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A two-part study in healthy volunteers to investigate the feasibility of a combined test medicine formulation

Submission date 17/06/2026	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 29/06/2026	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 29/06/2026	**Condition category** Other	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
The Sponsor is developing a combination product of the test medicines, 5-Hydroxytryptophan [5-HT] and Carbidopa, for the potential treatment of depression not responding adequately to available first-line treatments. The study will try to identify the pharmacokinetic profile (the level of test medicine in the blood) of the test medicine. It will also try to determine the dose of test medicines to use in the next stage of clinical trials. Safety and tolerability of the test medicines alone or in combination will also be assessed.

Who can participate?
Male and female volunteers aged between 18 and 60 years old.

What does the study involve?
This study will take place at 1 trial location in Nottingham, enrolling 28 participants (12 in Part 1 and 16 in Part 2).

Part 1 includes 5 study periods and volunteers will receive different doses and combination of doses of the test medicines on Day 1 of each period. Volunteers will be discharged 36 hours post-first dose (Day 2). There will be a minimum washout period of 7 days between the last dose in each period. After the final period volunteers will receive a follow-up telephone call 7 to 10 days post-final dose to check their continued well-being.

Part 2 includes 5 study periods and volunteers will receive radiolabelled test medicine and a radiolabelled drink for scintigraphy images to be taken, to identify where the test medicine is in the body. Volunteers will be discharged 36 hours post-dose (Day 2). There will be a minimum washout period of 7 days between the last dose in each period. After the final period volunteers will receive a follow-up telephone call 7 to 10 days post-final dose to check their continued well-being.

Volunteers' blood and urine will be taken throughout the study for analysis of the test medicine and for their safety. Volunteers are expected to be involved in this study for approximately 15 weeks from the screening visit until the follow up phone call.

What are the possible risks and benefits of participating?
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 depression will be of benefit to patients with this condition.

As this is a Phase I study, the most relevant population is healthy volunteers, and it is considered that the risk/benefit evaluation supports this. Females of childbearing potential (non-pregnant or lactating) will be allowed to participate as long as they comply with the contraception requirements detailed in the clinical protocol. 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.

In Part 2, volunteers will be exposed to 1.8 millisieverts (mSv) of radioactivity, which is equivalent to about 8 months of the average radiation exposure received in the UK each year (2.7 mSv). That amount of radiation poses negligible risk to the volunteers' health.

Volunteers may experience side effects from the test medicines in this study. Full information on possible side effects is provided to volunteers in the Participant Information Sheet and Informed Consent Forms. There is always a risk of unexpected side effects or an allergic reaction. To mitigate the risk, we'll ensure that volunteers meet the entry criteria for the study and monitor volunteers closely throughout the study.

There may be an extended period of fasting for the volunteers taking part in this study. To ensure an adequate fluid intake, the volunteers will be allowed ad libitum fluids and will be monitored for signs of dehydration and fatigue.

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.

As the test medicines act on the brain and nervous system, they may have an effect on the volunteers' mental health. So, we will assess volunteers at screening and after dosing using the Columbia-Suicide Severity Rating Scale (C-SSRS) questionnaire.

When given in large quantities, i.e. when given as a bolus dose, the test medicines (as powder for oral solution) may have an unpleasant taste. To mask this taste volunteers will be given a Listerine® Strip immediately prior to administration of the test medicines as a bolus.

Where is the study run from?
Evecxia Therapeutics Inc. (USA)

When is the study starting and how long is it expected to run for?
March 2020 until August 2021

Who is funding the study?
Evecxia Therapeutics Inc. (USA)

Who is the main contact?
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Contact information

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Public, Scientific

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EU Clinical Trials Register (EudraCT)
2019-004678-25

Integrated Research Application System (IRAS)
276262

Sponsor study code
EVX101-101

CRO study code
QSC201140

Study information

Scientific Title
A two-part study to evaluate the proof of concept of gastro-retentive formulation viability for a 5-Hydroxytryptophan/Carbidopa combination product and a pharmacoscintigraphic assessment of 5-Hydroxytryptophan/Carbidopa gastro-retentive formulation prototypes in healthy subjects

Study objectives
The trial will meet the following primary and secondary objectives:

Primary objectives - Part 1
1. To evaluate the pharmacokinetic (PK) profile of 5-hydroxytryptophan (5-HTP) and carbidopa, when 5-HTP Powder for Oral Solution and Carbidopa Powder for Oral Solutions are co administered as a sipping regimen (mimicking sustained release delivery)
2. To determine the 5-HTP Powder for Oral Solution dose which gives the desired 5 HTP exposure as a sipping regimen
3. To determine the Carbidopa Powder for Oral Solution dose which gives the desired 5-HTP exposure as a sipping regimen
4. To determine the 5-HTP:carbidopa ratio that provides at least a 200% or higher increase in 5-HTP plasma exposure compared with 5 HTP alone
Primary objectives - Part 2
1. To evaluate the in vivo gastroretentive (GR) properties of 5 HTP/carbidopa GR prototype tablet formulations using scintigraphic methods in the fed state after a high-fat meal
2. To evaluate the PK of 5-HTP/carbidopa GR prototype tablet formulations in the fed state after a high-fat meal

Secondary objectives - Part 1
1. To assess the safety and tolerability of 5-HTP when administered alone or in combination with carbidopa as a sipping regimen
2. To investigate the PK of 5-HTP Powder for Oral Solution and Carbidopa Powder for Oral Solution co-administered as a sipping regimen in the fed versus fasted state (optional)
3. To assess the relative bioavailability of 5-HTP and carbidopa co-administered as sustained release delivery (as mimicked by the sipping schedule) vs the immediate release (IR) administration, ie the entire 5-HTP dose and carbidopa administered at the same time as a bolus (optional)
Secondary objectives - Part 2
1. To determine the GR properties of a selected 5-HTP/carbidopa GR prototype tablet formulation when administered with a meal of alternative composition
2. To provide additional information on the safety and tolerability of 5-HTP/carbidopa GR prototype tablet formulations

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 24/02/2020, Wales Research Ethics Committee 2 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 2920 785 738; Wales.REC2@wales.nhs.uk), ref: 20/WA/0031

Primary study design
Interventional

Allocation
N/A: single arm study

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Sequential

Purpose
Formulation development

Study type(s)

Health condition(s) or problem(s) studied
Healthy volunteers

Interventions
In Part 1 volunteers receive reconstituted 5-HTP powder for oral solution alone in a sipping regimen split into 10 equal doses administered over 9 hours on one occasion, in combination with reconstituted carbidopa powder for oral solution in a sipping regimen split into 10 equal doses administered over 9 hours on 3 occasions, and reconstituted 5-HTP powder for oral solution alone administered as a single dose on one occasion. Doses are 250 mg 5-HTP alone and range from 250 mg/0.625 mg to 250 mg/10 mg 5-HTP/carbidopa.

In Part 2 volunteers receive radiolabelled 5-HTP/carbidopa gastro retentive (GR) prototype tablet as a single dose on 5 separate occasions. Doses range from 250 mg/0.625 mg to 250 mg /15 mg 5-HTP/carbidopa, radiolabelled with not more than (NMT) 1 MBq 111In.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
5-HTP powder for oral solution, Carbidopa powder for oral solution, Radiolabelled 5-HTP /carbidopa gastro retentive (GR) prototype tablet

Primary outcome(s)
1. Part 1: Measurement of the appropriate pharmacokinetic (PK) parameters of 5-HTP and carbidopa following administration of 5-HTP Powder for Oral Solution and Carbidopa Powder for Oral Solution in a sipping regimen including but not limited to: Tmax, Cmax, AUC(0-last), AUC(0 inf) and T1/2 measured using analysis of plasma samples at timepoints from pre-dose until 36 hours post-dose

2. Part 1: Measurement of Frel (exposure) of 5 HTP at different dose levels based on Cmax, AUC (0 last) and AUC(0-inf) measured using analysis of plasma samples at timepoints from pre-dose until 36 hours post-dose

3. Part 1: Measurement of Frel (exposure) of 5 HTP at different dose levels of carbidopa based on Cmax, AUC(0-last) and AUC(0-inf) measured using analysis of plasma samples at timepoints from pre-dose until 36 hours post-dose

4. Part 1: Measurement of Frel (exposure) of 5-HTP at different 5-HTP:carbidopa ratios based on Cmax, AUC(0-last) and AUC(0-inf) measured using analysis of plasma samples at timepoints from pre-dose until 36 hours post-dose

5. Part 2: A comparison of the in vivo transit and disintegration of 5-HTP/carbidopa GR prototype tablet formulations by measuring the following scintigraphic parameters: last time in stomach, gastric emptying (GE), small intestinal transit, colon arrival (CA), time and location of initial tablet disintegration (ITD) and complete tablet disintegration (CTD) measured using analysis of scintigraphic images at timepoints from immediately after dosing until 24 hours post-dose

6. Part 2: Measurement of the appropriate PK parameters of 5-HTP and carbidopa following administration of 5-HTP/carbidopa GR prototype tablet formulations including but not limited to: Tmax, Cmax, AUC(0-last), AUC(0 inf) and T1/2 measured using analysis of plasma samples at timepoints from pre-dose until 36 hours post-dose

Key secondary outcome(s)

1. Part 1: Safety and tolerability measured using incidence of adverse events (AEs), and assessment of physical examinations, safety laboratory tests, vital signs, and electrocardiograms (ECGs) at timepoints from written informed consent until discharge from the study at the final follow up call or unscheduled follow-up visit

2. Part 1: Comparison of the PK parameters AUC(0 last), AUC(0-inf) and Cmax of 5 HTP and carbidopa in the fed state versus fasted state (optional) measured using analysis of plasma samples at timepoints from from pre-dose until 36 hours post-dose

3. Part 1: Measurement of Frel of the sustained release delivery (as mimicked by the sipping schedule) vs the IR administration of 5 HTP and carbidopa, based on Cmax, AUC(0-last) and AUC (0-inf) (optional) measured using analysis of plasma samples at timepoints from pre-dose until 36 hours post-dose

4. Part 2: A comparison of the in vivo transit and disintegration of 5-HTP/carbidopa GR prototype tablet formulations by measuring the following: scintigraphic parameters – last time in stomach, GE, small intestinal transit, CA, time and location of ITD, and CTD; PK parameters - Tmax, Cmax, AUC(0-last), AUC(0 inf) and T1/2 measured using analysis of scintigraphic images at timepoints from immediately after dosing until 24 hours post-dose

5. Part 2: Safety and tolerability measured using incidence of AEs, and assessment of physical examinations, safety laboratory tests, vital signs, and ECGs. at timepoints from written informed consent until discharge from the study at the final follow up call or unscheduled follow-up visit

Completion date

31/08/2021

Eligibility

Key inclusion criteria
1. Healthy males or healthy females of non-childbearing potential
2. Age 18 to 60 years (Part 1) or 30 to 60 years (Part 2) of age at the time of signing informed consent
3. Body mass index (BMI) of 18.0 to 32.0 kg/m² inclusive, and a body weight of at least 50 kg at screening
4. Must be willing and able to communicate and participate in the whole study
5. Must provide written informed consent
6. Must agree to adhere to the contraception requirements defined in the clinical protocol

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
All

Total final enrolment
28

Key exclusion criteria
1. Subjects who have received any IMP in a clinical research study within the 90 days prior to Day 1
2. Subjects who are study site employees, or immediate family members of a study site or sponsor employee
3. History of any drug or alcohol abuse in the past 2 years
4. Regular alcohol consumption in males >21 units per week and females >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)
5. A confirmed positive alcohol breath test at screening or admission
6. Current smokers and those who have smoked within the last 12 months. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or admission
7. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
8. Females of childbearing potential including those who are pregnant or lactating (all female subjects must have a negative serum pregnancy test at screening and a negative urine pregnancy test at each admission). A woman is considered of childbearing potential unless she is permanently sterile (hysterectomy, bilateral salpingectomy, and 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). Bilateral tubal ligation

/occlusion is not considered a form of permanent sterilisation
9. Subjects with pregnant partners
10. Part 2 only: 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 (not applicable for Part 1)
11. Subjects who do not have suitable veins for multiple venepunctures/cannulation 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 allowed
13. Confirmed positive drugs of abuse test result
14. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) results
15. Presence or history of clinically significant cardiovascular, renal, hepatic, respiratory disease, neurological or psychiatric disorder, or other significant diseases as judged by the investigator
16. Presence of history of any GI disease including peptic ulceration, GI bleeding, ulcerative colitis, Crohn's Disease or Irritable Bowel Syndrome
17. Part 2 only: History of clinically relevant GI surgery (with the exception of appendectomy unless it was performed within the previous 12 months; not applicable for Part 1)
18. Acute diarrhoea or constipation in the 7 days before the predicted Day 1. If screening occurs >7 days before the 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
19. Subjects must be able to eat 90% of the FDA-approved high-fat breakfast, including bacon, in order to be eligible for dosing
20. Subjects with a history of cholecystectomy or gall stones
21. Subject answers "yes" to "Suicidal Ideation" Items 1 or 2 on the Columbia-Suicide Severity Rating Scale (C-SSRS) at screening
22. Serious adverse reaction or serious hypersensitivity to any drug (including serotonergic drugs such as anti-depressants and migraine medication) or the formulation excipients
23. Subjects who are taking, or have taken, any prescribed or over-the-counter drug or herbal remedies including medications used to treat depression, anxiety, bipolar disorder and schizophrenia (serotonergic drugs such as antidepressants, lithium, anticonvulsants, antipsychotics, anti-epileptics and anxiolytics) (other than 4 g of paracetamol per day) in the 14 days before IMP administration. Hormone replacement therapy is not permitted. Exceptions may apply on a case by case basis, if considered not to interfere with the objectives of the study, as determined by the PI
24. Presence or history of clinically significant allergy requiring treatment, as judged by the investigator. Hay fever is allowed unless it is active
25. Donation or loss of greater than 400 mL of blood within the previous 3 months
26. Evidence of current SARS-CoV-2 infection
27. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
06/03/2020

Date of final enrolment
31/08/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way, Ruddington Fields
Ruddington, Nottingham
England
NG11 6JS

Sponsor information

Organisation
Evecxia Therapeutics Inc.

Funder(s)

Funder type

Funder Name
Evecxia Therapeutics Inc.

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available