ISRCTN20653849 https://doi.org/10.1186/ISRCTN20653849

A study in healthy male volunteers designed to investigate how the test medicine [14C]-CORT125329 is taken up, broken down and removed by the body

Submission date
22/09/2022

Recruitment status
No longer recruiting

Registration date
21/10/2022

Overall study status
Completed

Last Edited
27/10/2022

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, CORT125329, for the potential treatment of antipsychotic-induced weight gain (AIWG). AIWG is the condition in which patients taking antipsychotic medications have a tendency to gain weight. In addition, antipsychotic drugs can increase the risk of patients developing cardiovascular disease (diseases of the heart/blood vessels). This study will aim to look at how the test medicine is taken up, broken down and removed by the body when given orally as capsules after food. To help investigate this, the test medicine will be radiolabelled. 'Radiolabelled' means that the test medicine has a radioactive component, in this case Carbon-14 which is a type of naturally occurring radioactivity. The safety and tolerability of this test medicine will also be studied.

Who can participate?
Healthy male volunteers aged between 45 and 70 years

What does the study involve?
Participants will be admitted to the clinic the evening before the day of dosing. On Day 1, after eating a standard breakfast, participants will receive a single 1200 mg dose of the radiolabelled test medicine as 12 x 100 mg capsules. Their blood, urine and faeces will be taken throughout the study for analysis of the test medicine and its breakdown products, and for their safety. A cerebrospinal fluid (CSF) sample will be taken on one occasion. Participants will remain in the clinic up to Day 11, but if the relevant radioactivity elimination criteria have been met for all participants before Day 11, they may be discharged early as a group. If the relevant criteria have not been met by Day 11, participants may remain in the clinic (up to Day 13). Home collection of urine and/or faeces may be required. Participants are expected to be involved in this study for about6 weeks from screening to the follow-up phone call.

What are the possible benefits and risks of participating?
Participants will get no medical benefit from taking part in this study. It is hoped that the

development of a product to improve the treatment of antipsychotic-induced weight gain will be of benefit to patients with this condition. 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 volunteers. 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. When investigating new medicines there is always a risk of unexpected side effects and occasionally allergic reactions. Participants will be closely monitored during the study. Participants may experience side effects from the test medicine in this study. Full information on possible side effects is provided in the Participant Information Sheet and Informed Consent Form (PIS/ICF). There will be an extended period of fasting for the participants. To ensure an adequate fluid intake, the subjects will be allowed fluids and will be monitored for signs of dehydration and fatigue. Blood samples will be collected during the study, which can cause soreness and bruising of the arm, but these problems usually clear up within a few days to weeks. ECG stickers on subjects' chests and limbs may cause some local irritation and may be uncomfortable to remove. Participants will be closely monitored and if any irritation occurs, appropriate care will be given. CSF samples will be collected. Collection of CSF will be via a lumbar puncture, which may cause some side effects, the most common ones being headaches and swelling/back pain around where the needle was inserted. These are usually mild and should get better after a few days. In some cases they can last for up to a week. The lumbar puncture will be carried out by a consultant anaesthetist. By taking part in the study the participants will be exposed to a small amount of radiation. Further information can be found in the PIS/ICF.

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

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

Who is funding the study?
Corcept Therapeutics (USA)

Who is the main contact?
Hazel Hunt, hhunt@corcept.com

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2022-002574-90

IRAS number
1006127

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CORT125329-141, IRAS 1006127

Study information

Scientific Title

An open label, single-dose, single-period study designed to assess the mass balance recovery, metabolite profile and metabolite identification of [14C]-CORT125329 in healthy male subjects

Acronym
QSC206122

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

Primary objectives:
1. To determine the mass balance recovery (amount of radioactivity recovered from urine and faeces) after a single oral dose of [14C]-CORT125329
2. To perform metabolite (breakdown product) profiling and structural identification from plasma, urine and faecal samples

Secondary objectives:
1. To determine the routes and rates of elimination of [14C]-CORT125329
2. To identify significant metabolites of CORT125329
3. To explore the oral pharmacokinetics (what the body does to the test medicine, PK) of CORT125329 further
4. To evaluate the extent of distribution of TR (total radioactivity) into blood cells
5. To provide additional safety and tolerability information for CORT125329
6. To determine if CORT125329 crosses the blood-brain barrier

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/10/2022, Health and Social Care Research Ethics Committee B (HSC REC B) (Unit 5, Lissue Industrial Estate West, Rathdown Walk, Moira Road, Lisburn, Co. Antrim, BT28 2RF, UK; +44 (0)28 9536 1400; RECB@hscni.net), ref: 22/NI/0155

Study design
Non-randomized open-label uncontrolled single-dose trial

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

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

Interventions
This is a non-randomized, open-label, uncontrolled, single-dose trial. This trial consists of a single study period involving up to 6 healthy male subjects, aged between 45 and 70 years. Following consumption of a standard breakfast, subjects will receive a single oral 1200 mg dose of the radiolabelled test medicine as 12 x 100 mg capsules. Subjects will remain in the clinic up to Day 11, they may be discharged early as a group if the relevant criteria have been met. If the relevant criteria have not been met by Day 11, subjects may remain in the clinic (up to Day 13). Home collections of urine and/or faeces may be required. A follow-up phone call will take place 5 to 8 days after the final collection period to ensure the ongoing wellbeing of the subjects. Subjects are expected to be involved in this study for approximately 6 weeks from screening to follow-up phone call.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
[14C]-CORT125329 Lipid Capsule, LFCS Type III, 100 mg (NMT 0.825 MBq)

Primary outcome measure
1. Total radioactivity (TR) measured using liquid chromatography-radio-detection with subsequent mass spectrometry on blood samples collected from Day 1 to Day 11 and urine and faecal samples collected from Day 1 to Day 11
2. Metabolite profiling, structural identification, and quantification analysis using blood samples from Day 1 to Day 5 and urine and faecal samples collected from Day 1 to Day 11. This may be extended until the mass balance criteria are met.

Secondary outcome measures
1. Total radioactivity/metabolite profiling using liquid chromatography-radio-detection with subsequent mass spectrometry on urine and faeces collected from Day 1 to Day 11. This may be extended until the mass balance criteria are met.
2. Metabolic profiling and ID using liquid chromatography-radio-detection with subsequent mass spectrometry on blood samples collected from Day 1 to Day 5
3. TR and PK measured using liquid chromatography-radio-detection with subsequent mass spectrometry on blood samples collected from Day 1 to Day 11
4. Adverse events monitored from signing the informed consent form until the follow-up phone call. Subjects will undergo safety tests, ECGs, vital signs measurements and physical examinations at screening, and at intervals from admission until final discharge
5. Total radioactivity and concentration of drug in CSF sample measured using liquid chromatography/mass spectrometry, collected on Day 1

Overall study start date
20/09/2022

Completion date

29/12/2022

Eligibility

Key inclusion criteria
1. Must provide written informed consent
2. Must be willing and able to communicate and participate in the whole study
3. Aged 45 to 70 years inclusive at the time of signing informed consent
4. Must agree to adhere to the contraception requirements defined in the clinical study protocol.
5. Healthy male subjects
6. Body mass index of 18.0 to 32.0 kg/m² as measured at screening
7. Must have regular bowel movements (i.e., average stool production of ≥1 and ≤3 stools per day)

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
6

Key exclusion criteria
1. Serious adverse reaction or serious hypersensitivity to any drug or formulation excipients; allergy to lidocaine
2. Presence or history of clinically significant allergy requiring treatment, as judged by the Investigator.
3. History of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or gastrointestinal (GI) disease, neurological or psychiatric disorder, as judged by the Investigator
4. Subject had any form of cancer within the 5 years before screening for this study, with the exception of basal cell and/or squamous cell cancer of the skin that has been treated completely and is without evidence of local recurrence or metastasis
5. Subject has a history and/or symptoms of adrenal insufficiency
6. Subject has a history of clinically significant GI disease including gastroesophageal reflux disease, malabsorption syndrome, colon cancer, chronic colitis, Crohn’s disease, inflammatory bowel disease, gastroparesis, cholecystectomy, constipation, chronic diarrhoea, obstruction, GI bleeding, and/or peptic ulcers
7. Subject has a condition that could be aggravated by glucocorticoid antagonism (e.g., asthma, any chronic inflammatory condition). Subjects with inactive seasonal hay fever may be included. 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 prior to screening
8. History of additional risk factors for torsades de pointes (e.g., heart failure, hypokalaemia, family history of long QT syndrome)

9. Undergone a lumbar puncture within 6 weeks before Day 1
10. Medical history or evidence of mass occupying lesion in brain or spinal cord or history of spinal cord injury, which could preclude the procedure of lumbar puncture and CSF collection
11. Evidence or history of clinically significant back pain, back pathology and/or back injury (e.g degenerative disease, spinal deformity or spinal surgery) that may predispose to complications or technical difficulties in the conduct of a lumbar puncture
12. Evidence or history of significant active bleeding or coagulation disorder
13. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the Investigator or delegate at screening
14. Evidence of SARS-CoV-2 infection within 2 weeks of IMP administration
15. Clinically significant abnormal clinical chemistry, haematology, coagulation or urinalysis as judged by the Investigator. Subjects with Gilbert's Syndrome are allowed.
16. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results
17. Subject has active renal and/or hepatic disease as demonstrated by ALT and/or AST >1.5 times the upper limit of normal at screening or on admission
18. Evidence of renal impairment at screening, as indicated by an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73m2 using Modification of Diet in Renal Disease (MDRD) equation /Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI; 2009) equation
19. Platelet count below lower limit of normal; prothrombin time and/or activated partial thromboplastin time above the upper limit of normal at screening
20. Subjects with a QTcF interval of >450 msec at screening or baseline (before first dose of study medication)
21. Supine heart rate (HR) at rest of <40 bpm or >100 bpm. Blood pressure (BP) outside the following ranges: diastolic BP 40-90; and 90-160 (subjects aged ≥45 years). Heart rate and BP can be retested twice in the supine position at intervals of 5 minutes on a given day at screening and pre-dose
22. Subjects who have received any IMP in a clinical research study within the 90 days prior to Day 1, or participated in CORT125329-140 (QSC203060) at any time
23. Radiation exposure, excluding background radiation but including that from the present study, diagnostic x-rays and other medical exposures, exceeding 5 mSv in the last 12 months or 10 mSv in the last 5 years. No occupationally exposed worker, as defined in the Ionising Radiation Regulations 2017, shall participate in the study
24. Donation of blood or plasma within the previous 3 months prior to screening or loss of greater than 400 ml of blood

Please see the clinical protocol for a full list of exclusion criteria.

Date of first enrolment
22/11/2022

Date of final enrolment
29/12/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Quotient Sciences Limited
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Funder(s)

Funder type
Industry

Funder Name
Corcept Therapeutics (United States)

Results and Publications

Publication and dissemination plan
1. Internal report
2. Submission to regulatory authorities

The findings of this Phase I study will be shared with the Sponsor, Corcept Therapeutics, 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.

Intention to publish date
29/12/2023

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 the confidential nature of the data.

IPD sharing plan summary
Not expected to be made available