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A study of the gastrointestinal behaviour of a novel oral treatment (EDP2393) in healthy male volunteers

Submission date
26/05/2023

Recruitment status
No longer recruiting

Registration date
05/06/2023

Overall study status
Completed

Last Edited
11/01/2024

Condition category
Skin and Connective Tissue Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
This study is designed to assess the release in the body and gastrointestinal (digestive system) transit behaviour of capsules containing EDP2939 to enable the selection of the optimum capsule size and polymer thickness for future clinical studies with EDP2939. EDP2939 is a pharmaceutical preparation of extracellular vesicles (EVs) of a single strain of Prevotella histicola bacteria, currently in clinical development for the treatment of psoriasis. It is available as polymer-coated capsules.

Who can participate?
Healthy male volunteers aged 18 to 60 years

What does the study involve?
The following treatments are being dosed throughout this study:
Treatment A: Radiolabelled EDP2939 size 0 capsule with ~14 mg polymer coating
Treatment B: Radiolabelled EDP2939 size 2 capsule with ~6 mg polymer coating
Treatment C: Radiolabelled EDP2939 size 2 capsule with ~8 mg polymer coating
Treatment D: Radiolabelled EDP2939 size 2 capsule with ~10 mg polymer coating
The primary purpose of this study is to understand the site and time of disintegration of the four capsules in the body. Participants will attend a maximum of four assessment visits and will be dosed in fasted or fed states. The researchers will use scintigraphic imaging to visualise the gastric emptying of each treatment (when they leave the stomach) and confirm the site of release in the gastrointestinal tract. They will also use this technique to determine how quickly the treatment breaks up in the body. To look at these parameters they will add a small amount of radioactive material to the capsule (99mTC-DTPA).

What are the possible benefits and risks of participating?
Participants will not benefit from the treatment. The inclusion and exclusion criteria have been chosen in order to enable a uniform study population and to minimise possible risks in relation to the administration of the EDP2939 capsules. Based on extensive clinical exposure with a similar medication called EDP1815 (a pharmaceutical preparation that contains Prevotella

histicola and the extracellular vesicles which comprise EDP2939) the clinical risks associated with EDP2939, including at doses to be used in this study, are anticipated to be minimal, and there are to date no expected adverse events before this study. The study medicine has also been given to laboratory animals at doses higher than those given in this study. There were no obvious side effects related to the study medicine in animals.
The radioisotope to be used in this study, technetium-99m (99mTc), will be complexed with diethylenetriaminepentaacetic acid (DTPA) which prevents absorption of the radioisotope from the gastrointestinal tract. The maximum radiation dose each subject will receive from this study will be 0.4 mSv. This is equivalent to about 8 weeks of average natural background radiation in the UK, or five transatlantic flights. In addition to monitoring the radiation dose the subjects receive in this study, the researchers will take into account previous radiation doses, e.g. from x-rays and scans to ensure that they do not exceed recommended maximum exposure.

Where is the study run from?
Evelo Biosciences Inc. (USA)

When is the study starting and how long is it expected to run for?
December 2022 to May 2023

Who is funding the study?
Evelo Biosciences Inc. (USA)

Who is the main contact?
Dr Lyn Corry, lyn.corry@bddpharma.com

Contact information

Type(s)
Principal investigator

Contact name
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Additional identifiers

Integrated Research Application System (IRAS)
1007114

Protocol serial number

, Sponsor Protocol: EDP2939-102

Study information

Scientific Title
A Phase I, single-centre, open-label, crossover study in healthy volunteers using scintigraphy to evaluate the gastrointestinal behaviour of EDP2939 oral dosage forms

Study objectives
To assess site and time to onset of disintegration/release with EDP2939 capsules of different sizes and polymer coating weights in fasted and/or fed states.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/03/2023, London - Westminster Research Ethics Committee (Equinox House, City Link, Nottingham, NG42 4LA, UK; +44 207 104 8066; westminster.rec@hra.nhs.uk), ref: 23/LO /0035

Study design
Single-centre open-label crossover design in up to 12 healthy male volunteers

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Psoriasis

Interventions
The following four treatment arms were included in this study:
Treatment arm 1: Radiolabelled EDP2939 size 0 capsule with ~14 mg polymer coating dosed in the fed state
Treatment arm 2: Radiolabelled EDP2939 size 2 capsule with ~6 mg polymer coating dosed in the fed state
Treatment arm 3: Radiolabelled EDP2939 size 2 capsule with ~8 mg polymer coating dosed in the fed state
Treatment arm 4: Radiolabelled EDP2939 size 2 capsule with ~8 mg polymer coating dosed in the fasted state

The dose (strength) of EDP2939 in each capsule will be 3.9 x e12 equivalent particle number (eTPN).

Participants will attend a maximum of four assessment visits.

Each treatment arm consisted of a single visit to the study site with each visit lasting a maximum of 13.5 hours. On each of the four treatment arms (1, 2, 3, 4) subjects were dosed with a single

capsule radiolabelled to contain approximately 4 MBq 99mTc DTPA at the time of dosing. All subjects received the same treatment as each other at the study visits. There was a minimum of 3 days between treatment arms. Scintigraphic imaging was used to assess the gastrointestinal behaviour of each treatment. The intervention was not continued to be made available to participants once the study was complete.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
EDP2939

Primary outcome(s)
Site and time to onset of disintegration/release with EDP2939 capsules of different sizes and polymer coating weights in fasted and/or fed states using scintigraphic data generated from the acquisition of scintigraphic images using a gamma camera. Images were taken at dosing then every 5 minutes until complete disintegration of the capsule was observed, after which images were taken every 15 minutes until the dispersed radioactivity reached the colon.

Key secondary outcome(s))
1. Radiolabel release kinetics of each EDP2939 dosage form
2. Gastrointestinal transit parameters of each EDP2939 dosage form
3. The effect of food on gastric performance
The above outcome measures were evaluated using scintigraphic data generated from the acquisition of scintigraphic images taken by a gamma camera. Images were taken at dosing then every 5 minutes until complete disintegration of the capsule was observed, after which images were taken every 15 minutes until the dispersed radioactivity reached the colon.

Completion date
31/05/2023

Eligibility

Key inclusion criteria
1. Male subjects between 18 and 60 years of age inclusive
2. Body weight between >50.0 kg
3. Body mass index between 18 and 30 kg/m², inclusive
4. Understands and is willing, able and likely to comply with all study procedures including consumption of meals provided and restrictions
5. Demonstrates understanding of the study and willingness to participate as evidenced by voluntary written informed consent (signed and dated) obtained before any trial-related activities
6. Good general health with (in the opinion of the Principal Investigator [PI], or medically qualified designee) no clinically significant and/or relevant abnormalities of medical history or prior to dosing evaluations, including physical examination, vital signs and ECG and screening clinical laboratory results.
7. Unless the subject has had a vasectomy (with confirmed sterility) more than 12 weeks prior to the study starting, must be willing to abstain from sexual intercourse and be abstinent from

penile-vaginal intercourse as their usual and preferred lifestyle (abstinent on a long-term and persistent basis) and agree to remain abstinent for 90 days after the last dose of IMP, with women of childbearing potential for the duration of the trial and for 90 days after the last assessment visit OR agree to use a condom during each episode of penile-vaginal intercourse, in addition to female their partner (if a person who could become pregnant) using a highly effective form of contraception.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
60 years

Sex
Male

Total final enrolment
12

Key exclusion criteria
1. Medical history:
1.1. Current or recurrent disease/condition that, in the opinion of the PI or medically qualified designee responsible, could affect study conduct; the safety of the subject as a result of participation; and/or the ability of the subject to complete the study or laboratory assessments. For example: hepatic disorders, renal insufficiency, congestive heart failure, conditions known to impact gastric emptying such as migraine or diabetes mellitus and relevant non-self-limiting GI disorders.
1.2. Current or relevant previous history of severe or unstable psychiatric illness, that may require treatment or make the subject unlikely to fully complete the study, or that presents undue risk from the study medication or procedures
1.3. History of previous surgical intervention which could affect GI transit and/or function for example gastric surgery, vagotomy or known adhesions with previous obstructive symptoms
1.4. Haematological or biochemical blood test at screening outside normal ranges and deemed clinically significant by the PI or medically qualified designee
1.5. Any contraindication to the gamma scintigraphy procedure
1.6. As a result of a physical examination or screening investigations available prior to dosing evaluations, the PI or medically qualified designee/physician responsible considers the volunteer unfit for the study
1.7. Measured body temperature >38°C (infection control procedure)
2. Medications:
2.1. Subject is scheduled to take prescribed medication within 14 days prior to the first or any subsequent assessment visit which, in the opinion of the PI or medically qualified designee

responsible, will interfere with the study procedures or has the potential to affect gastric emptying and/or gut transit or compromise safety
2.2. Subject is scheduled to take over-the-counter (OTC) medication, including vitamins, pro and prebiotics and natural or herbal remedies, within 48 hours prior to the first or any subsequent assessment visit unless approved by the PI or medically qualified designee
3. Alcohol/substance abuse:
3.1. Recent history (within the last year) of alcohol or other substance abuse
3.2. Subject has an average weekly alcohol intake of greater than 14 units
3.3. Subject has positive urine drugs of abuse test at screening or prior to dosing evaluation
3.4. Subject has a positive breath alcohol test at screening or prior to dosing evaluation
4. Smoking:
4.1. Subject has recently discontinued smoking (less than 3 months)
4.2. Subject is currently a smoker or user of nicotine-containing products
4.3. Subject has a positive urine cotinine test at screening or prior to dosing evaluation
5. Allergy/intolerance:
5.1. Subject has a history of allergy to any component of the dosage form or any other allergy, which, in the opinion of the PI or medically qualified designee responsible, contraindicates their participation
5.2. Subject has an allergy to any of the contents of the standardised meals
5.3. Subject is vegetarian or vegan
6. Clinical Studies
6.1. Participation in another clinical study (inclusive of final post-study examination) or receipt of an investigational drug within the 12 weeks before the screening visit, or five elimination half-lives of the previous study drug, whichever is longer
6.2. Subject whose participation in this study will result in participation in more than four studies over a 12-month period
7. Personnel:
7.1. An employee of the Sponsor or study site or members of their immediate family
8. Radiation exposure:
8.1. Subject has a total dosimetry value which, in the opinion of the PI or medically qualified designee/physician responsible, contraindicates their participation
9. Family planning:
Subjects who are intending to father a child or donate sperm up to the 90 days following the last dose of IMP in the study or are unwilling or unable to follow the precautions outlined in inclusion criteria 7
10. Blood:
10.1. Blood donation or significant blood loss within 3 months of screening and for the duration of the study
10.2. Difficulty accessing veins for cannulation or blood sampling
11. Other:
Subject has any non-removable metal objects such as metal plates, screws etc in their chest or abdominal area which in the opinion of the PI or medically qualified designee could affect the study conduct

Date of first enrolment
27/03/2023

Date of final enrolment
17/04/2023

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
BDD Pharma Ltd
Bio-Imaging Centre
Basement Medical Block
Glasgow Royal Infirmary
Glasgow
United Kingdom
G4 0SF

Sponsor information

Organisation
Evelo Biosciences Inc.

Funder(s)

Funder type
Industry

Funder Name
Evelo Bioscience Inc.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study are not expected to be made available due to this being a Phase I healthy volunteer study.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			11/01/2024	No	No
HRA research summary			26/07/2023	No	No