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A study in healthy volunteers to discover how the test medicine interacts with other approved medicines

Submission date
31/03/2023

Recruitment status
No longer recruiting

Registration date
06/06/2023

Overall study status
Completed

Last Edited
22/09/2023

Condition category
Other

[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, miricorilant, for the potential treatment of antipsychotic-induced weight gain (AIWG) and non-alcoholic steatohepatitis (NASH). AIWG is a condition in which patients taking antipsychotic medications tend to gain weight. In addition to weight gain, antipsychotic medications increase insulin resistance thereby increasing the risk of patients developing cardiovascular disease (diseases that affect the heart and blood vessels). NASH develops from non-alcoholic fatty liver disease (NAFLD), which is a range of conditions caused by a build-up of fat in the liver and is usually seen in overweight or obese people. A healthy liver should contain little or no fat.

Who can participate?
Healthy adult volunteers

What does the study involve?
This one-part, healthy subject drug-drug interaction study aims to assess the pharmacokinetics (PK, what the body does to the drug) of five approved marketed medicines when given with and without the test medicine, miricorilant in fed conditions (with food). This study will take place at one non-NHS site and will consist of a single study period involving up to 30 healthy male or female (of non-childbearing potential) subjects, aged between 18 and 60. Subjects will be admitted on the evening of Day -1. Subjects will receive an oral dose of repaglinide (0.5 mg tablet); tolbutamide (500 mg tablet); midazolam (2.5 mg oral solution); dolutegravir (50 mg tablet); rosuvastatin (10 mg tablet) on two occasions (on the mornings of Day 1 and Day 10). On the mornings of Day 4 to Day 12, subjects will receive 400 mg of miricorilant, as 8 x 50 mg tablets. Subjects will be discharged on Day 13 and will receive a follow-up phone call, 4 to 11 days post-final test medicine dose.

Subjects' blood and urine will be taken throughout the study for analysis of the test medicine and marketed medicines, as well as for their safety. Subjects are expected to be involved in this study for approximately 7 weeks from screening to the follow-up call.

What are the possible benefits and risks of participating?
Participants will get no medical benefit from taking part in this study. We hope that the development of a product to improve the treatment of antipsychotic-induced weight gain (AIWG) and non-alcoholic steatohepatitis (NASH) will be of benefit to patients with either of these conditions.

1. As this is a Phase I study, the most relevant population is healthy volunteers. It is considered that the risk/benefit evaluation in this study supports the use of healthy subjects.

2. There is always a risk that the stipend in healthy subject 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. Subjects will be closely monitored during the study.

4. Subjects may experience side effects from the test medicine and/or marketed medicines in this study. Full information on possible side effects is provided to volunteers in the Participant Information Sheet and Informed Consent Form.

5. There will be an extended period of fasting for the subjects taking part in this study. Subjects will be provided with a light snack and then fast from all food and drink (except water) for a minimum of 10 hours each day before dosing. To ensure an adequate fluid intake, subjects will be allowed water up to 1 hour before each scheduled dosing time and will be provided with 240 mL of water at the dosing time and again at 1-hour post-dose. Thereafter, water will be allowed ad libitum. Decaffeinated fluids will be allowed ad libitum from lunchtime on each day of dosing.

6. Blood samples will be collected during the study. Collection of these samples can cause soreness and bruising of the arm but these problems usually clear up within a few days to weeks.

7. ECG stickers on volunteers' chests and limbs may cause some local irritation and may be uncomfortable to remove. Subjects will be closely monitored and if any irritation occurs, appropriate care will be given.

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

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

Who is funding the study?
Corcept Therapeutics (USA)

Who is the main contact?
recruitment@weneedyou.co.uk

Contact information

Type(s)
Principal investigator

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Dr Sharan Sidhu

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1007538

Protocol serial number
CORT118335-855, IRAS 1007538

Study information

Scientific Title
An open-label, drug-drug interaction study designed to evaluate the potential effect of miricorilant on cytochrome P450 2C8, 2C9, 3A4, uridine-diphospho-glucuronosyltransferase 1A1 enzyme activity, and breast cancer resistance protein activity using probe substrates in healthy male and female subjects

Study objectives
The study is not hypothesis testing. The objectives are as follows:

Primary objective:
To determine the effect of miricorilant at steady state on the oral pharmacokinetics (how the test medicine is taken up by the body; PK) of repaglinide, tolbutamide, midazolam, dolutegravir and rosuvastatin in healthy men and women

Secondary objective:
To provide additional safety and tolerability information for miricorilant

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 06/09/2023, London - Hampstead REC (Ground Floor, Temple Quay House, Health Research Authority, Bristol, BS1 6PN, United Kingdom; +44 (0)2071048345, (0)2071048189; hampstead.rec@hra.nhs.uk), ref: 23/LO/0227

Study design
Open-label drug-drug interaction study

Primary study design
Interventional

Study type(s)
Other, Safety

Health condition(s) or problem(s) studied
1. Non-alcoholic steatohepatitis (NASH)
2. Antipsychotic-induced weight gain (AIWG)

Interventions
This is a non-randomised, open-label trial. This one-part, healthy subject drug-drug interaction study aims to assess the pharmacokinetics (PK, what the body does to the drug) of five approved marketed medicines when given with and without the test medicine, miricorilant in fed conditions (with food). This study will take place at one non-NHS site and will consist of a single-study period involving up to 30 healthy men or women (of non-childbearing potential), aged between 18 and 60. Subjects will be admitted on the evening of Day -1. Subjects will receive an

oral dose of repaglinide (0.5 mg tablet); tolbutamide (500 mg tablet); midazolam (2.5 mg oral solution); dolutegravir (50 mg tablet); and rosuvastatin (10 mg tablet) on two occasions (on the mornings of Day 1 and Day 10). On the mornings of Day 4 to Day 12, subjects will receive 400 mg of miricorilant, as 8 x 50 mg tablets. Subjects will be discharged on Day 13 and will receive a follow-up phone call, 4 to 11 days post-final test medicine dose. The subject's blood will be taken throughout the study for analysis of the test medicine and marketed medicines. Blood and urine samples will also be taken throughout to monitor ongoing subject safety. Subjects are expected to be involved in this study for approximately 7 weeks from screening to the follow-up call. Subjects are expected to be involved in this study for approximately 7 weeks from screening to the follow-up phone call.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Miricorilant, repaglinide, tolbutamide, midazolam, dolutegravir, rosuvastatin

Primary outcome(s)
Pharmacokinetic (PK) parameters Cmax, AUC(0-last) and AUC(0-inf) comparing repaglinide, tolbutamide, midazolam, dolutegravir and rosuvastatin administered before and after multiple dose administration of miricorilant collected from days 1 to 13

Key secondary outcome(s))
Safety and tolerability information for all study products and procedures are assessed by:
1. Incidence of adverse events (AEs) measured by monitoring for adverse events from signing the informed consent form until the follow-up phone call (before day -1 to day 23)
2. Measurement of vital signs, electrocardiograms, laboratory safety tests and physical examinations at screening, and at intervals from admission until discharge (day -1 to day 13).

Completion date
16/11/2023

Eligibility

Key inclusion criteria
1. Provide written informed consent
2. Willing and able to communicate and participate in the whole study
3. Aged 18 to 60 years inclusive at the time of signing the informed consent
4. Agree to adhere to the contraception requirements defined in the clinical protocol
5. Male subjects or non-pregnant, non-lactating female subjects of non-childbearing potential
6. Participants who are healthy as determined by medical evaluation including medical history, physical examination, vital signs, 12-lead ECGs, screening clinical laboratory profiles (haematology, clinical chemistry, and urinalysis), as deemed by the Investigator or designee
7. Body mass index (BMI) of 19.0 to 32.0 kg/m2 as measured at screening
8. Body weight ≥50 kg at screening

Participant type(s)

Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
60 years

Sex
All

Key exclusion criteria
1. Serious adverse reaction or serious hypersensitivity to any drug or formulation excipients
2. Presence or history of clinically significant allergy requiring treatment, as judged by the Investigator. Hay fever is allowed unless it is active
3. History of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or gastrointestinal disease (including cholecystectomy), bleeding disorder, neurological or psychiatric disorder, as judged by the Investigator.
4. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the Investigator or delegate at screening
5. Clinically significant abnormal clinical chemistry (including AST and/or ALT >1.5 × the upper limit of the reference range or CK >1.5 × ULN), haematology or urinalysis as judged by the Investigator (laboratory parameters are listed in the clinical protocol). Subjects with Gilbert's Syndrome are allowed
6. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or (HIV) 1 and 2 antibody results
7. Evidence of renal impairment at screening, as indicated by an estimated glomerular filtration rate (eGFR) of <80 mL/min/1.73 m2 using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI; 2009) equation
8. Female subjects of childbearing potential including those who are pregnant or lactating (all female subjects must have a negative highly sensitive serum (at screening) or urine (at admission) pregnancy test)
9. Clinically significant ECG abnormalities or vital sign abnormalities at screening or baseline (pre-first dose) including but not limited to:
9.1. QTcF > 450 msec based on a single ECG at screening, and based on the mean of 3 supine ECGs performed at least 2 minutes apart at Day 1 pre-dose
9.2. Supine heart rate (HR) at rest of <40 bpm or >100 bpm at screening and pre-(first) dose
9.3. Blood pressure (BP) outside the following ranges: diastolic BP 40-90 mmHg; systolic BP 90-140 mmHg (subjects aged 18-45 years) and 90-160 mmHg (subjects aged >45 years) at screening or before the first dose of study medication (NIMPs or IMP). HR and BP can be retested twice in the supine position at intervals of approximately 5 minutes on a given day
10. Subjects who have received any IMP or NIMP in a clinical research study within the 90 days prior to Day 1, or less than 5 elimination half-lives prior to Day 1, whichever is longer
11. Subjects who report having received miricorilant in the 6 months before the first dose of miricorilant in this study

12. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood
13. Subjects who are taking, or have taken, any prescribed or over-the-counter drug or vitamins /herbal remedies (other than up to 4 g of paracetamol per day in the 14 days before first NIMP administration). COVID-19 vaccines are accepted as concomitant medications
14. Subjects who are currently using glucocorticoids or have a history of systemic glucocorticoid use at any dose within 12 calendar months before the first NIMP administration, or 90 days for inhaled glucocorticoids. Subjects who have received up to two single doses of a glucocorticoid in another study more than 90 days before the first dose of study medication will not be excluded from taking part in the study for this reason
15. Any contraindication to the use of repaglinide, tolbutamide, midazolam, dolutegravir, rosuvastatin as per the Summary of Product Characteristics (SMPC) for each product
16. History of any drug or alcohol abuse in the past 2 years
17. Regular alcohol consumption in male subjects >21 units per week and in female subjects >14 units per week (1 unit = ½ pint beer, or a 25 mL shot of 40% spirit, 1.5 to 2 units = 125 mL glass of wine, depending on the type)
18. A confirmed positive alcohol breath test at screening or admission
19. Current smokers and those who have smoked within the last 12 months
20. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or admission
21. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
22. Confirmed positive drugs of abuse test result (drugs of abuse tests are listed in the clinical protocol) at screening or admission
23. Male subjects with pregnant or lactating partners
24. Subjects who are, or are immediate family members of, a study site or Sponsor employee
25. Failure to satisfy the Investigator of fitness to participate for any other reason

Date of first enrolment
13/06/2023

Date of final enrolment
16/11/2023

Locations

Countries of recruitment
United Kingdom

England

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Sponsor information

Organisation
Corcept Therapeutics (United States)

ROR
https://ror.org/03ey3qt70

Funder(s)

Funder type
Industry

Funder Name
Corcept Therapeutics

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 commercial sensitivity.

IPD sharing plan summary
Not expected to be made available