ISRCTN38693215 https://doi.org/10.1186/ISRCTN38693215

First in human study to assess the safety, tolerability and pharmacokinetics of EDI048 in healthy volunteers

Submission date
09/02/2022

Recruitment status
No longer recruiting

Registration date
22/04/2022

Overall study status
Completed

Last Edited
20/10/2022

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
The sponsor is developing the test medicine, EDI048 for the potential treatment of cryptosporidiosis. Cryptosporidiosis is an infection caused by parasites that causes watery diarrhoea. These infections can be potentially life threatening in vulnerable populations.
This study will evaluate the safety (side effects), how the body processes the treatment (pharmacokinetics), and what the treatment does to the body (pharmacodynamic effects) of the drug EDI048 in healthy volunteers.
This is a phase I study, looking at how this drug works in the human body and the safety of this drug in healthy volunteers. This trial does not test if the drug helps to improve health.

Who can participate?
This two-part healthy volunteer study will enrol approximately 64 males and females, aged between 18 and 55 (inclusive), in a non-NHS UK site, to assess the safety and tolerability of the test medicine.

What does the study involve?
Part A will consist of 4 groups (8 volunteers per group), who will be randomised (chosen at random) to receive a single dose of EDI048 or placebo (dummy test medicine).
Part B will consist of 4 groups (8 volunteers per group) who will be randomised to receive a single dose of EDI048 or placebo (dummy test medicine) every 12 hours for 5.5 days.
EDI048 or placebo (dummy test medicine) will be given as an oral liquid by mouth and each group will receive a higher dose than the previous group, providing the data shows it is safe to do so.
Volunteers will be discharged on Day 8 (Part A) and Day 13 (Part B). They will then receive a follow up phone call on 30 days post final dose.
Volunteer's blood and urine will be taken throughout the study for analysis of the test medicine and for their safety.
Volunteers are expected to be involved in this study for approximately 8.5 weeks (Part A) or 9 weeks (Part B) from screening to the follow up call.

What are the possible benefits and risks of participating?
Benefits:
None
Risks:
1. For a Phase I study, the most relevant population is healthy volunteers and it is considered that the risk/benefit evaluation supports this. Only women of non-child bearing potential will be enrolled since the properties of EDI048 on fertility and fetal development have not been fully characterized to date.
2. There is always a risk that the stipend in healthy volunteer studies could represent coercion. The time spent in the clinic, travel, inconvenience and other expenses factor in calculating the stipend. Perception of risk is not considered in this calculation.
3. When investigating new medicines there is always a risk of unexpected side effects and occasionally allergic reactions. Volunteers will be closely monitored during the study.
4. Volunteers may experience side effects from the test medicine in this study. Full information on possible side effects is provided to volunteers in the Participant Information Sheet and Informed Consent Form(s)
5. There will be an extended period of fasting for the volunteers taking part in this study. To ensure an adequate fluid intake, the volunteers will be placed under a strict fluid intake regime and will be monitored for signs of dehydration and fatigue.
6. Blood samples will be collected during the study. Collection of these samples can cause soreness and bruising of the arms but these problems usually clear up within a few days to a few weeks.
7. ECG stickers on volunteers' chests and limbs may cause some local irritation and may be uncomfortable to remove but volunteers will be closely monitored to ensure any local irritation does not persist.
8. The risk to participants in this trial may be minimized by compliance with the eligibility criteria and study procedures, close clinical monitoring particularly facilitated by domiciling during the treatment period, as well as a post study safety contact 30 days post last treatment.

Where is the study run from?
Quotient Sciences Ltd (UK)

When is the study starting and how long is it expected to run for?
February 2022 to November 2022

Who is funding the study?
Novartis Pharma (Switzerland)

Who is the main contact?
Clinical Trial Information Desk, Clinicaltrial.enquiries@novartis.com

Contact information

Type(s)
Scientific

Contact name
Dr Clinical Trial Information Desk

Contact details

Forum 1, Novartis Campus Basel
Basel
Switzerland
4056
+41 61 324 1111
Clinicaltrial.enquiries@novartis.com

Additional identifiers

Clinical Trials Information System (CTIS)
2021-006567-19

Integrated Research Application System (IRAS)
1004992

Protocol serial number
CEDI048A02101

Study information

Scientific Title
A first-in-human, randomized, participant and investigator blinded, placebo controlled, single and multiple ascending dose study to assess the safety, tolerability and pharmacokinetics of EDI048 in healthy volunteers

Study objectives
1. Safety and tolerability of single and multiple oral doses of EDI048 in healthy volunteers
2. To assess the pharmacokinetics (PK) of EDI048 and metabolites (QPL621 and FRK011) in blood (plasma) and urine (SAD only) following administration of single and multiple oral doses

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, London Bridge Research Ethics Committee (London HRA Centre, 2nd Floor, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 1048124; londonbridge.rec@hra.nhs.uk), ref: 22/LO/0107

Primary study design
Interventional

Study design
Interventional double blind randomized parallel group placebo controlled trial

Study type(s)
Other

Health condition(s) or problem(s) studied
Cryptosporidium infections

Interventions
This is a first-in-human study to evaluate the safety, tolerability, and pharmacokinetics of single ascending doses and multiple ascending doses of EDI048 administered orally in healthy volunteers.
The study population will comprise of healthy females of non child bearing potential and healthy males between the ages of 18 and 55 years inclusive. Approximately 64 participants will be enrolled and randomized to receive EDI048 or placebo. Up to 16 additional participants, in 2 additional cohorts may be randomized if additional SAD or MAD cohorts are necessary.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
EDI048

Primary outcome(s)
1. Adverse events (to assess tolerability of the test medicine) will be collected by often asking the volunteers how they are feeling, from the start of the trial until follow up.
2. Additional safety assessments (e.g. vital signs, ECGs and laboratory safety tests) will be performed using standard phase 1 unit monitoring methods from start of screening until the end of the study. Volunteers will be in the study for approximately 65 days.

Key secondary outcome(s)
Blood samples will be collected and the pharmacokinetics of the test medicine in plasma will be serially assessed, after a single dose, and after repeated doses (administered twice daily for 5.5 days) up to 48 hrs post last dose (day 6 morning dose only), using LC-MS/MS bioanalytical assay method.

Completion date
04/11/2022

Eligibility

Key inclusion criteria
1. Healthy male and female participants 18 to 55 years of age included, and in good health as determined by past medical history, physical examination, vital signs, electrocardiogram, and laboratory tests at screening.
2. Participants must weigh at least 50 kg to participate in the study, and must have a body mass index (BMI) within the range of 18.0 - 30.0 kg/m^2. BMI = Body weight (kg) / [Height (m)]^2
3. At screening and baseline, vital signs (systolic and diastolic blood pressure and pulse rate) will be assessed in the supine position after the participant has rested for at least three (3) minutes, and again in the standing position. Supine vital signs should be within the following ranges:
4. Oral body temperature between 35.0-37.5 °C
5. Systolic blood pressure, 90-139 mmHg
6. Diastolic blood pressure, 50-89 mmHg
7. Pulse rate, 40-90 bpm

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Participants who have received any IMP in a clinical research study within 90 days or 5 half-lives of enrollment, whichever is longer; or longer if required by local regulations.
2. History of multiple and recurring allergies or allergy or hypersensitivity to any of the study treatments, excipients or drugs of similar chemical classes. Hay fever is allowed unless it is active at time of screening or if there is a risk that it may become active during the study.
3. Pregnant or nursing (lactating) women, assessed at screening and baseline.
4. Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant.
5. Sexually active males unwilling to use a condom during intercourse while taking investigational drug and for 7 days after stopping the investigational drug.

Date of first enrolment
25/04/2022

Date of final enrolment
23/10/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way
Ruddington Fields
Nottingham
United Kingdom
NG11 6JS

Sponsor information

Organisation
Novartis Pharma AG (Switzerland)

Funder(s)

Funder type
Industry

Funder Name
Novartis Pharma

Alternative Name(s)
Novartis Deutschland GmbH, Novartis Pharma GmbH, Novartis Deutschland

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan
The findings of this Phase I study will be shared with the Sponsor, Novartis, only. As these findings are confidential due to commercial sensitivity, it is not appropriate to share the results of this study with other researchers at this time.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No