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A study in healthy volunteers to investigate how the test medicine CORT113176 is taken up by the body when given with food and without food

Submission date
09/02/2022

Recruitment status
No longer recruiting

Registration date
09/03/2022

Overall study status
Completed

Last Edited
09/06/2022

Condition category
Nervous System Diseases

[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, CORT113176, for the potential treatment of amyotrophic lateral sclerosis (ALS), a rare disease with few treatment options. ALS involves progressive degeneration of motor neurons (nerve cells) in both the brain and the spinal cord leading to progressive muscle weakness, relentless disability, and death, typically within 3 to 5 years from symptom onset. The aim of this study is to evaluate the pharmacokinetics (what the body does to the drug) of CORT113176 softgel capsules when administered as single oral doses in healthy volunteers, and to assess the effect of food on CORT113176.

Who can participate?
Healthy volunteers aged 18 to 60 years

What does the study involve?
After a screening assessment, volunteers will enter the clinical unit on Day -1 and will be dosed with the test medicine on Day 1, either with or without food. Volunteers will be discharged on Day 4. There will then be a minimum of 7 days between doses and volunteers will return to the clinical unit for period 2. Volunteers will be dosed with the same dose of the test medicine as in period 1, in the opposite fed/fasted state. Blood and urine samples will be collected from volunteers throughout the study for analysis of the test medicine and for safety assessments. Volunteers are expected to be involved in this study for about 6 weeks from screening to follow up.

What are the possible benefits and risks of participating?
As this is a Phase I study, the most relevant population is healthy volunteers, who will get no medical benefit from taking part in the study. 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. Volunteers will be closely monitored during the study. Volunteers may experience side effects from the test medicine in this study. If excessive glucocorticoid receptor (GR) antagonism is suspected, standard supportive care (including fluid resuscitation as indicated) and medical therapy will be administered without delay. The effects of excessive GR antagonism should be reversible by the administration of a GR agonist, for example dexamethasone, and intravenous fluids. Possible side effects include headache, pain in extremity, joint pain and stiffness, back pain, feeling sick and vomiting. This is not expected when receiving a single dose on two occasions. There will be an extended period of fasting for the volunteers taking part in this study. Volunteers will be monitored for signs of dehydration and fatigue. 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. ECG stickers on volunteers' chests and limbs may cause some local irritation and may be uncomfortable to remove but volunteers will be closely monitored to ensure any local irritation does not persist. CORT113176 does not demonstrate evidence of phototoxic potential (skin irritation). The test medicine will be given orally.

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

When is the study starting and how long is it expected to run for?
February 2022 to May 2022

Who is funding the study?
Corcept Therapeutics (USA)

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

Contact information

Type(s)
Scientific

Contact name
Dr Sharan Sidhu

Contact details
Mere Way
Ruddington Fields
Nottingham
United Kingdom
NG11 6JS
+44 (0)330 3031000
recruitment@weneedyou.co.uk

Type(s)
Scientific

Contact name

Dr Sharan Sidhu

Contact details
Mere Way
Ruddington Fields
Nottingham
United Kingdom
NG11 6JS
+44 (0)330 3031000
recruitment@weneedyou.co.uk

Type(s)
Principal investigator

Contact name
Dr Sharan Sidhu

Contact details
Mere Way
Ruddington Fields
Nottingham
United Kingdom
NG11 6JS
+44 (0)330 3031000
recruitment@weneedyou.co.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2022-000181-18

Integrated Research Application System (IRAS)
1005009

Protocol serial number
CORT113176-654, QSC207407, IRAS 1005009

Study information

Scientific Title
A Phase I single-dose study to evaluate the pharmacokinetics of CORT113176 softgel capsules in healthy subjects

Study objectives
1. Evaluate the pharmacokinetics (PK, what the body does to the test medicine) of CORT113176 softgel capsules when administered as single oral doses in healthy subjects
2. Assess the PK of CORT113176 following co-administration with food, relative to fasting conditions
3. Obtain additional safety and tolerability data

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/03/2022, Fast Track Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, UK; Tel: not available; fasttrack.rec@hra.nhs.uk), REC ref: 22/FT/0029

Study design
Randomized crossover study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Amyotrophic lateral sclerosis (ALS)

Interventions
This is a single-centre, randomised, open-label, crossover Phase I study in healthy adult volunteers to assess the effect of food on the pharmacokinetics (PK) of CORT113176 when given by mouth as softgel capsules. There will be two groups of participants, each comprising eight healthy volunteers. Each participant will take two single doses of CORT113176 softgel capsules: one after an overnight fast, and one after a standard breakfast. One group of participants will take 150 mg CORT113176 (2 x 75 mg softgel capsules); the other group will take 300 mg CORT113176 (4 x 75 mg softgel capsules).

Blood samples will be taken before, and frequently after, dosing to measure the amount of CORT113176.

Participants will be screened during the 4 weeks before the study starts. They will have two study sessions: during each session, they will stay on the ward for 5 nights and take a single dose of CORT113176. They will return to the ward for a follow-up visit at about 1 week after their final study session. Participants will take about 6 weeks to complete the study.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
CORT113176

Primary outcome(s)
Pharmacokinetic (PK) characteristics calculated from levels of CORT113176 measured using high-performance liquid chromatography (HPLC) analysis of blood samples collected throughout the trial between screening and day 7

Key secondary outcome(s))
1. Participant-identified adverse events assessed by questionnaire throughout the trial between screening and day 7
2. Other safety events identified by standard Phase I facility monitoring (blood test, clinical laboratory tests, urine samples, safety labs, ECG and physical examination findings) throughout the trial between screening and day 7

Completion date
21/05/2022

Eligibility

Key inclusion criteria
1. Healthy male subjects or non-pregnant, non-lactating healthy female subjects of non-childbearing potential (women of non-childbearing potential, as defined in the clinical protocol)
2. Age 18 to 60 years at the time of signing informed consent
3. Body mass index of 18.0 to 30.0 kg/m² as measured at screening
4. Weight of ≤102 kg at screening
5. Must be willing and able to communicate and participate in the whole study
6. Must provide written informed consent
7. Must agree to adhere to the contraception requirements defined in the clinical protocol

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
35

Key exclusion criteria
1. Subjects who have received any investigational medicinal product (IMP) in a clinical research study within the 90 days before the first dose in this study, or less than 5 elimination half-lives prior to the first dose, whichever is longer
2. Subjects who are, or are immediate family members of, a study site or Sponsor employee
3. Subjects who have previously been administered IMP in this study.
4. Evidence of current SARS-CoV-2 infection or required to self-isolate in accordance with current government guidelines
5. History of any drug or alcohol abuse in the past 2 years
6. Regular alcohol consumption in male subjects >21 units per week and 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)
7. A confirmed positive alcohol breath test at screening or admission
8. Current smokers and those who have smoked within the last 6 months before the first dose in this study. A confirmed breath carbon monoxide (CO) reading of greater than 10 ppm at screening or admission
9. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 6 months before the first dose in this study
10. Female subjects of childbearing potential including those who are pregnant or lactating (all female subjects must have a negative pregnancy test at screening and admission). A woman is considered of childbearing potential unless she is permanently sterile (hysterectomy, bilateral salpingectomy and/or bilateral oophorectomy) or is postmenopausal (had no menses for 12 months without an alternative medical cause and a serum follicle-stimulating hormone concentration ≥40 IU/L).
11. Male subjects with pregnant or lactating partners
12. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the Investigator or delegate at screening
13. Clinically significant abnormal clinical chemistry, haematology or urinalysis as judged by the Investigator. Subjects with Gilbert's syndrome are allowed
14. Confirmed positive drugs of abuse test result
15. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) results
16. Subject has active renal and/or hepatic disease, as evidenced by:
16.1. An estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m^2 using Modification of Diet in Renal Disease (MDRD) equation at screening
16.2. ALT and/or AST >1.5 times the upper limit of normal at screening or on admission
16.3. Subjects with borderline results can have these tests repeated once
17. History of clinically significant cardiovascular, renal, hepatic, endocrine, metabolic, respiratory, gastrointestinal (GI), neurological or psychiatric disorder, as judged by the Investigator
18. Subject had any form of cancer within the 5 years before the 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
19. Subject has a history and/or symptoms of adrenal insufficiency
20. 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
21. 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
22. Subjects with a QTcF interval of >450 msec at screening or baseline (before the first dose of study medication), based on the mean of three ECGs
23. History of additional risk factors for torsades de pointes (e.g., heart failure, hypokalaemia, family history of long QT syndrome)
24. Supine heart rate (HR) at rest of <40 bpm or >100 bpm. 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). Heart rate and BP can be retested twice in the supine position at intervals of 5 min on a given day at screening and admission.
25. Serious adverse reaction or serious hypersensitivity to any drug or the formulation excipients
26. Donation or loss of greater than 400 ml of blood or plasma within the previous 3 months

Date of first enrolment
17/03/2022

Date of final enrolment
17/05/2022

Locations

Countries of recruitment
United Kingdom

England

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

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 the study being a phase I single-dose study in healthy volunteers to assess the pharmacokinetics of an investigational drug

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No