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A study in healthy males to assess how the radiolabelled test medicine RO7223280 is broken down, processed and removed from the body

Submission date
19/07/2022

Recruitment status
No longer recruiting

Registration date
25/07/2022

Overall study status
Completed

Last Edited
22/07/2022

Condition category
Other

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Antibiotics are medicines used to prevent and treat bacterial infections. Antibiotic resistance occurs when bacteria adapt and change in response to the use of these medicines in such a way that medicines can no longer kill them. One of the bacterial strains which has resistance to multiple antibiotics is Acinetobacter baumannii. This bacteria type is most commonly found in hospitals leading to hospital-acquired bacterial infections in people with a compromised immune system.

The aim of this study is to test the study drug (RO7223280) designed for the treatment of hospital-acquired (or nosocomial) bacterial pneumonia (HABP), ventilator-associated bacterial pneumonia (VABP), and bloodstream infections (BSI) caused by A. baumannii. The study looks to see how quickly and to what extent RO7223280 is distributed, broken down (metabolized), and eliminated from the human body (pharmacokinetics). For this study, RO7223280 is radioactively labelled with carbon-14 (14C). In this way, RO7223280 can be traced in blood, plasma, urine, and faeces.

Who can participate?
Healthy male volunteers aged between 35 to 64 years old

What does the study involve?
Once enrolled, participants will need to be a part of this study for up to 22 days. This study will have three parts:
1. A screening period of 28 days, where certain tests would be done to determine if the participant is eligible to take part in the study
2. A treatment period, where eligible participants will be enrolled and will receive a single 1-hour infusion into the vein (intravenous) of 14C-labelled-RO7223280 on Day 1 in the research centre. Participants will be required to stay in the research centre for a period of at least 16 days (15 nights). The stay might be extended to 22 days if a participant has not passed at least 95% of

radioactivity out of their bodies.
3. A follow-up period during which participants will have to return to the research centre at approximately 7 days after the last urine and faeces samples are collected

What are the possible benefits and risks of participating?
Participants will receive monetary compensation of €4021 for participation in the entire study. Reserve participants (individuals who are approved for screening but do not take part in the study) will receive a compensation of €529. The information gained from this study may help investigators to increase their knowledge about the effects of RO7223280 and help in the search for better treatment of bacterial infections.
Participants may have side effects from the drug RO7223280. These can be mild to severe and even life-threatening, and they can vary from person to person.

The potential side effects associated with RO7223280 or study procedures are listed below:
Risks associated with RO7223280:
RO7223280 might have (serious) side effects that are still unknown. In addition to unknown side effects, there is a (small) chance that an allergic reaction will occur. This can be caused by the study compound or other ingredients that are used to prepare the formulation. The most common side effects observed previously were infusion-related effects such as itching, flushing, shortness of breath etc. Other side effects include headache and, skin inflammation, and skin bruising caused by infusion needles.

Coronavirus test:
Samples for the coronavirus test will be taken from the back of the participant's nose and throat using swabs. Taking the samples can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the throat may cause the participant to gag. When the sample is taken from the back of the nose, the participant may experience a stinging sensation and the eyes may become watery.

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 September 2022

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

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-001155-16

Protocol serial number
BP43532

Study information

Scientific Title
Open-label, non-randomized study investigating the excretion balance, pharmacokinetics, and metabolism of a single intravenous dose of [14C]-labelled RO7223280 in healthy male participants

Study objectives
The purpose of the study is to characterise mass balance, rates, and routes of elimination of [14C/12C]-labelled RO7223280, using conventional analytical methods. The study will also assess the pharmacokinetics (PK) of total drug-related [14C]-radioactivity, [12C]-RO7223280 and its metabolite(s), as appropriate.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/07/2022, The Independent Ethics Committee (Medisch Ethische Toetsings Commissie) of the Foundation Evaluation of Ethics in Biomedical Research (Stichting Beoordeling Ethiek Biomedisch Onderzoek, Doctor Nassaulaan 10, 9401 HK Assen, Netherlands; +31 592 40 58 71; info@stbebo.nl), ref: RPU21555-21555X

Study design
Open-label non-randomized interventional study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Healthy participants

Interventions
Participants will receive a single dose of [14C/12C]-RO7223280, 1000 milligrams (mg) with a total radioactivity of 1.8 megabecquerel (MBq) [48 microcurie (µCi)] administered as 1-hour intravenous (IV) infusion under fasted conditions on Day 1.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
[14C/12C]-RO7223280

Primary outcome(s)
1. Total drug-related [14C]-radioactivity of [14C]-labelled RO7223280 measured as cumulative percentage of [14C]-radioactive dose recovered (%Fe) in urine and faecal samples collected at pre-dose and multiple timepoints post-dose up to Day 22
2. Cumulative amount of total drug-related [14C]-radioactivity of [14C]-labelled RO7223280 during the sampling period, calculated as the sum of amount of total drug-related [14C]-radioactivity excreted (Ae) for each collection interval measured from urine and faecal samples collected at pre-dose and multiple timepoints post-dose up to Day 22
3. Maximum observed blood or plasma concentration (Cmax) of [14C]-Radioactivity and plasma concentration of [12C]-RO7223280 (and its metabolite(s), as appropriate) measured from blood or plasma samples collected at pre-dose and multiple timepoints post-dose up to Day 22
4. Time to maximum observed blood or plasma concentration (Tmax) of [14C]-radioactivity and plasma concentration of [12C]-RO7223280 (and its metabolite(s), as appropriate) measured from blood or plasma samples collected at pre-dose and multiple timepoints post-dose up to Day 22
5. Area under the plasma or blood concentration versus time curve from time zero to the last measurable concentration (AUClast) of [14C]-radioactivity and of [12C]-RO7223280 (and its metabolite(s), as appropriate) measured from blood or plasma samples collected at pre-dose and multiple timepoints post-dose up to Day 22
6. Area under the plasma or blood concentration versus time curve from time zero extrapolated to infinity (AUCinf) of [14C]-radioactivity and of [12C]-RO7223280 (and its metabolite(s), as appropriate) measured from blood or plasma samples collected at pre-dose and multiple timepoints post-dose up to Day 22
7. Apparent terminal half-life (T1/2) of [14C]-radioactivity and of [12C]-RO7223280 (and its metabolite(s), as appropriate) measured from blood or plasma samples collected at pre-dose and multiple timepoints post-dose up to Day 22
8. Terminal rate constant calculated by linear regression of the log-transformed terminal part of the concentration-time curve (λz) of [14C]-radioactivity and of [12C]-RO7223280 (and its metabolite(s), as appropriate) measured from blood or plasma samples collected at pre-dose and multiple timepoints post-dose up to Day 22
9. Clearance (CL) of [12C]-RO7223280 measured from plasma samples collected at pre-dose and multiple timepoints post-dose up to Day 22
10. Volume of distribution at steady-state (Vss) of [12C]-RO7223280 measured from plasma samples collected at pre-dose and multiple timepoints post-dose up to Day 22
11. Blood-to-plasma ratio of total drug-related [14C]-radioactivity measured from blood or plasma samples collected at pre-dose and multiple timepoints post-dose up to Day 22

Key secondary outcome(s))
1. Concentration of human metabolites of RO7223280 (as appropriate) measured in plasma, blood, urine, and faecal samples collected at pre-dose and multiple timepoints post-dose up to Day 22
2. Percentage of participants with adverse events (AEs) and severity of AEs, with severity being determined according to National Cancer Institute-Common Terminology Criteria for Adverse Events Version 5.0 (NCI CTCAE V5.0) from screening up to 7 days after the final collection of samples (up to approximately 8 weeks)
3. Number of participants with change from baseline in vital signs measured using temperature, pulse rate, respiratory rate, systolic and diastolic blood pressure from screening up to 7 days after the final collection of samples (up to approximately 8 weeks)
4. Number of participants with change from baseline in physical examination parameters measured by assessments of the cardiovascular, respiratory, gastrointestinal, dermatological, neurological, and musculoskeletal systems, in addition to head, eyes, ears, nose, throat, neck and lymph nodes from screening up to 7 days after the final collection of samples (up to approximately 8 weeks)
5. Number of participants with change from baseline in electrocardiogram (ECG) readings measured using triplicate 12-lead ECG from screening up to 7 days after the final collection of samples (up to approximately 8 weeks)
6. Number of participants with change from baseline in laboratory test results measured using blood and urine samples from screening up to 7 days after the final collection of samples (up to approximately 8 weeks)

Completion date
07/09/2022

Eligibility

Key inclusion criteria
1. Able and willing to provide written informed consent and comply with the study protocol according to International Council for Harmonisation (ICH) and local regulations
2. Male participants aged 35 to 64 years old (inclusive) at screening
3. Healthy male participants. Health status is defined by the absence of evidence of any active or chronic disease following a detailed medical and surgical history, a complete physical examination including vital signs, 12-lead ECG, hematology, clinical chemistry, serology, coagulation, and urinalysis.
4. Participants must weigh at least 50 kilograms (kg) and must have a body mass index (BMI) within the range of 18-32 kilograms per square meter (kg/m^2) (inclusive) at screening

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
35 years

Upper age limit
64 years

Sex
Male

Key exclusion criteria
1. History of any clinically significant gastrointestinal, renal, hepatic, broncho-pulmonary, neurological, psychiatric, cardiovascular, endocrinological, haematological or allergic disease, metabolic disorder, cancer, or cirrhosis
2. History or evidence of any medical condition potentially altering the absorption, distribution, metabolism, or elimination of drugs. Surgical history of the gastrointestinal tract affecting gastric motility or altering the gastrointestinal tract (with the exception of uncomplicated appendectomy and hernia repair)
3. History or presence of clinically significant ECG abnormalities based on the average of the triplicate ECG recordings (e.g., PQ/PR interval >210 milliseconds (ms), QTcF >450 ms) or cardiovascular disease (e.g., cardiac insufficiency, coronary artery disease, cardiomyopathy, congestive heart failure, family history of congenital long QT syndrome, family history of sudden death)
4. History of malignancy
5. Evidence of human immunodeficiency virus (HIV) infection and/or positive for human HIV antibodies
6. Presence of hepatitis B surface antigen or positive hepatitis C antibody test result at screening or within 3 months prior to study drug administration
7. History of hypersensitivity to any of the excipients in the formulation of RO7223280
8. Infrequent bowel movements (less than once per 24 hours on average)
9. Regular work with ionizing radiation or radioactive material
10. Participants who plan to attempt to father children within 3 months after the study drug administration
11. Participants who have been exposed to ionizing radiations within one year prior to study drug administration

Date of first enrolment
11/07/2022

Date of final enrolment
09/08/2022

Locations

Countries of recruitment
Netherlands

Study participating centre
PRA Health Sciences
Van Swietenlaan 6
Groningen
Netherlands
9728 NZ

Sponsor information

Organisation
Roche (United States)

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

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