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A study to assess safety, tolerability, and processing by the body of multiple doses of zosurabalpin administered through a tube inserted into a vein in the arm of healthy participants

Submission date 28/09/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 29/09/2023	**Overall study status** Completed	
Last Edited 04/12/2023	**Condition category** Other	

Plain English summary of protocol

Background and study aims
Acinetobacter is a group of germs (bacteria) commonly found in soil and water causing infections in different parts of the body such as blood, urinary tract, and lungs. These bacteria are constantly finding new ways to defeat the effects of the drugs used to kill them (antibiotics) and treat the infections they cause. This is called antibiotic-resistance. Carbapenems were a mainstay of treatment for antibiotic-resistant acinetobacter. However, these bacteria have developed resistance to carbapenems too. Zosurabalpin is an experimental drug, which means that Health Authorities (like the U.S. Food and Drug Administration and European Medicines Agency) have not approved zosurabalpin for the treatment of antibiotic-resistant bacterial infections.
The purpose of this study is to find out whether zosurabalpin at different doses has any effects (good or bad) and what happens to zosurabalpin once it is in the participant's body (this is called pharmacokinetics [PK]).

Who can participate?
Healthy males and females of 18 to 64 years of age

What does the study involve?
Participants will need to be a part of this study for about 8 weeks. The study will have four parts:
1. Screening Period: Potential participants will be screened to check if they are eligible to participate in the study. Screening visit will take place from up to 32 days until 4 days before study treatment.
2. Treatment period: Participants will have to come to the clinic 3 days before the start of the study treatment (i.e., zosurabalpin). The study treatment will be administered via a tube inserted into vein in participant's arm from Day 1 to Day 10 and the participants will have to stay in the clinic until all assessments are completed on Day 14.

3. Ambulatory Visit: Participants will have to revisit the clinic on Day 16 after being discharged to assess the potential effects of zosurabalpin on the body.
4. Follow-up Visit: Participants will have to come back to the clinic again on Day 24 (+ or - 2 days) so that the study doctors can check the participants' health after treatment is completed.

What are the possible benefits and risks of participating?
Participants will receive zosurabalpin purely for research purposes; it is not intended that they will receive any benefit from it. The participants will not receive any additional benefit from participating in this study, but the information that is learned may help people with antibiotic-resistant bacterial infections.

Participants may have side effects from the drug or procedures used in this study, and they can be mild to severe, and they can vary from person to person.

Risks associated with zosurabalpin:
Zosurabalpin has had limited testing in humans; therefore, all the potential side effects are not known at this time. The known side effects of this drug, as well as potential side effects are listed below.
1. Allergic reactions on treatment with zosurabalpin, which can be in the form of itching, difficulty breathing, a rash, and/or drop in blood pressure.
2. Reactions due to the administration of the drug through a tube inserted into vein in participant's arm: symptoms may include chills, fever, nausea, headache, high or low blood pressure, fast heart rate, flushing, itching, and shortness of breath.
3. Reaction at the site of the injection: symptoms may include itchiness, pain, and redness.

Risks associated with study treatment administration:
The study treatment will be given through a PICC line that will be placed into a vein in the participant's arm and passed through to the larger veins near the participant's heart. The participant may experience a mild discomfort or sensation of warmth and pain during the procedure, and there is a small chance of infection from placing the needle into a vein in the arm.

There may be a risk in exposing an unborn child to the study treatment, and not all potential risks are known at this time. Women and men must take precautions to avoid exposing an unborn child or a breastfed baby to the study treatment. Participants who are pregnant, or currently breastfeeding cannot take part in the study.

Where is the study run from?
F. Hoffmann-La Roche Ltd (Switzerland)

When is the study starting and how long is it expected to run for?
June 2023 to February 2024

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

Who is the main contact?
global.trial_information@roche.com

Contact information

Type(s)

Public

Contact name
Dr Clinical Trials

Contact details
Building 1
Grenzacherstrasse 124
Basel
Switzerland
CH-4070
+41 616878333
global.trial_information@roche.com

Additional identifiers

Clinical Trials Information System (CTIS)
2023-505411-20-00

Protocol serial number
BP44773

Study information

Scientific Title
A non-randomized, open-label, non-controlled, adaptive, multiple-dose study to investigate the safety, tolerability, and pharmacokinetics of zosurabalpin following intravenous administration in healthy participants

Study objectives
The purpose of this study is to assess the safety and tolerability of zosurabalpin (and its metabolite(s) as appropriate) following multiple intravenous (IV) dose administration of zosurabalpin via a peripherally inserted central catheter (PICC) line in healthy participants.

Ethics approval required
Ethics approval required

Ethics approval(s)
Submitted 12/09/2023, MREC of the foundation BEBO (Dr. Nassaulaan 10, Assen, 9401 HK, Netherlands; +31(0)592-405871; info@stbebo.nl), ref: Nil known

Primary study design
Interventional

Study design
Phase I single center open-label non-randomized non-controlled parallel-group adaptive multiple ascending dose (MAD) interventional study

Study type(s)
Treatment

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

Interventions
Participants will be enrolled in multiple cohorts to receive zosurabalpin from Day 1 to Day 10, at the assigned doses, as an IV infusion through a PICC line. Subsequent doses will be selected in an adaptive manner during the study conduct.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)
Incidence and Severity of Adverse Events (AEs), as Assessed by National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5.0 (NCI CTCAE v5.0) From Screening up to Day 24

Key secondary outcome(s)
1. Plasma Pharmacokinetic (PK) Parameters of Zosurabalpin Measured Using a Validated Liquid Chromatography Mass Spectrometry (LC-MS/MS) Assay From Day 1 up to Day 16
2. Urine PK Parameters of Zosurabalpin Measured Using a Validated LC-MS/MS Assay From Samples Collected on Multiple Time-points From Day 1 to Day 11

Completion date
25/02/2024

Eligibility

Key inclusion criteria
1. Able and willing to provide written informed consent and to comply with the study protocol.
2. Participants must weigh at least 50 kilogram (kg) and must have a body mass index (BMI) within the range of 18 to 32 kg per square meter (kg/m2) (inclusive) at screening.
3. Health status is defined by 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 electrocardiogram (ECG), hematology, blood chemistry, serology, coagulation, and urinalysis.
4. Participants must agree to remain abstinent or at least one highly effective contraceptive method.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
64 Years

Sex
All

Key exclusion criteria
1. History of any clinically significant gastrointestinal, renal, hepatic, bronchopulmonary, neurological, psychiatric, cardiovascular, endocrinological, hematological or allergic disease, metabolic disorder, cancer, or cirrhosis.
2. Concomitant disease or condition that could interfere with, or treatment of which might interfere with, the conduct of the study.
3. History of malignancy.
4. Use of glucocorticoids and other immunosuppressive medications within 30 days (or within 5 times the elimination half-life, whichever is longer) prior to Day 1 and until follow-up.
5. Are currently enrolled in, have participated in, or plan to participate in this or any other clinical study involving an investigational medicinal product (IMP) or medical device study from within the 30 days directly preceding screening or within 5 times the elimination half-life, if known (whichever is longer), until the completion of the follow-up visit.
6. Participation in four or more interventional clinical studies within 12 months prior to enrollment (Day 1).
7. Donation of blood or blood products for transfusion over 100 mL in the last 30 days or 500 mL in the last 3 months or had significant blood loss within 3 months prior to the first study treatment administration.
8. Participants with insufficient venous access.
9. History of hypersensitivity to any of the excipients in the formulation of zosurabalpin.

Date of first enrolment
18/10/2023

Date of final enrolment
31/01/2024

Locations

Countries of recruitment
Netherlands

Study participating centre
ICON
Groningen
Netherlands
9728 NZ

Sponsor information

Organisation
F. Hoffmann-La Roche Ltd

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche Ltd

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