A Randomized, Double-blind, Placebo-controlled, Single Ascending Dose and Multiple Ascending Dose Study to Investigate the Safety, Tolerability, and Pharmacokinetics of REC-3964 in Healthy Subjects

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Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON53684

Source
ToetsingOnline

Brief title
SAD PK study with REC-3964

Condition

- Other condition
- Bacterial infectious disorders

Synonym
Bacterial infection in the bowel

Health condition

Clostridium difficile

Research involving
Human

Sponsors and support

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

Intervention

Keyword: MAD, REC-3964, SAD

Outcome measures

Primary outcome

To evaluate the safety and tolerability of single ascending doses (SAD) and multiple ascending doses (MAD) of REC-3964 administered orally to healthy subjects.

Secondary outcome

Secondary Objectives:

• To characterize the pharmacokinetics (PK) of REC-3964 and its enantiomer, REC-3974, in plasma and urine following single and multiple oral doses of REC-3964 in healthy subjects.

Exploratory Objectives:

• To investigate the metabolite profile of REC-3964 in plasma following single and multiple oral doses of REC-3964 in healthy subjects.

• To investigate the potential genetic variants influencing the PK of REC-3964

in healthy subjects.

• To investigate potential blood biomarkers of REC-3964 activity following

single and multiple oral doses in healthy subjects.

• To evaluate changes in cytochrome P450 (CYP)3A activity following multiple

oral doses of REC-3964 in healthy subjects.

• To estimate the fraction of unbound REC-3964 in plasma following single oral

doses of REC-3964 in healthy subjects.

Study description

Background summary

REC-3964 is a new compound that may potentially be used for the treatment of Clostridium difficile infections. An infection with this bacterium is known to cause the release of toxins in the gut leading to stomach pain (abdominal pain) and watery diarrhea. Severe infections can occur when normal gut bacteria are disrupted and can lead to hospitalization or even death. REC-3964 is found to have a suppressing effect on these toxins and protects cells in the gut in this manner. Contrary to antibiotics, REC-3964 is found to not alter normal bacteria in the gut. REC 3964 may potentially be used for the treatment of (acute) severe cases of Clostridium difficile infections.

Study objective

REC-3964 is a new investigational drug, meaning that it has not yet been approved or marketed in the Netherlands or anywhere else at this time.

In this study, REC-3964 is investigated in humans for the first time. REC-3964 has not been used by humans before. It has been extensively tested in the laboratory and on animals.

The purpose of this study is to test the safety and tolerability of REC-3964 when it is taken by healthy subjects.

In this study, we will also investigate how quickly and to what extent REC-3964 is absorbed, transported, and eliminated from the body.

The study will also include collecting a blood sample for genotyping to look at

the effect of your genetic information on your body*s response to REC-3964.

Study design

Part A

Screening -> Day -28 up to Day -2

Treatment period - Arrival -> Day -2
Treatment period - In-house stay -> Day -2 up to Day 3
Treatment period - Departure -> Day 3

Follow-up -> Between Day 6 and Day 8

Part B

Screening -> Day -28 up to Day -2

Treatment period - Arrival -> Day -2
Treatment period - In-house stay -> Day -2 up to Day 16
Treatment period - Departure -> Day 16

Follow-up -> Between Day 18 and Day 22

Intervention

Part A
Starting dose 50 mg REC-3964 or placebo orally once on D1 (doses in subsequent groups to be determined).

Part B
Starting dose to be determined REC-3964 or placebo orally from D1 to D14: One time, two times (every 12 hours) or three times (every 8 hours) each day

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula (a tube in a vein in the arm) can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment (bruising) of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, sweating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take about 102 (Part A) or 199 (Part B) milliliters (mL) of blood from screening to follow-up. This amount does not cause any problems in

adults. To compare: a blood donation involves 500 mL of blood being taken each time. If the investigator thinks it is necessary for the safety of a subject, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

Heart tracing
To make a heart tracing, electrodes (small, plastic patches) will be placed on arms, chest and legs. To monitor the electrical activity of the heart over a longer period, electrodes (small, plastic patches) will be placed on the chest and abdomen. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Meals
Standardized meals will be given.

Coronavirus test
Samples for the coronavirus test will be taken from the back of the nose and throat using swabs. Taking the samples only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the throat may cause subjects to gag. When the sample is taken from the back of the nose, they may experience a stinging sensation and the eyes may become watery.

Contacts

Public
Recursion Pharmaceuticals, Inc.

S Rio Grande St. 41
Salt Lake City UT 84101
US
Scientific
Recursion Pharmaceuticals, Inc.

S Rio Grande St. 41
Salt Lake City UT 84101
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Subject is male or female aged >= 18 to <= 65 years. For Cohort A6 and potentially for Cohort B5, subject is male or female aged > 65 years (note: there is no upper limit for the subject*s age).
2. Subject must provide written informed consent prior to initiation of any study procedures.
3. Subject*s body mass index is between 18 and 32 kg/m2, inclusive, with a minimum body weight of 50 kg.
4. Subject is healthy as determined by medical history, physical examination, vital signs, and 12 lead ECG. For any abnormalities, the subject may be included only if the Investigator judges the abnormalities or deviations from normal to be not clinically significant.
5. Subject*s clinical laboratory test results (hematology including reticulocyte count, biochemistry, coagulation, urinalysis, comprehensive metabolic panel, and complete blood count) are clinically acceptable as determined by the Investigator at Screening and Admission.

Exclusion criteria

1. Subject 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 subject at risk.
2. Subject has any condition that, in the opinion of the Investigator, could affect drug absorption (eg, stomach or intestinal surgery such as cholecystectomy or bariatric surgery, gastroesophageal reflux disease, irritable bowel syndrome, or celiac disease).
3. Subject has a known history of hypersensitivity to the drug class or its excipients.
4. Subject has a history of alcohol or substance abuse within 1 year prior to screening for study participation, or is currently using alcohol, drugs of abuse, or any prescribed or over-the-counter medication in a manner, which, in the opinion of the Investigator, indicates abuse.

5. Subject has been treated with prescription, over-the-counter, dietary, or herbal supplements that are CYP3A inhibitors or inducers within 14 days before the first dose of study drug: eg, ketoconazole, itraconazole, voriconazole, posaconazole, clarithromycin, telithromycin, nefazodone, rifampin, rifapentine, rifabutin, grapefruit juice, Valencia oranges, or St. John*s Wort.

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:	Completed
Start date (anticipated):	17-08-2022
Enrollment:	106
Type:	Actual

Ethics review

Approved WMO Date:	13-07-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-08-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	18-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-03-2023
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	EUCTR2022-002403-38-NL
CCMO	NL81881.056.22

Study results

Date completed: 09-05-2023

Results posted: 18-01-2024

First publication
28-11-2023

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File