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A study in healthy male volunteers to investigate how the radiolabelled test medicine [14C]-CORT125236 is taken up, broken down and removed from the body (Part 1) and to investigate how the test medicine CORT125236 is taken up by the body in healthy male and female volunteers when given as a new tablet recipe with and without food (Part 2)

Submission date 15/08/2024	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 11/10/2024	**Overall study status** Completed	
Last Edited 11/02/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine as a potential treatment for solid tumours (cancer) in combination with chemotherapy or other cancer medicines. Solid tumours represent approximately 90% of adult human cancers. They can develop in many parts of the human body. This study aims to answer:
1. How much test medicine enters the bloodstream and how quickly the body gets rid of it?
2. Does food affect the blood levels of the test medicine?
3. How does the body break down and get rid of the test medicine?
This study will also provide more information on the safety and tolerability of the test medicine and any side effects.

Who can participate?
Healthy men aged 30 to 65 years in Part 1 and healthy men and women who are unable to have a baby, aged 18 to 55 years in Part 2.

What does the study involve?
In Part 1, volunteers will be given a single dose of test medicine to find out how the body breaks down and gets rid of the test medicine. The test medicine will be ‘radiolabelled’ and contain a small amount of radioactivity (Carbon-14). In Part 2, the blood levels of the test medicine will be compared after it's given in a new tablet form (recipe) with and without food and at two

different dose levels. This study will take place at 1 site in Nottingham. In Part 1, volunteers will receive a single dose of radiolabelled test medicine in capsules by mouth. They will stay in the clinic for up to 13 nights and take up to 6 weeks to finish the study. In Part 2, volunteers will receive 3 single doses of test medicine as tablets by mouth. They will stay in the clinic for 4 nights on 3 occasions, attend 3 return visits and 1 follow up visit, and take up to 9 weeks to finish the study.

Samples will be collected to:
1. Do safety tests (blood and urine)
2. Measure the amount of the test medicine (blood, Part 1/2; urine and faeces, Part 1 only)
3. Measure the amount of radioactivity and breakdown products of the test medicine (blood, urine and faeces, Part 1 only)

What are the possible benefits and risks of participating?
Volunteers may experience side effects from the test medicine. The test medicine is early in development so there is little information about its effects in humans. Full information on possible side effects is in the Participant Information Sheet and Informed Consent Forms (PIS-ICF). There is always a risk of unexpected side effects or an allergic reaction. To mitigate the risk, the study team will ensure that volunteers meet the entry criteria for the study and monitor volunteers closely throughout the study.

In Part 1, volunteers will be exposed to up to 0.8 milliSieverts (mSv) of radioactivity during the study, which is equivalent to about 107 days' exposure to the average yearly background radiation in the UK (2.7 mSv). That amount of radiation poses negligible risk to the volunteers' health but volunteers should not take part in another ADME study involving radiation for approximately 1 year. Volunteers who participate in Part 2 will not be exposed to radiation.

The screening tests might be of benefit if we find an important medical problem, but they might reveal something that the volunteer would prefer not to know about. If there are medically important findings in our tests at screening, or during the study, we will inform the volunteer's GP.

Volunteers will be confined to the clinic during the study and must make outpatient visits and comply with the lifestyle restrictions described in the PIS-ICF, including periods of fasting from food and drink except water and short periods during which they will be allowed no fluids.

The test medicine might harm unborn children, so all volunteers must follow the restrictions on the donation of sperm or eggs and use acceptable contraception. Were a volunteer, or a partner of a volunteer, to become pregnant during the study, the study team would ask permission to follow up on the pregnancy.

Volunteers will undergo many tests and procedures during the study.
*Blood sampling can cause soreness and bruising of the arms but these problems usually clear up within a few days to a few weeks. Susceptible volunteers may faint when we take blood samples; volunteers must lie down when we take blood samples to mitigate that risk.
*ECG stickers may cause local skin irritation.

Healthy volunteers will get no medical benefit from the test medicine; however, the aims of the study can be most efficiently met in volunteers with no concurrent medical conditions and who do not need to take concomitant medication that might interfere with the study objectives or increase the risk of the study. The risk/benefit evaluation in this study supports the use of healthy volunteers.

Volunteers will receive payment for participating in the study. There is always a risk that payment could represent coercion. However, payment will be based on committed time, inconvenience, and travel and other expenses, not on risk. An ethics committee will review the payment to ensure that it is fair.

Where is the study run from?
Corcept Therapeutics Incorporated (USA)

When is the study starting and how long is it expected to run for?
August 2024 to December 2024

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

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

Contact information

Type(s)
Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Integrated Research Application System (IRAS)
1010259

Protocol serial number
CORT125236-151

Study information

Scientific Title
A two-part, open-label, single-dose study designed to assess the mass balance recovery, metabolite profile and metabolite identification of [14C]-CORT125236 in healthy male subjects and to assess pharmacokinetics of CORT125236 tablet, including food effect in healthy subjects

Study objectives
Primary objectives:
1. To determine the mass balance recovery after a single oral dose of [14C]-CORT125236 (Part 1).
2. To perform metabolite profiling and structural identification from plasma, urine and faecal samples (Part 1).
3. To determine the exposure of CORT125236 following administration of CORT125236 tablets at two dose levels, including relative bioavailability in the fed and fasted states (Part 2).

Secondary objectives:
1. To determine the routes and rates of elimination of [14C]-CORT125236 (Part 1).
2. To identify the chemical structure of each metabolite accounting for more than 10% of circulating total radioactivity (TR) or accounting for 10% or more of the dose in excreta (Part 1).
3. To explore further the oral PK following single doses of CORT125236 lipid-filled capsules (Part 1).
4. To evaluate the extent of the distribution of TR into blood cells to explore further the oral PK following single doses of CORT125236 lipid-filled capsules (Part 1).
5. To provide additional safety and tolerability information for CORT125236 (Parts 1 and 2).

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 07/10/2024, South Central – Berkshire Research Ethics Committee (Health Research Authority, 2 Redman Place,, London, E20 1JQ, United Kingdom; +44 (0)207 104 8178, 207 104 8182, 207 104 8233; berkshire.rec@hra.nhs.uk), ref: 24/SC/0217

Primary study design
Interventional

Study design
Two-part open-label single-dose study

Study type(s)
Other, Safety

Health condition(s) or problem(s) studied
Medical condition: Solid tumours
Medical condition in lay language: Solid tumours
Therapeutic areas: Diseases [C] - Cancer [C04]

Interventions
This is a 2-part study. Part 1 is a single-period, single-dose, open-label study in healthy male subjects. Part 2 is an open-label, part-randomised, 3-way crossover study in healthy male and female subjects. Part 1 assesses how the body breaks down and gets rid of the test medicine. The test medicine will be radiolabelled and contain a small amount of radioactivity (Carbon-14). Part 2 assesses the pharmacokinetics (PK, what the body does to the drug) of the test medicine after it's given as a new tablet formulation, with and without food at two different dose levels. This study will take place at one non-NHS site, and it is planned to enrol 6 healthy male subjects aged 30 to 65 in Part 1, and 6 healthy male or female (of non-childbearing potential) subjects aged 18 to 55 in Part 2. Subjects will be admitted in the evening of Day -1 in both study parts. In Part 1, subjects will receive an oral dose of 300 mg test medicine radiolabelled with Carbon-14, as 5 x 60 mg capsules, on Day 1, and will be discharged on Day 11. In Part 2, subjects will receive single oral doses of 200 mg test medicine (as 4 x 50 mg tablets) on Day 1 of Periods 1 and 2, in either the fed or fasted state. A computer will decide the order in which they receive these doses. In Period 3 of Part 2, subjects will receive a different dose of test medicine, taken either with or without food. Subjects in Part 2 will be discharged on Day 4 of each study period, have a follow-up visit on Day 5 of each study period, and a final follow-up visit on Day 10 of Period 3. Subject's blood and urine (and faeces in Part 1) will be taken throughout the study for analysis of the test medicine, its breakdown products and amount of radioactivity (Part 1), as well as for their safety. Subjects are expected to be involved in this study for approximately 6 weeks from screening to discharge in Part 1, and 9 weeks from screening to discharge in Part 2.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
[14C]-CORT125236 Lipid Capsule, 60 mg (NMT 1.61 MBq), CORT125236 Tablet, 50 mg

Primary outcome(s)
Part 1: Assessment of mass balance measured using urine and faecal samples taken from Day 1 to Day 11, or until mass balance criteria are met
Part 1: Metabolite profiling and structural identification measured using blood, urine and faecal samples taken from Day -1 until Day 11
Part 2: Pharmacokinetic parameters measured using blood samples taken from Day 1 until Day 5 of each period

Key secondary outcome(s)
Part 1: Pharmacokinetic parameters measured using urine and faecal samples taken from Day -1 until Day 11, or until mass balance criteria are met
Part 1: Identification of the chemical structure of each metabolite measured using blood, urine and faecal samples taken from Day -1 until Day 11
Part 1: Exploration of oral pharmacokinetic parameters measured using blood samples taken from Day -1 until Day 11

Part 1: Evaluation of whole blood:plasma concentration ratios for total radioactivity measured using blood samples taken from Day 1 until Day 11
Parts 1 and 2: Safety and tolerability measured using the incidence of adverse events, physical examinations, and changes from baseline for vital signs, electrocardiograms and laboratory safety tests from Day -1 until the final follow-up visit

Completion date
30/12/2024

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 30 to 65 years (Part 1) or aged 18 to 55 (Part 2) inclusive at the time of signing informed consent.
4. Must agree to adhere to the contraception requirements defined in the Clinical Protocol.
5. Healthy male subjects (Parts 1 and 2) or non-pregnant, non-lactating female subjects of non-childbearing potential (Part 2 only) according to the assessment of the investigator, as based on a complete medical history including a physical examination, vital signs, 12-lead ECG, and laboratory safety tests without any clinically significant abnormalities. Safety bloods, urinalysis, ECGs and vital signs are to be re-checked at admission/pre-dose.
6. Body mass index (BMI) of 18.0 to 30.0 kg/m² as measured at screening
7. Weight ≥50 kg at screening.
8. Must have regular bowel movements (i.e. average stool production of ≥1 and ≤3 stools per day) for Part 1 only.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 11/10/2024:

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.
3. History of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or gastrointestinal disease, neurological or psychiatric disorder, as judged by the Investigator.
4. Acute diarrhoea or constipation in the 7 days before the predicted Day 1. If screening occurs > 7 days before Day 1, this criterion will be determined on Day 1. Diarrhoea will be defined as the passage of liquid faeces and/or a stool frequency of greater than 3 times per day. Constipation will be defined as a failure to open the bowels more frequently than every other day (Part 1 only).
5. Subject had any form of cancer within the 5 years before first dose in 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.
6. Subject has a history and/or symptoms of adrenal insufficiency.
7. Subject has a history of clinically significant gastrointestinal disease including gastroesophageal reflux disease, malabsorption syndrome, colon cancer, chronic colitis, Crohn's disease, inflammatory bowel disease, gastroparesis, cholecystectomy, constipation, chronic diarrhoea, obstruction, gastrointestinal bleeding, and/or peptic ulcers.
8. Subject has any history of clinically significant recurrent back pain, as judged by the Investigator.
9. Subject has any history of clinically significant recurrent ear infections, including otitis externa, as judged by the Investigator.
10. Subject has any condition or history of any condition that could be aggravated by glucocorticoid antagonism (e.g., asthma, any chronic inflammatory condition and including autoimmune disease or rheumatic disease) or glucocorticoid activation (e.g., immunodeficiency, active infection). 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.
11. Subjects who do not have suitable veins for multiple venepunctures/cannulations as assessed by the Investigator or delegate at screening.
12. Clinically significant abnormal clinical chemistry, haematology or urinalysis as judged by the Investigator. Subjects with Gilbert's Syndrome are not allowed.
13. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results.
14. 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.
15. Female subjects (Part 1) or female subjects of childbearing potential (Part 2) including those who are pregnant or lactating. A woman is considered of childbearing potential unless she is permanently sterile (hysterectomy, bilateral salpingectomy, and bilateral oophorectomy) or is post-menopausal (had no menses for 12 months without an alternative medical cause and a serum follicle stimulating hormone [FSH] concentration ≥40 IU/L) All female subjects must have a negative highly sensitive urine (or serum) pregnancy test.
16. Clinically significant ECG abnormalities or vital sign abnormalities at screening or baseline (pre-first dose of IMP) including but not limited to:
16.1. QTcF > 450 msec based on a single ECG at screening and pre-(first) dose.
16.2. Supine heart rate (HR) or ventricular rate at rest of <40 bpm or >100 bpm at screening and pre-(first) dose.
16.3. Blood pressure (BP) outside the following ranges: diastolic BP 40-90 mmHg; systolic BP 90-140 mmHg at screening or before the first dose.
16.4. ECGs and HR and BP can be retested twice in the supine position at intervals of approximately 5 minutes on a given day.
17. 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.
18. Subjects who report to have received CORT125236 in a previous study part. Subjects who have taken part in Part 1 of this study may not take part in Part 2 of this study (and vice versa).
19. Radiation exposure, including that from the present study, excluding background radiation but including 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 (Part 1 only).
20. Subjects who have been administered IMP in an ADME study in the last 12 months (Part 1 only).
21. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood.
22. Subjects who are taking, or have taken, any prescribed medication (including vaccines) or over-the-counter drug or herbal remedies (other than up to 4 g of paracetamol per day) in the 14 days before IMP administration. Exceptions may apply, as determined by the Investigator in consultation with the Medical Monitor, if each of the following criteria are met: medication with a short half-life if the washout is such that no PD activity is expected by the time of dosing with IMP; and if the use of medication does not jeopardise the safety of the trial subject; and if the use of medication is not considered to interfere with the objectives of the study.
23. 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 products before first dose of study medication. Subjects who have used enzyme inducers within 30 days before the first dose of study medication will also be excluded. 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.
24. History of any drug or alcohol abuse in the past 2 years.
25. 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 type).
26. A confirmed positive alcohol breath test at screening or admission.
27. Current smokers and those who have smoked within the last 12 months.
28. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months.
29. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or admission.
30. Confirmed positive drugs of abuse test result at screening or admission.
31. Male subjects with pregnant or lactating partners.
32. Subjects who are, or are immediate family members of, a study site or Sponsor employee.
33. Failure to satisfy the Investigator of fitness to participate for any other reason.

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Previous exclusion criteria:

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14.4. ECGs and HR and BP can be retested twice in the supine position at intervals of approximately 5 minutes on a given day.
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16. Subjects who report to have received CORT125236 in a previous study part. Subjects who have taken part in Part 1 of this study may not take part in Part 2 of this study (and vice versa).
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19. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood.
20. Subjects who are taking, or have taken, any prescribed medication (including vaccines) or

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21. 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 products before first dose of study medication. Subjects who have used enzyme inducers within 30 days before the first dose of study medication will also be excluded. 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.
22. History of any drug or alcohol abuse in the past 2 years.
23. 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 type).
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29. Male subjects with pregnant or lactating partners.
30. Subjects who are, or are immediate family members of, a study site or Sponsor employee.
31. Failure to satisfy the Investigator of fitness to participate for any other reason.

Date of first enrolment
28/10/2024

Date of final enrolment
23/12/2024

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 (United States)

ROR
https://ror.org/03ey3qt70

Funder(s)

Funder type
Industry

Funder Name
Corcept Therapeutics Incorporated

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