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A study in healthy male volunteers to look at the effects of the test medicine, miricorilant, on weight gain caused by the approved medicine olanzapine

Submission date
11/05/2023

Recruitment status
No longer recruiting

Registration date
01/06/2023

Overall study status
Completed

Last Edited
01/09/2023

Condition category
Nutritional, Metabolic, Endocrine

[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, for the treatment of mental disorders such as schizophrenia, tend to gain weight. Antipsychotic medications also 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, 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.

This one-part healthy subject proof of concept study aims to assess whether the test medicine reduces the weight gain caused by the approved medicine, olanzapine.

Who can participate?
This study will take place at one non-NHS site and will consist of a single study period involving up to 70 healthy male subjects, aged 18-55 years.

What does the study involve?
Subjects will be randomised to 1 of 2 treatment regimens in which they will be orally dosed with olanzapine (10 mg) and either miricorilant (100 mg) or placebo. All regimens will be dosed in the morning for 21 consecutive days. Subjects will be admitted to the clinical unit on the evenings of Days -1, 7, 14 and 21, and dosed in the clinical unit on Days 1 to 4, Day 8 and Day 15. Subjects will be discharged from the clinical unit following dosing on Days 4, 8 and 15 and will proceed with home dosing on Days 5 to 7, Days 9 to 14, and Days 16 to 21. Subjects will be discharged for the last time on Day 22 and will return 12 to 16 days post-final test medicine dose for a follow-up visit.

Subject’s blood will be taken during the study for analysis of the test medicine. Subject’s blood and urine will also be collected for safety testing. Subjects are expected to be involved in this study for approximately 9 weeks from screening to the follow-up visit.

What are the possible benefits and risks of participating?
Benefits:
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/or non-alcoholic steatohepatitis (NASH) will be of benefit to patients with either of these conditions.
Risks:
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 approved medicine in this study. Full information on possible side effects is provided to subjects in the Participant Information Sheet and Informed Consent Form.
5. 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.
6. 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?
May 2023 to December 2023

Who is funding the study?
Corcept Therapeutics Incorporated (USA)

Who is the main contact?
Dr Sharan Sidhu, sharan.sidhu@quotientsciences.com

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1007798

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CORT118335-857, IRAS 1007798

Study information

Scientific Title
A randomised, double blind, placebo-controlled study to evaluate the effect of low dose miricorilant on olanzapine-induced weight gain in healthy subjects (QSC301120)

Study objectives
To evaluate the impact of low dose miricorilant 100 mg on olanzapine-induced weight gain following 21 days of daily dosing with co-administered miricorilant and olanzapine vs olanzapine and placebo.

Secondary objectives:
1. To evaluate the impact of low dose miricorilant 100 mg on olanzapine-induced weight gain following 7 and 14 days of daily dosing with co-administered miricorilant and olanzapine vs olanzapine and placebo.
2. To determine the pharmacokinetics (how the test medicine is taken up by the body, PK) of miricorilant and its metabolite, CORT118335-P9.
3. To evaluate the impact of low dose miricorilant 100 mg on glucose, insulin, homeostatic model assessment of insulin-resistance (HOMA-IR), triglycerides and cholesterol following 7, 14 and 21 days of daily dosing with co-administered miricorilant and olanzapine vs olanzapine and placebo.
4. To evaluate the impact of low dose miricorilant 100 mg on olanzapine-induced changes in waist-to-hip ratio following 7, 14 and 21 days of daily dosing with co-administered miricorilant and olanzapine vs olanzapine and placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 31/08/2023, HSC REC A (ORECNI, Business Services Organisation, Lissue Industrial Estate West, Rathdown Walk, Moira Road, Lisburn, Co. Antrim, BT28 2RF, United Kingdom; +44 28 9536 1400; RECA@hscni.net), ref: 23/NI/0058

Study design
Interventional double blind randomized parallel group placebo controlled trial

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Antipsychotic-induced weight gain (AIWG)

Interventions
This is a randomised, double blind, placebo-controlled trial. This one-part, healthy subject proof of concept study aims to assess whether the test medicine, miricorilant, dosed with food, reduces the weight gain caused by the approved medicine, olanzapine. This study will take place at one non-NHS site and will consist of a single study period involving up to 70 healthy men, aged between 18 and 55. Subjects will be randomised to 1 of 2 treatment regimens in which they will be orally dosed with olanzapine (10 mg) and either miricorilant (100 mg) or placebo. All regimens will be dosed in the morning for 21 consecutive days. Subjects will be admitted to the clinical unit on the evenings of Days -1, 7, 14 and 21, and dosed in the clinical unit on Days 1 to 4, Day 8 and Day 15. Subjects will be discharged from the clinical unit following dosing on Days 4, 8 and 15 and will proceed with home dosing on Days 5 to 7, Days 9 to 14, and Days 16 to 21. Subjects will be discharged for the last time on Day 22 and will return 12 to 16 days post-final test medicine dose for a follow-up visit. Subject’s blood will be taken during the study for analysis of the test medicine. Subject’s blood and urine will also be collected for safety testing. Subjects are expected to be involved in this study for approximately 9 weeks from screening to the follow-up visit.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
CORT118335 Tablets 100 mg [Miricorilant], Olanzapine film-coated tablets 10 mg

Primary outcome(s)
Change in body weight evaluated by analysis of body weight measurements taken from Day 1 and Day 22.

Key secondary outcome(s))
1. Change in body weight evaluated by analysis of body weight measurements taken from Day 1 and Days 8 and 15.
2. PK parameters for miricorilant and its metabolite, CORT118335-P9, as applicable, evaluated

by analysis of blood samples collected from Day 1 to Day 22.
3. Changes in plasma or serum concentrations of glucose, insulin, triglyceride and cholesterol and HOMA-IR from baseline evaluated by analysis of blood samples collected from Day 1 and Days 8, 15 and 22.
4. Changes in waist-to-hip ratio compared to baseline evaluated by analysis of waist-to-hip ratio measurements taken on Day 1 and Days 8, 15 and 22.
5. Safety, evaluated by monitoring adverse events (AEs) from signing the informed consent form until the follow-up visit (prior to Day -1 until Day 35±2) and results from safety tests, ECGs, vital signs measurements and physical examinations at screening, and at intervals from pre-dose on Day 1 to Day 22 and on Day 35±2.
6. Incidence and degree of increases in hepatic aminotransferases compared to baseline evaluated by analysis of blood samples collected from Day 1 to Day 22.

Completion date
14/12/2023

Eligibility

Key inclusion criteria
1. Provide written informed consent
2. Willing and able to communicate and participate in the whole study
3. Male
4. Aged 18 to 55 years inclusive at the time of signing informed consent
5. Agree to adhere to the contraception requirements defined in the Clinical Protocol
6. Healthy as determined by medical evaluation including medical history, physical examination, vital signs, 12-lead ECG, clinical laboratory profiles (haematology, clinical chemistry and urinalysis), as deemed by the Investigator or designee
7. BMI of 18.0 to 25.0 kg/m² as measured at screening
8. Stable body weight as indicated by assessment at screening and pre-dose Day 1. Pre dose Day 1 body weight to be within ±2.0% of screening body weight (measured in the morning following a minimum 8 hour fast)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
55 years

Sex
Male

Key exclusion criteria

1. Serious adverse reaction or serious hypersensitivity to any drug or formulation excipients (including lactose)
2. Presence or history of clinically significant allergy requiring treatment, as judged by the Investigator. Subjects with inactive seasonal hay fever may be included
3. H istory of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or gastrointestinal disease (including cholecystectomy and gall stones), neurological or psychiatric disorder, as judged by the Investigator
4. Subject has a condition that could be aggravated by glucocorticoid and/or mineralocorticoid antagonism (e.g. asthma, any chronic inflammatory condition, postural hypotension/orthostatic symptoms). Subjects with childhood (aged less than 18 years) asthma may be included provided they have had no symptoms and required no treatment for at least 5 years
5. History of additional risk factors for torsades de pointes (e.g. heart failure, hypokalaemia, family history of long QT syndrome)
6. Lack of suitable veins for multiple venepunctures/cannulation as assessed by the Investigator or delegate at screening
7. Clinically significant abnormal clinical chemistry (including ALT, AST and/or bilirubin more than the ULN at screening), haematology or urinalysis as judged by the Investigator
8. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results
9. Subject has renal impairment as evidenced by an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m2 using Modification of Diet in Renal Disease (MDRD) equation at screening
10. Clinically significant ECG abnormalities or vital sign abnormalities at screening or baseline (Day 1 pre-dose) including but not limited to:
10.1. QTcF >450 msec
10.2. Supine heart rate (HR) at rest of >100 bpm
10.3. 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)
10.4. HR and BP can be retested twice in the supine position at intervals of approximately 5 minutes on a given day
11. Subjects who have received any IMP 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
12. Subjects who have received miricorilant in study QSC300704 in the 6 months prior to the first dose of miricorilant in this study
13. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood
14. 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 IMP administration. COVID-19 vaccines are accepted concomitant medications
15. Subjects who are currently using glucocorticoids or have a history of systemic glucocorticoid use at any dose within the last 12 months or 3 months for inhaled glucocorticoids. Subjects who have received up to two single doses of a glucocorticoid in another study more than 3 months before first dose of study medication will not be excluded from taking part in the study
16. Any contraindication to the use of olanzapine as per the SmPC
17. History of any drug or alcohol abuse in the past 2 years
18. Regular alcohol consumption >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 type).
19. A confirmed positive alcohol breath test at screening or admission
20. Current smokers and those who have smoked within the last 12 months
21. Current users of e-cigarettes and nicotine replacement products and those who have used

these products within the last 12 months
22. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or admission
23. Confirmed positive drugs of abuse test result at screening or admission
24. Pregnant or lactating sexual partners
25. Is, or is an immediate family member of, a study site or Sponsor employee
26. Failure to satisfy the Investigator of fitness to participate for any other reason

Date of first enrolment
10/08/2023

Date of final enrolment
06/11/2023

Locations

Countries of recruitment
United Kingdom

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

Sponsor information

Organisation
Corcept Therapeutics Incorporated (USA)

Funder(s)

Funder type
Industry

Funder Name
Corcept Therapeutics Incorporated (USA)

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Data sharing statement to be made available at a later date