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A study to investigate the effects of food and administration of different forms of mavodelpar on the safety and concentration of mavodelpar in the blood

Submission date
10/10/2023

Recruitment status
No longer recruiting

Registration date
10/10/2023

Overall study status
Completed

Last Edited
28/02/2025

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
The purpose of this study is to evaluate the study drug, mavodelpar (formerly known as REN001) in two different formulations (existing capsule formulation and new tablet formulation). The main objectives of the study are as follows:
1. To evaluate and compare the bioequivalence (assessment of whether the two formulations can be considered the same in terms of concentration levels in the blood at various timepoints) of mavodelpar when it is administered as an oral tablet versus an oral capsule.
2. To investigate the effect of food on the concentration of mavodelpar in the blood following administration of mavodelpar in both a fasted state (without food) and a fed state (following a high-fat, high-calorie meal).
3. To investigate the concentration of mavodelpar in the blood, how this changes over a period of time and to measure if and how this concentration differs when mavodelpar is administered as an oral tablet versus an oral capsule.
4. To determine the safety and tolerability (the degree to which side effects of the study drug can be tolerated) of mavodelpar when it is administered as a single dose in different forms i.e., as an oral tablet versus an oral capsule and following administration in a fasted state (without food) and fed state (following a high-fat, high-calorie meal).
The purpose of the study is to evaluate the four elements described above when mavodelpar is given as a single dose in two different forms over three treatment periods in the presence and absence of food.

Who can participate?
A total of up to 32 participants are needed to fully complete this study. Participants must be healthy adult males and females aged between 18 and 60 years.

What does the study involve?
Across the three treatment periods, each participant will receive:
1. A single dose of mavodelpar (100 milligrams [mg]) in the form of an oral capsule (2 x 50 mg)

following a high-fat, high-calorie meal
2. A single dose of 100 mg mavodelpar in the form of an oral tablet (1 x 100 mg) following a high-fat, high-calorie meal and
3. A single dose of 100 mg mavodelpar in either the form of a capsule or tablet in a fasted state.
Each dose in each treatment period will be separated by a period of at least 10 days. The study will consist of a screening visit (between 35 and 1 day prior to the first dose), three treatment periods (consisting of a maximum of 7 days with 3 overnight stays per treatment period from Day -1 to Day 3 and 3 single day return visits on Days 4-6) and a post-study follow-up visit on Day 6 of treatment period 3.

What are the possible benefits and risks of participating?
Taking part in this study is not expected to provide participants with any direct medical benefit. However, the information from this study may help improve the treatment of diseases associated with dysfunction in the process of metabolism and cellular energy production.
Full information on possible side effects/risks are provided to volunteers in the Participant Information Sheet and Informed Consent Form.
Throughout the study the health of the participants will be regularly monitored and appropriate treatment for any medical condition will be provided if required. All doctors employed by Simbec-Orion are trained and certified in Advanced Life Support Procedures in order to deal with a medical emergency. Nurses and other clinical staff are also trained in emergency procedures. Simbec-Orion also has an agreement with Prince Charles Hospital for referral of participants if required following a medical emergency.

Where is the study run from?
Simbec-Orion Clinical Pharmacology Unit (UK)

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

Who is funding the study?
Reneo Pharma Ltd (UK)

Who is the main contact?
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Contact information

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Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-003704-32

Integrated Research Application System (IRAS)
1006936

Protocol serial number
REN001-105

Study information

Scientific Title
A Phase I, randomized, open-label, single-dose, three-period crossover bioequivalence and food effect study with orally administered mavodelpar tablet and capsule formulations in healthy subjects

Study objectives
The primary objectives of this study are:
1. To assess the single-dose pharmacokinetic bioequivalence of the mavodelpar tablet formulation (100 mg x 1; test), compared to mavodelpar capsule formulation (50 mg x 2; reference), when administered after a high-fat, high-caloric meal to healthy subjects.
2. To assess the effect of a high-fat, high-calorie meal on the pharmacokinetics (PK) of the mavodelpar tablet formulation in healthy subjects following a single-dose administration.
3. To assess the effect of a high-fat, high-calorie meal on the pharmacokinetics (PK) of the mavodelpar capsule formulation in healthy subjects following a single-dose administration.

The secondary objectives of this study are:
1. To assess the safety and tolerability of mavodelpar administered as a single dose of 100 mg in either capsule or tablet formulation and under fed and fasted states in healthy subjects.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 30/08/2023, Wales Research Ethics Committee 2 (Wales Research Ethics Committee 2, Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 (0)2920 230457; Wales.REC2@wales.nhs.uk), ref: 23/WA/0128

2. Approved 30/08/2023, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, United Kingdom; +44 (0)20 3080 6000; info@mhra.gov.uk), ref: CTA 49733/0007/001-0001

Primary study design
Interventional

Study design
A randomized, open-label crossover trial of bioequivalence and food effect in up to 32 healthy volunteers

Study type(s)
Other

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

Interventions
This is a Phase I, open-label, randomized, three-period crossover study in healthy subjects to assess bioequivalence of the mavodelpar tablet formulation (100 mg) vs the mavodelpar capsule formulation (2 x 50 mg) administered in the fed condition. The study will also investigate the effect of a high-fat, high-caloric meal on the pharmacokinetics (PK) of both the tablet formulation and capsule formulation compared to fasting conditions (food effect).

After completing a screening period (Day -35 to Day -1), up to 32 eligible healthy volunteer subjects will be randomized to complete three sequential treatment periods in an order determined by the treatment sequence they are randomized to. Subjects will receive the following in a randomized order over three treatment periods:

1. A single oral dose of 100 mg (50 mg x 2) mavodelpar in capsule formulation following a high-fat, high-caloric meal (n = 32)
2. A single oral dose of 100 mg mavodelpar (100 mg x 1) in tablet formulation following a high-fat, high-caloric meal (n = 32)
3. In a third treatment period, participants will be split randomly across two allocations (16 vs. 16 subjects) as follows:
3.1. A single oral dose of 100 mg (50 mg x 2) mavodelpar in capsule formulation following a period of fasting (n = 16)
3.2. A single oral dose of 100 mg (100 mg x 1) mavodelpar in tablet formulation following a period of fasting (n = 16)

Post Study Follow-Up safety assessments will be performed on the last day (Day 6) of the final treatment period (Treatment Period 3) or, if a subject withdraws, as close to 5 days after their last dose as possible.

The study took place in the Clinical Pharmacology Unit of Simbec-Orion Clinical Pharmacology under medical and nursing supervision. It is expected that the total duration of the study for each subject will be approximately 2–3 months from Screening to last visit.

Screening (Day – 35 to Day -1)
Screening assessments will be performed from Day -35 to Day -1 to ensure the eligibility of subjects.

Treatment Periods 1 - 3 (Day -1 to Day 6)
Subjects will enter the Clinical Pharmacology Unit on Day -1 of each treatment period to complete scheduled assessments. All subjects will be required to fast overnight for a minimum of 10 h before dosing on Day 1. On Day 1 of each treatment period, when scheduled to receive their dose under fasted conditions subjects will take their tablet or capsule (dependent on randomization) with approximately 240 mL (8 oz) of water and remain fasted until at least 4 h after dosing. When scheduled to receive their dose under fed conditions subjects will take their tablet or capsule (dependent on randomization) with approximately 240 mL (8 oz) of water after completely consuming a high-fat, high-caloric meal. Subjects will start consuming the designated meal 30 minutes prior to administration of mavodelpar and subjects must fully consume the meal within 30 minutes of starting.

Subjects will remain in the clinical unit until Day 3 of each treatment period (after completion of the 48-h post-dose assessments) and will then return on Day 4, Day 5, and Day 6 as outpatients to complete the required assessments. In the instance that enrolled subjects have difficulty travelling to the Clinical Pharmacology Unit to complete outpatient visits, they may remain at the Clinical Pharmacology Unit or alternative accommodation (i.e., hotel) may be arranged.
A minimum of 10 days washout will separate doses (i.e., dosing in Treatment Period 2 can occur 10 days after the dose in Treatment Period 1).

Post-Study Follow-Up
A Post-Study Follow-Up visit will be conducted at the last outpatient visit of the final Treatment Period (Day 6 of Treatment Period 3) (or, if a subject withdraws, as close to 5 days after their last dose as possible). If all follow-up assessments are satisfactory to the Principal Investigator (or delegate), the subject will be discharged from the study. If any AEs are ongoing, or any assessments are not satisfactory, subjects may be recalled to the unit for follow-up assessments until the Principal Investigator (or delegate) is satisfied the subject may be discharged from the study. Subjects will be advised to return or contact the Clinical Pharmacology Unit at any time during the study if they feel they may be experiencing any adverse effects.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Mavodelpar (REN001)

Primary outcome(s)
Pharmacokinetic (PK) parameters derived from analysis of plasma samples for concentrations of mavodelpar: Cmax, AUClast and AUCinf. PK blood samples will be collected for measurement of mavodelpar (M351 and M527 may also optionally be measured from the same sample as an exploratory analysis) at the following timepoints: pre-dose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, 16, 24, 36, 48, 72, 96 and 120 h for each treatment period.

Key secondary outcome(s)
1. Additional mavodelpar PK parameters derived from analysis of plasma samples for concentrations of mavodelpar: Tmax, t½, λz, CL/F and Vz/F. PK samples will be collected at the following timepoints: pre-dose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, 16, 24, 36, 48, 72, 96 and 120-h for each treatment period.
2. Adverse Events (AEs) and Serious Adverse Events (SAEs) recorded from the point of informed consent up to post-study follow-up visit.
3. Absolute values and changes from baseline in clinical laboratory parameters (biochemistry, hematology, coagulation and
urinalysis) measured at Screening, Day -1 & Day 3 (of each treatment period) and post-study follow-up visit
4. Absolute values and changes from baseline in vital signs (systolic/diastolic blood pressure, pulse and oral body temperature) measured at Screening, Day -1, Day 1 (pre-dose, 2 hr & 6 hr post-dose) of each treatment period and post-study follow-up visit.

Completion date
13/11/2023

Eligibility

Key inclusion criteria
1. Healthy male and female subjects, between 18 and 60 years of age, inclusive at Screening.
2. Female subjects: negative pregnancy test at Screening (Serum) and Day -1 of the first treatment period (Urine).
3. Must agree to adhere to the contraception requirements defined in the study protocol.
4. A body mass index (BMI) of 18-32 kg/m2 at Screening (BMI = body weight (kg) / [height (m)]2)
5. No clinically significant history of previous allergy/sensitivity to mavodelpar or any of the excipients contained within the IMP.
6. No clinically significant abnormal test results for serum biochemistry, haematology, coagulation and/or urine analyses within 35 days before the first dose administration of the IMP.
7. Negative urinary drugs of abuse (DOA) screen (including alcohol), determined within 35 days before the first dose administration of the IMP (N.B.: A positive test result may be repeated at the Investigator's discretion).
8. Negative human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg) and hepatitis C virus antibody (HCV Ab) test results at Screening.
9. No clinically significant abnormalities in 12-lead electrocardiogram (ECG) determined within 35 days before first dose of IMP including a PR interval >220 ms, QT interval heart rate corrected using Fridericia's formula (QTcF) > 450ms.
10. No clinically significant abnormalities in vital signs (blood pressure, pulse and oral temperature) determined within 35 days before first dose of IMP.
11. Must be available to complete the study (including the follow-up visit).
12. Must satisfy an Investigator about his/her fitness to participate in the study.
13. Must provide written informed consent to participate in the study.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
All

Total final enrolment
32

Key exclusion criteria
1. A clinically significant history of gastrointestinal disorder likely to influence IMP administration and absorption.
2. Use of prescription or non-prescription drugs, including vitamins, herbal and dietary supplements within 35 days or 5 half-lives (whichever is longer) prior to the first dose of IMP. The exceptions are paracetamol (which may be taken as an analgesic to a maximum of 2 g in 24 h) and ibuprofen (which may be taken as an analgesic to a maximum of 1.2 g in 24 h).
3. Evidence of significant renal, hepatic, central nervous system, respiratory, cardiovascular or metabolic dysfunction.
4. Veins not suitable for venepuncture and cannulation.
5. Presence or history of clinically significant allergy requiring treatment, as judged by the Investigator. Hay Fever is allowed unless active.
6. A clinically significant history of drug or alcohol use (defined as the consumption of more than 14 units [for male and female subjects] of alcohol a week) within the past two years.
7. Inability to communicate well with the Investigators (i.e., language problem, poor mental development or impaired cerebral function).
8. Participation in a New Chemical Entity (NCE) clinical study within the previous 3 months or five half-lives, whichever is longer, or a marketed drug clinical study within the 30 days or five half-lives, whichever is longer, before the first dose of IMP. (The washout period between studies is defined as the period of time elapsed between the last dose of the previous study and the first dose of the next study).
9. Donation or loss of 450 mL or more blood within the 3 months before the first dose of IMP or plans to donate blood in the 3 months following completion of the study.
10. Dietary restrictions (e.g., restrictions for medical, religious or cultural reasons, etc) that would prevent the subject from consuming a standardised meal, the high-fat, high-caloric meal, and gelatine capsule.
11. Unwilling or unable to swallow gelatine capsules.
12. Users of nicotine products i.e., current smokers or ex-smokers who have smoked within the 6 months prior to Screening or users of cigarette replacements (i.e., e-cigarettes, nicotine patches or gums).

13. Female subjects who are pregnant, breastfeeding or lactating.
14. Received, or intend to receive, a COVID-19 vaccine injection within 35 days prior to first dose of IMP.

Date of first enrolment
11/09/2023

Date of final enrolment
11/10/2023

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Simbec Research Limited
Simbec House Merthyr Tydfil Industrial Park
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Sponsor information

Organisation
Reneo Pharma Ltd (United Kingdom)

Funder(s)

Funder type
Industry

Funder Name
Reneo Pharma Ltd (United Kingdom)

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 because of their high commercial sensitivity and the negligible benefit to the public of publication of results of non-therapeutic clinical trials.

IPD sharing plan summary
Not expected to be made available