index is between 18 and 32 kg/m2, inclusive, with a minimum body weight of 50 kg.
4. Participant is healthy, as determined by pre-study medical history,physical examination (including neurologic examination), vital signs, and 12-lead ECG.

Exclusion criteria

1. Participant has any clinically significant laboratory abnormality or illness which, in the opinion of the Investigator, could interfere with the conduct or interpretation of the study or put the participant at risk.
2. Participant has a history of gall bladder disorder or complication, including cholelithiasis.
3. Participant has a history of abnormal left ventricular ejection fraction.
4. Participant has a history of corneal erosions, corneal degenerations, active or recurrent keratitis, and other forms of serious ocular surface inflammatory conditions.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-02-2022
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	25-01-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	07-02-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2021□006909□30-NL
CCMO	NL80312.056.22

Study results