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A study in healthy volunteers to investigate how the test medicine, zavacorilant, is taken up by the body when given in different dose levels, with food and without food

Submission date
25/01/2024

Recruitment status
No longer recruiting

Registration date
21/03/2024

Overall study status
Completed

Last Edited
21/03/2024

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 zavacorilant (also known as CORT125329) for the potential treatment of neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS - also known as Motor Neurone Disease), Huntington's disease (HD), and Alzheimer's disease (AD). Neurodegenerative diseases occur when nerve cells in the brain, spinal cord or body lose function over time and ultimately die. These diseases affect millions of people worldwide. It's common for patients to have a higher level of cortisol (a steroid hormone produced by the adrenal gland), which is known to affect the nervous system. The test medicine reduces the effects of cortisol and has shown beneficial effects in a mouse model of ALS.
This study will compare side effects and blood levels in healthy volunteers after the test medicine is given with and without food (relative bioavailability) and at increasing dose levels.

Who can participate?
Healthy men and women who are unable to have a baby, aged 18 to 60 years

What does the study involve?
Six volunteers will receive two single doses of test medicine as capsules, one fasted and one fed. They'll stay in the clinic for up to 4 nights each dose, and take up to 7 weeks to finish the study.
Twelve volunteers will receive a single dose of test medicine as capsules, either fasted or fed. They'll stay in the clinic for up to 4 nights, and take up to 6 weeks to finish the study.
The researchers will collect blood and urine samples to complete safety tests and measure the amount of test medicine and one of its breakdown products (in blood).

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 neurodegenerative diseases such ALS, HD and AD will be of benefit to patients with these conditions.
Volunteers may experience side effects from the test medicine. Full information on possible side

effects is in the Participant Information Sheet and Informed Consent Forms (PIS/ICFs). There is always a risk of unexpected side effects or an allergic reaction. To mitigate the risk, the researchers will ensure that volunteers meet the entry criteria for the study and monitor volunteers closely throughout the study.
Our 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 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'll 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 researchers would ask permission to follow up 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, 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?
Quotient Sciences Limited (UK)

When is the study starting and how long is it expected to run for?
January 2024 to June 2024

Who is funding the study?
Corcept Therapeutics (USA)

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

Contact information

Type(s)
Public, Scientific

Contact name
Ms Hazel Hunt

Contact details

149 Commonwealth Drive
Menlo Park
United States of America
CA 94025
+1 (0)650 6882862
hhunt@corcept.com

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

Integrated Research Application System (IRAS)
1009209

Protocol serial number
CORT125329-142

Study information

Scientific Title
A Phase I pharmacokinetic assessment of zavacorilant softgel capsule formulation, including dose proportionality and food effect in healthy subjects

Acronym
QSC301567

Study objectives
1. To determine the exposure of zavacorilant following administration of zavacorilant softgel capsules at increasing dose levels, including relative bioavailability in the fed and fasted states.
2. To assess the exposure of a zavacorilant metabolite following administration of the zavacorilant softgel capsules.
3. To provide additional safety and tolerability information for zavacorilant.

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 08/03/2024, Health and Social Care Research Ethics Committee B (HSC REC B) (Unit 5, Lissue Industrial Estate West, Rathdown Walk, Moira Road, Lisburn, BT28 2RF, United Kingdom; +44 (0)28 9536 1400; recb@hscni.net), ref: 24/NI/0002

Primary study design
Interventional

Study design
Interventional single-centre open-labelled pharmacokinetic study including dose proportionality and food effect assessment

Study type(s)
Other

Health condition(s) or problem(s) studied
Neurological diseases including amyotrophic lateral sclerosis (ALS), Huntington’s disease (HD) and Alzheimer’s disease (AD)

Interventions
This is a part-randomized, uncontrolled trial. This three-cohort, healthy subject study aims to compare side effects and blood levels of the test medicine zavacorilant after being given with and without food (relative bioavailability), and at increasing dose levels. The study will take place at one non-NHS site and will consist of three cohorts of six healthy volunteers. In Cohort 1, subjects will be randomized to receive 250 mg zavacorilant once in the fed and once in the fasted state in a crossover manner over 2 periods. In Cohorts 2 and 3, subjects will receive up to 750 mg zavacorilant in either the fed or fasted state in a single period. For each period, subjects will be admitted to the clinical unit on the evening of Day -1, dosed in the clinical unit on Day 1 and discharged from the clinical unit on Day 4. For Cohort 1, there will be a minimum of 7 days between dosing occasions. Subject’s blood will be taken during the study for analysis of the test medicine and one of its breakdown products. The subject’s blood and urine will also be collected for safety testing. Subjects are expected to be involved in this study for approximately 6-7 weeks from screening to final discharge.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)
Pharmacokinetic (PK) parameters for zavacorilant measured using plasma samples, including but not limited to: Tmax, Cmax, AUC(0-last), AUC(0-inf), and T1/2, collected from days 1 to 4 at each period

Key secondary outcome(s)
1. PK parameters for a zavacorilant metabolite measured using plasma samples, including but not limited to: Tmax, Cmax, AUC(0-last), AUC(0-inf), and T1/2, collected from days 1 to 4 at each period

2. Safety and tolerability evaluated by assessment of adverse events (AEs), vital signs, electrocardiograms (ECGs), physical examinations and laboratory safety tests from signing informed consent to the follow-up phone call

Completion date
04/06/2024

Eligibility

Key inclusion criteria
Informed Consent and Compliance:
1. Must provide written informed consent
2. Must be willing and able to communicate and participate in the whole study

Demographics and Contraception:
3. Aged 18 to 60 years inclusive at the time of signing informed consent
4. Must agree to adhere to the contraception requirements defined in the Clinical Protocol

Baseline Characteristics:
5. Healthy male subjects and healthy female subjects of non-childbearing potential according to the assessment of the Investigator, as based on a complete medical history including a physical examination, vital signs, 12-lead ECG, and clinical laboratory tests without any clinically significant abnormalities.
6. Body mass index (BMI) of 18.0 to 30.0 kg/m2 as measured at screening
7. Weight 50-102 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
Medical/Surgical History and Mental Health:
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 GI disease, neurological or psychiatric disorder, as judged by the Investigator. Gilbert's syndrome is not permitted.
4. Subjects with a history of cholecystectomy or gallstones

Physical Examination:
5. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the Investigator or delegate at screening

Diagnostic Assessments:
6. Clinically significant abnormal clinical chemistry, haematology or urinalysis as judged by the Investigator (laboratory parameters are listed in the protocol). Subjects with Gilbert's Syndrome are allowed.
7. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results
8. Evidence of renal impairment as indicated by:
8.1. An estimated glomerular filtration rate (eGFR) of <80 mL/min/1.73m2 using the Modification of Diet in Renal Disease (MDRD) at screening
8.2. ALT and/or AST >1.5 times the upper limit of normal at screening
9. Female subjects of childbearing potential including those who are pregnant or lactating (all female subjects must have a negative highly sensitive 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 [FSH] concentration ≥40 IU/L)
10. Clinically significant ECG abnormalities or vital sign abnormalities at screening or baseline (pre-first dose of IMP) including but not limited to:
10.1. QTcF > 450 msec based on a single ECG at screening and pre-(first) dose
10.2. Supine heart rate (HR) at rest of 40-100 bpm at screening and pre-(first) dose
10.3. BP outside the following ranges: diastolic BP 40-90 mmHg; systolic BP 90-140 mmHg at screening or before the first dose
10.4. ECGs and HR and BP can be retested twice in the supine position at intervals of approximately 5 minutes on a given day

Prior Study Participation:
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. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood

Prior and Concomitant Medication:
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 the first IMP administration. Exceptions may apply, as determined by the Investigator and agreed by the Sponsor, if each of the following criteria are met: medication with a short half-life if the washout is such that no pharmacodynamic activity is expected by the time of dosing with IMP; the use of medication does not jeopardise the safety of the trial subject; and the use of medication is not considered to interfere with the objectives of the study.
14. Subjects who are currently using glucocorticoids or have a history of systemic glucocorticoid agonist use at any dose within the last 12 months or 3 months for inhaled products before the first dose of IMP. Subjects who have received up to two single doses of a glucocorticoid in another study more than 3 months before the first dose of study medication will not be excluded from taking part in the study.

Lifestyle Characteristics:
15. History of any drug or alcohol abuse in the past 2 years
16. 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)
17. A confirmed positive alcohol breath test at screening or admission
18. Current smokers and those who have smoked within the last 12 months
19. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
20. A confirmed breath carbon monoxide reading of greater than 10 at screening or admission
21. Confirmed positive drugs of abuse test result (drugs of abuse tests are listed in the protocol) at screening or admission

Other:
22. Male subjects with pregnant or lactating partners
23. Subjects who are, or are immediate family members of, a study site or Sponsor employee
24. Failure to satisfy the Investigator of fitness to participate for any other reason

Date of first enrolment
27/03/2024

Date of final enrolment
04/06/2024

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

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

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