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A study in healthy volunteers to look at how the test medicine, COMP360, is taken up by the body when given as two different strength capsules

Submission date
18/06/2022

Recruitment status
No longer recruiting

Registration date
09/08/2022

Overall study status
Completed

Last Edited
18/10/2022

Condition category
Mental and Behavioural Disorders

[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, COMP360, for the potential treatment of treatment-resistant depression. Depression is a common mental health problem that can cause people to experience low mood, loss of motivation or pleasure, feelings of guilt or low self-worth, disturbed sleep, changes in appetite, and low energy, and concentration. Patients with treatment-resistant depression see no improvement in their symptoms with standard depression medication.

Who can participate?
Healthy male/female volunteers aged between 18 to 55 years old

What does the study involve?
This two-period healthy volunteer study will try to identify how the test medicine is taken up by the body when given at the same dose in different strengths, as well as the safety and tolerability of the test medicine.

Volunteers will receive both of the following treatments, one at each of the study visits in a random order (either test then reference or reference then test): 25 mg COMP360 given as 1 x 25 mg capsule (test regimen) or 25 mg COMP360 given as 5 x 5 mg capsules (reference regimen).

In Treatment Period 1, at least 14 volunteers will receive an oral dose of COMP360 25 mg, either as a single capsule or as multiple capsules in a fed state. Volunteers will be discharged on Day 2 and have a washout period of 14 days before returning for the next study period.

In Treatment Period 2, at least 14 volunteers will receive an oral dose of COMP360 25 mg, either as a single capsule or as multiple capsules in a fed state. Volunteers will be discharged on Day 2 and will receive a follow-up call 5-11 days post final dose.

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 up to 8 weeks from screening to the follow-up call.

What are the possible benefits and risks 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 treatment-resistant 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 the risk/benefit evaluation in this study supports the use of healthy volunteers. Females of childbearing potential (non-pregnant or lactating) will be allowed to participate as long as they comply with the contraception requirements.
There is 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.
There is 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 and/or the reference product in this study. Full information on possible side effects is provided in the PIS/ICF.
There will be two overnight periods of fasting in this study of at least 10 hours before a light meal is provided prior to each dosing. Water will be allowed ad libitum except for 1 hour before and after dosing, and food can be eaten four hours after doing. Healthy volunteers will be monitored for signs of dehydration and fatigue.
Collection of blood samples during the study 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 chests and limbs may cause some local irritation and be uncomfortable to remove but healthy volunteers will be closely monitored to ensure any local irritation does not persist.
As the test medicine is CNS acting with psychedelic effects and may have an effect on healthy volunteers' mental health, the medicine will be administered alongside therapist psychological support. Questionnaires and scales will be used to regularly monitor these effects during the study and rescue medications will be available, if required. The questionnaire and scales will be performed by an appropriately trained physician.

Where is the study run from?
COMPASS Pathfinder Limited (United Kingdom)

When is the study starting and how long is it expected to run for?
June 2022 to January 2023

Who is funding the study?
COMPASS Pathfinder Limited (United Kingdom)

Who is the main contact?
1. Dr Guy Goodwin (Scientific) (United Kingdom)
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2. Ms Zainib Shabir (Public) (United Kingdom)
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Contact information

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Integrated Research Application System (IRAS)
1005916

Protocol serial number
COMP105

Study information

Scientific Title
A phase I, open-label, randomised-sequence, two-way crossover study to assess the relative oral bioavailability of 25 mg and 5 mg strength capsules of COMP360 in healthy volunteers

Acronym
QSC207869

Study objectives
1. To assess the relative oral bioavailability (the proportion of the test medicine taken up by the body when given in two forms) of a single oral dose of COMP360 25 mg administered as a 1 × 25 mg capsule versus a single oral dose of COMP360 25 mg administered as 5 × 5 mg capsules in healthy volunteers
2. To compare the pharmacokinetics (what the body does to the test medicine, PK) of a single oral dose of COMP360 25 mg administered as a 1 × 25 mg capsule versus a single oral dose of COMP360 25 mg administered as 5 × 5 mg capsules in healthy volunteers
3. To compare the safety and tolerability of a single oral dose of COMP360 25 mg administered as a 1 × 25 mg capsule versus a single oral dose of COMP360 25 mg administered as 5 × 5 mg capsules in healthy volunteers

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/08/2022, North East - York Research Ethics Committee (Room 002, TEDCO Business Centre, Viking Industrial Park, Jarrow, NE32 3DT, United Kingdom; +44 (0)2071048057; york.rec@hra.nhs.uk), ref: 22/NE/0106

Primary study design
Interventional

Study design
Phase I open-label randomized-sequence two-way crossover study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Treatment-resistant depression

Interventions
Volunteers will receive both of the following treatments, one at each of the study visits in a random order (either test then reference or reference then test): 25 mg COMP360 given as 1 x

25 mg capsule (test regimen) or 25 mg COMP360 given as 5 x 5 mg capsules (reference regimen), in the fed state.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
COMP360

Primary outcome(s)
1. Plasma PK parameters for psilocin, measured by analysing blood samples taken on the day of dosing for a 24-hour period, in both treatment periods, as per the clinical protocol:
1.1. Peak exposure of psilocin (Cmax)
1.2. Area under the concentration-time curve from zero to 24 hours (AUC0-24h) of psilocin
1.3. Area under the concentration-time curve from zero to infinity (AUC0-inf) of psilocin

Key secondary outcome(s)
The endpoints will be measured by analysing blood samples taken on the day of dosing for a 24-hour period, in both treatment periods, as per the clinical protocol
1. Plasma PK parameters for psilocin, psilocybin, 4-hydroxyindoleacetic acid (4-HIAA) and psilocin-O-glucuronide including:
1.1. Area under the concentration-time curve from zero to 24 hours (AUC0-24h)
1.2. Area under the concentration-time curve from zero to infinity (AUC0-inf)
1.3. Peak exposure (Cmax)
1.4. Time to reach peak exposure (tmax)
1.5. Time to the first measurable timepoint (tlag)
1.6. Elimination half-life (t1/2)
1.7. Last measurable concentration (Clast)
1.8. Apparent total clearance of the drug from plasma after oral administration (CL/F) (psilocybin only)
1.9. Apparent volume of distribution at terminal phase (Vd/F) (psilocybin only)

2. Safety endpoints measured via physical examinations and through psychiatric assessment questionnaires throughout the study, from screening (Day -28) until the follow-up phone call (up to 6 days post-dosing in period 2):
2.1. Adverse events (AEs)
2.2. Electrocardiogram (ECG)
2.3. Vital signs
2.4. Clinical laboratory tests
2.5. Suicidality assessed via the Columbia-Suicide Severity Rating Scale (C-SSRS)
2.6. Brief Psychiatric Rating Scale – positive symptoms subscale (BPRS+)

Completion date
04/01/2023

Eligibility

Key inclusion criteria

1. Signed ICF
2. Male or female aged between 18 and 55 years old at screening
3. Body mass index between 18.5 and 30.0 at screening
4. Weight ≥50 kg at screening
5. Non-smoker (including e-cigarettes) for at least 12 months prior to screening
6. Willing to comply with fasting and food intake requirements
7. Able to complete all protocol required assessments and agree to comply with all study visits

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 16/08/2022:
1. Current or clinically relevant history of any psychotic disorder, bipolar disorder, borderline personality disorder, major depression, panic disorder, post-traumatic stress disorder, generalised anxiety disorder, obsessive-compulsive disorder, or eating disorder, as assessed by a structured clinical interview (Mini International Neuropsychiatric Interview, Version 7.0.2 [MINI Version 7.0.2] and Mini International Neuropsychiatric Interview, Version 7.0.2 – Plus borderline personality module [MINI-Plus])
2. A history of suicide attempts, suicidal ideation or suicidal behaviour as determined by the C-SSRS at Screening or at Day 1; or clinical assessment of significant suicidal risk or risk of self-injury identified during participant interview
3. Satisfying diagnostic criteria for alcohol or substance use disorder, as determined by Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) (MINI 7.0.2) within 12 months prior to Screening
4. Use of pharmacological compounds for psychiatric or neurological conditions acting on the central nervous system within 30 days (or five half-lives, whichever is longer) prior to Screening
5. In first-degree relatives, a history of psychotic disorders or mood disorders, including bipolar disorders and depressive disorders
6. Other personal circumstances or behaviour judged by the investigator to be incompatible with the establishment of rapport or the safe exposure to COMP360
7. Exposure to psilocybin or any other psychedelics, such as ayahuasca, mescaline, LSD, or peyote within 12 months prior to Screening. Additionally, participants must agree not to use psychedelics other than COMP360 for the duration of the study.
8. Pregnancy, lactating or planning a pregnancy
9. Engagement in sexual intercourse which could result in pregnancy, must agree to use a highly effective contraceptive method throughout their participation in the study and for 3 months after their final COMP360 administration. Participants of childbearing potential must have a negative serum pregnancy test at Screening, and a negative urine pregnancy test the day prior

to COMP360 administration (Day -1 of each treatment period).
10. Participants should be informed not to donate eggs for the duration of the study period and for 30 days after their final COMP360 administration, or to donate sperm for the duration of the study period, and for at least three months after their final COMP360 administration
11. Cardiovascular conditions:
11.1. Lifetime history of stroke
11.2. Lifetime myocardial infarction
11.3. Clinically significant arrhythmia (<1 year prior to signing the ICF) or tachycardia (resting heart rate over 100 beats per minute)
11.4. Blood pressure >140/90 mmHg at screening or prior to COMP360 administration on Day 1, following triplicate readings
11.5. Elongated QT interval corrected by Fridericia (QTcF; interval >450 msec for men and >470 msec for women) at screening or prior to COMP360 administration on Day 1, following triplicate readings.
12. Type 1 diabetes mellitus or uncontrolled type 2 diabetes mellitus (defined by haemoglobin A1c [HbA1c] >8% at Screening) or a history of diabetic ketoacidosis, hyperglycaemic coma, or severe hypoglycaemia with loss of consciousness (<3 months prior to signing of ICF)
13. Seizure disorder
14. Recent substance use within the last month (excluding alcohol), such as but not limited to cannabis, cocaine, ketamine, opiates, MDMA, and psilocybin, or a confirmed positive urine drugs screen for illicit substances or drugs of abuse at screening and/or Day 1
15. Current enrolment in any investigational drug or device study, or participation in such within 90 days or five half-lives (whichever is longer) of screening
16. Abnormal and clinically significant results on the physical examination or laboratory tests at screening or Day -1; the vital signs or ECG at screening or Day 1, that in the investigator's opinion may constitute a risk for an individual who is exposed to COMP360
17. Any other clinically significant cardiovascular, pulmonary, gastrointestinal, hepatic, renal or any other major concurrent illness that, in the opinion of the investigator, may interfere with the interpretation of the study results or constitute a health risk for the participant if they take part in the study
18. Participants with aspartate aminotransferase, alanine aminotransferase, gammaglutamyl transferase or total bilirubin levels >1.5 x the upper limit of normal at Screening or Day -1. These laboratory evaluations may be repeated once at the discretion of the investigator. If the repeat test is <1.5 x the upper limit of normal, the participant may be included only if the investigator considers that the previous finding will not introduce additional risk factors and will not interfere with interpretation of safety data.
19. Positive test for hepatitis B surface antigen (HBsAg), anti-hepatitis C antibody (anti HCV) or known human immunodeficiency virus I and II (anti-HIV I/II) at Screening
20. Intake of >21 units of alcohol weekly in males and >14 units of alcohol weekly in females, consumption of alcohol within 48 hours of Screening, or from within 48 hours of Day -1 of each treatment period. One unit is equivalent to half a pint of beer or one 25 mL measure of 40% spirits, 1.5 to 2 units is equivalent to one125 mL glass of wine.
21. Habitual and heavy consumption of caffeinated beverages (>8 cups of coffee or equivalent per day) at Screening; and/or unable to refrain from use of (methyl) xanthine (eg coffee, tea, cola, chocolate) for 48 hours prior to, and for the duration of, each residential study visit
22. Use of any prescription or non-prescription medications, including herbal and nutritional supplements, or over-the-counter medications (eg ibuprofen, aspirin) within 15 days or five half-lives (whichever is longer) of first COMP360 administration and throughout the study. By exception, the participant may take paracetamol (≤2 g/day for up to 48 hours prior to first dosing) and oral contraceptives.
23. COVID-19 vaccination within seven days of first COMP360 administration
24. Donation of blood or plasma of >400 mL within three months prior to first COMP360

administration until four weeks after final COMP360 administration
25. Hypersensitivity to the investigational product or any of the excipients
26. Presence or history of clinically significant allergy requiring treatment, as judged by the investigator. Hay fever is allowed unless it is active.
27. Participants who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at Screening
28. Evidence of current SARS-CoV-2 infection or residual symptoms from a previous infection Screening or Day -1 of each treatment period
29. A confirmed positive alcohol breath test at Screening or Day -1 of each treatment period
30. A confirmed positive urine cotinine test at Screening or Day -1 of each treatment period
31. Participants who are, or are immediate family members of, a study site or sponsor employee
32. Failure to satisfy the investigator of fitness to participate for any other reason

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Previous exclusion criteria:
1. Current or clinically relevant history of any psychotic disorder, bipolar disorder, borderline personality disorder, major depression, panic disorder, post-traumatic stress disorder, generalised anxiety disorder, obsessive-compulsive disorder, or eating disorder, as assessed by a structured clinical interview (Mini International Neuropsychiatric Interview, Version 7.0.2 [MINI Version 7.0.2] and Mini International Neuropsychiatric Interview, Version 7.0.2 – Plus borderline personality module [MINI-Plus])
2. A history of suicide attempts, suicidal ideation or suicidal behaviour as determined by the C-SSRS at Screening or at Day 1; or clinical assessment of significant suicidal risk or risk of self-injury identified during participant interview
3. Satisfying diagnostic criteria for alcohol or substance use disorder, as determined by Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) (MINI 7.0.2) within 12 months prior to Screening
4. Use of pharmacological compounds for psychiatric or neurological conditions acting on the central nervous system within 30 days (or five half-lives, whichever is longer) prior to Screening
5. In first-degree relatives, a history of psychotic disorders or mood disorders, including bipolar disorders and depressive disorders
6. Other personal circumstances or behaviour judged by the investigator to be incompatible with the establishment of rapport or the safe exposure to COMP360
7. Exposure to psilocybin or any other psychedelics, such as ayahuasca, mescaline, LSD, or peyote within 12 months prior to Screening. Additionally, participants must agree not to use psychedelics other than COMP360 for the duration of the study.
8. Pregnancy, lactating or planning a pregnancy
9. Engagement in sexual intercourse which could result in pregnancy, must agree to use a highly effective contraceptive method throughout their participation in the study and for 3 months after their final COMP360 administration. Participants of childbearing potential must have a negative serum pregnancy test at Screening, and a negative urine pregnancy test the day prior to COMP360 administration (Day -1 of each treatment period).
10. Participants should be informed not to donate eggs for the duration of the study period and for 30 days after their final COMP360 administration, or to donate sperm for the duration of the study period, and for at least three months after their final COMP360 administration
11. Cardiovascular conditions:
11.1. Lifetime history of stroke
11.2. Lifetime myocardial infarction
11.3. Clinically significant arrhythmia (<1 year prior to signing the ICF) or tachycardia (resting heart rate over 100 beats per minute)
11.4. Blood pressure >140/90 mmHg at screening or prior to COMP360 administration on Day 1,

following triplicate readings
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12. Type 1 diabetes mellitus or uncontrolled type 2 diabetes mellitus (defined by haemoglobin A1c [HbA1c] >8% at Screening) or a history of diabetic ketoacidosis, hyperglycaemic coma, or severe hypoglycaemia with loss of consciousness (<3 months prior to signing of ICF)
13. Seizure disorder
14. Recent substance use within the last month (excluding alcohol), such as but not limited to cannabis, cocaine, ketamine, opiates, MDMA, and psilocybin, or a confirmed positive urine drugs screen for illicit substances or drugs of abuse at screening and/or Day 1
15. Current enrolment in any investigational drug or device study, or participation in such within 90 days or five half-lives (whichever is longer) of screening
16. Abnormal and clinically significant results on the physical examination or laboratory tests at screening or Day -1; the vital signs or ECG at screening or Day 1, that in the investigator's opinion may constitute a risk for an individual who is exposed to COMP360
17. Any other clinically significant cardiovascular, pulmonary, gastrointestinal, hepatic, renal or any other major concurrent illness that, in the opinion of the investigator, may interfere with the interpretation of the study results or constitute a health risk for the participant if they take part in the study

Date of first enrolment
24/10/2022

Date of final enrolment
29/12/2022

Locations

Countries of recruitment
United Kingdom

England

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Sponsor information

Organisation
COMPASS Pathfinder Limited

Funder(s)

Funder type
Industry

Funder Name
COMPASS Pathfinder Limited

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 full datasets being commercially sensitive and potentially used to support marketing authorisation applications.

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