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A study in healthy male volunteers to investigate how the test medicine COMP360 [14C]-psilocybin is taken up, broken down and removed from the body

Submission date
20/07/2024

Recruitment status
No longer recruiting

Registration date
18/09/2024

Overall study status
Completed

Last Edited
27/01/2025

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, low energy and concentration. Patients with treatment-resistant depression see no improvement in their symptoms with standard depression medication. In this study, healthy 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' - it will contain a small amount of radioactivity (Carbon-14) - so that we can track it in the body. This study on healthy volunteers aims to answer whether the test medicine causes any important side effects, how much test medicine enters the bloodstream and how quickly the body gets rid of it.

Who can participate?
Healthy male volunteers aged 30-55 years old

What does the study involve?
This study will take place at one non-NHS site in Nottingham. Volunteers will receive a single dose of radiolabelled test medicine, in a capsule by mouth. They will stay in the clinic for up to 10 nights and take up to 5 weeks to finish the study. During the study blood and urine samples will be collected to do safety tests. Over at least 8 days, many blood samples will be taken and volunteers will collect all their urine and faeces so that we can measure the amount of test medicine and its breakdown products.

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 treatment-resistant depression will be of benefit to patients with this condition.

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 Form. 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.

As the test medicine is CNS acting with psychedelic effects and may have an effect on healthy volunteer's 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.

Volunteers will be exposed to 3.8 milliSieverts (mSv) of radioactivity during the study, which is equivalent to about 17 months' exposure to average background radiation in the UK (2.7 mSv). This equates to the radiation dose that would result from 2.5 CT scans of the head (1.6 mSv each). That amount of radiation poses negligible risk to the volunteers' health but volunteers should not take part in this study if they have had 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.

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 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'll be allowed no fluids.
The test medicine might harm unborn children, so all volunteers must follow the restrictions on the donation of sperm and use acceptable contraception. Were a partner of a volunteer to become pregnant during the study, we 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?
Compass Pathfinder Limited

When is the study starting and how long is it expected to run for?
July 2024 to January 2025

Who is funding the study?
Compass Pathfinder Limited

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

Contact information

Type(s)
Public, Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
1010247

Protocol serial number
COMP 103, QSC301617

Study information

Scientific Title

A phase I, open-label, single-dose, mass balance study to investigate the absorption, distribution, metabolism, and excretion of COMP360 [14C]-psilocybin in healthy male participants

Study objectives
Primary objectives:
1. To assess the PK of total radioactivity in blood and plasma, and excretion of total radioactivity in urine and faeces and all excreta (urine and faeces combined) following a single oral dose of COMP360 [14C]-psilocybin 10 mg in healthy participants.
2. To identify and determine the relative abundance of metabolites including those accounting for >10% of total radioactivity of COMP360 [14C]-psilocybin in plasma, urine and faeces after a single oral dose of COMP360 [14C]-psilocybin 10 mg in healthy participants.

Secondary objectives:
1. To investigate the distribution of total radioactivity into red blood cells after a single oral dose of COMP360 [14C]-psilocybin 10 mg in healthy participants.
2. To identify the chemical structure of each metabolite accounting for more than 10% of circulating total radioactivity.
3. To further investigate the oral pharmacokinetics of psilocin (in plasma and urine) and its metabolites (4 HIAA and psilocin-O-glucuronide in plasma).
4. To assess the safety and tolerability of COMP360 [14C]-psilocybin 10 mg in healthy participants.
5. To investigate the quality and intensity of the psychedelic experience of a single oral dose of COMP360 [14C]-psilocybin 10 mg in healthy participants.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 03/10/2024, North East - York Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8143; york.rec@hra.nhs.uk), ref: 24/NE/0118

Primary study design
Interventional

Study design
Interventional non-randomized open-label study

Study type(s)
Safety

Health condition(s) or problem(s) studied
Treatment-resistant depression (TRD). Study to be conducted in healthy volunteers

Interventions
This is a non-randomised, open-label study assessing the mass balance recovery, absorption, distribution, metabolism and excretion of a single dose of the test medicine. Participants will receive a single radiolabelled dose of the test medicine as a capsule via the mouth. Participants are expected to be involved with the study for approximately 5 weeks from screening to discharge.

Intervention Type

Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
COMP360 [14C]-Psilocybin Capsule, 10 mg (NMT 2.3 MBq) [Psilocybin]

Primary outcome(s)
Evaluated from assessment of blood samples taken from Day 1 to Day 8:
1. Radioactivity in blood and plasma PK parameters:
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)

The below endpoints will be evaluated through the assessment of blood samples taken from Day 1 to Day 8, and urine and faecal collections taken from Day 1 to Day 10:
2. Amount of radioactivity recovered in urine and faeces and all excreta (urine and faeces combined) as:
For urine and faeces:
2.1. Ae (total radioactivity)
2.2. %Ae (total radioactivity expressed as a percentage of the dose)
2.3. Cum Ae (cumulative recovery of total radioactivity)
2.4. Cum %Ae (cumulative recovery expressed as a percentage of the dose)
For all excreta combined:
2.5. Ae (total radioactivity)
2.6. % Ae (total radioactivity expressed as a percentage of the dose)
2.7. Cum Ae (total) (Cumulative recovery of total radioactivity)
2.8. Cum % Ae (total) (Cumulative recovery expressed as a percentage of the dose)
3. Metabolite profiling for plasma, urine, and faeces assessed as a single AUC pool per participant and pooled sample across all volunteers at 2 time-points.

Key secondary outcome(s)
1. The distribution of total radioactivity into red blood cells assessed as blood-to-plasma ratios for total radioactivity evaluated from assessment of blood samples taken from Day 1 to Day 8

The below endpoints will be evaluated through the assessment of blood samples taken from Day 1 to Day 8, and urine and faecal collections taken from Day 1 to Day 10:
2. Metabolites identified in plasma, urine and faeces samples will be structurally identified using radiochromatographic data where the metabolite represents:
2.1. Greater than 10% of the total radioactivity in plasma
2.2. Greater than 10% of the administered dose in excreta
3. Plasma PK parameters for psilocin, 4-hydroxyindoleacetic acid (4 HIAA) and psilocin-O-glucuronide:
3.1. Area under the concentration-time curve from zero to 24 hours (AUC0-24h)
3.2. Area under the concentration-time curve from zero to infinity (AUC0-inf)
3.3. Peak exposure (Cmax)

3.4. Time to reach peak exposure (tmax)
3.5. Time to the first measurable timepoint (tlag)
3.6. Elimination half-life (t1/2)
3.7. Last measurable concentration (Clast)
4. Urine PK Parameters for psilocin:
4.1. Cumulative urinary excretion in urine for eachtime interval (Ae0-t)
4.2. Fraction (% dose) excreted in urine (Fe0-t)
4.3. Maximum rate of urinary excretion (Rmax)
4.4. Time of maximal urinary excretion (TRmax)
4.5. Elimination half-life (t1/2Z)

5. Safety assessed based on adverse event, ECG, vital signs, laboratory results, C-SSRS results and BPRS+ results from Day 1 to up to Day 10.

6. Summary of the 5D-ASC scores post COMP360 [14C]-psilocybin administration on Day 1

7. Summary of the Psychedelic intensity ratings post COMP360 [14C]-psilocybin administration assessed using questionnaire results on Day 1

Completion date
23/01/2025

Eligibility

Key inclusion criteria
1. Signed ICF.
2. Healthy Male aged 30 - 55 years at Screening.
3. Body mass index (BMI) of 18 - 32kg/m² at Screening.
4. Minimum weight of 50kg at Screening.
5. Regular bowel movements (average stool production of ≥1 and ≤3 stools per day).
6. Non-smoker (including e-cigarettes) for at least 12 months prior to Screening.
7. Willing to comply with fasting and food intake requirements.
8. Willing to comply with contraception requirements.
9. Participant is judged to have sufficient English language competence that under ordinary circumstances they are able to complete all protocol required assessments without any assistance or alteration to the copyrighted assessments, and agreement to comply with all study visits.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
30 Years

Upper age limit

55 Years

Sex
Male

Total final enrolment
6

Key exclusion criteria
1. Current or lifetime history of any psychotic disorder or bipolar disorder, as assessed by a structured clinical interview (Mini International Neuropsychiatric Interview, Version 7.0.2 [MINI 7.0.2] or documented via available medical records.
2. Borderline personality disorder as demonstrated by medical history or the Mini International Neuropsychiatric Interview Plus (MINI plus) – borderline personality disorder module.
3. Current or clinically relevant history of major depression, panic disorder, post-traumatic stress disorder, generalised anxiety disorder, obsessive-compulsive disorder, or eating disorder as assessed by the MINI 7.0.2 or documented via available medical records.
4. A history of suicide attempts, suicidal ideation or suicidal behaviour as determined by the Columbia-Suicide Severity Rating Scale (C-SSRS) at Screening, Day -1 or at Day 1; or clinical assessment of suicidal risk or risk of self-injury identified during other participant assessments.
5. Alcohol or substance use disorder within the 12 months prior to Screening as assessed by the MINI 7.0.2 or documented via available medical records.
6. Use of pharmacological compounds for psychiatric or neurological conditions acting on the central nervous system within the last 30 days or five half-lives (whichever is longer) prior to Screening.
7. In first-degree relatives, a history of psychotic disorders or bipolar disorder.
8. Other personal circumstances or behaviour judged by the investigator to be incompatible with the establishment of rapport or safe exposure to COMP360 [14C]-psilocybin.
9. Exposure to psilocybin, or any other classic psychedelics, such as ayahuasca, mescaline, lysergic acid diethylamide (LSD), dimethyltryptamine (DMT), 5-Methoxy-N,N-dimethyltryptamine (5-MeO-DMT), or peyote during the past three months prior to Screening, including microdosing. Additionally, the participant must agree not to use psychedelics for the duration of the study follow-up so as not to confound results.
10. Participants who are planning a pregnancy.
11. Participants with pregnant or lactating partners.
12. Participants who engage in sexual intercourse which could result in pregnancy, and who do not agree to use a highly effective contraceptive method throughout their participation in the study and for three months following COMP360 [14C]-psilocybin administration.
13. Participants who plan to donate sperm within the study period or within three months following COMP360 [14C]-psilocybin administration.
14. Presence of active gastrointestinal disease or other condition (eg gastrectomy, bariatric surgery, small bowel or large bowel resection) that may interfere significantly with the absorption of drugs.
15. Acute diarrhoea or constipation in the 7 days before administration of investigational medicinal product (IMP) in the study. If screening occurs >7 days before the day of administration, this criterion will be determined on the morning prior to administration.
16. Cardiovascular conditions: lifetime history of stroke, lifetime myocardial infarction, uncontrolled hypertension (resting blood pressure >140/90 mmHg), tachycardia (resting heart rate over 100 beats per minute), elongated QT interval corrected by Fridericia (QTcF; interval >450 ms) or clinically significant arrhythmia.
17. 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 the signing of ICF).
18. Seizure disorder.
19. Substance use within the last month (excluding alcohol) including but not limited to cannabis, cocaine, ketamine, opiates, and 3,4 MDMA or a confirmed positive urine drug screen for illicit drugs or drugs of abuse at Screening and/or Day -1.
20. 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.
21. Abnormal and clinically significant results on the physical examination, vital signs, electrocardiogram (ECG), or laboratory tests at Screening or Day -1 that in the investigator's opinion may constitute a risk for an individual who is exposed to COMP360 [14C]-psilocybin.
22. Any other clinically significant cardiovascular, pulmonary, gastrointestinal, hepatic, renal, endocrine, metabolic, 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.
23. Hypersensitivity to the investigational product or any of the excipients.
24. Participants with aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase >1.1 x the upper limit of normal (ULN) or total bilirubin levels >ULN at Screening or Day -1. Additionally, participants with creatinine clearance as determined by the Cockcroft-Gault method of <80ml/min at Screening. These laboratory evaluations may be repeated once at the discretion of the investigator. If the repeat test is <1.1 × ULN for aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase or <ULN for total bilirubin levels, 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 the interpretation of safety data.
25. Positive test for hepatitis B surface antigen (HBsAg), anti-hepatitis C antibody (anti-HCV) or human immunodeficiency virus I and II (anti-HIV I/II) at Screening.
26. Presence or history of clinically significant allergy requiring treatment, as judged by the investigator. Hay fever is allowed unless the participant is actively experiencing a hay fever reaction on Day -1 or Day 1.
27. Intake of >21 units of alcohol weekly, consumption of alcohol within 48 hours of Screening, or from within 48 hours of Day 1. 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 one 125 mL glass of wine.
28. Habitual and heavy consumption of caffeinated beverages (>8 cups of coffee or equivalent per day) at Screening; and/or unable to refrain from the use of (methyl) xanthine (eg coffee, tea, cola, chocolate) from 48 hours prior to and for the duration of the residential study visit.
29. Use of any prescription or non-prescription medications, including herbal and nutritional supplements, or over-the-counter (OTC) medications (eg ibuprofen, aspirin) within 15 days or five half-lives (whichever is longer) of COMP360 [14C]-psilocybin administration and throughout the study. By exception, the participant may take paracetamol (≤2 g/day for up to 48 hours prior to dosing) and a mild laxative if an individual participant has not experienced a bowel movement in any 36-hour period post-dose. Rescue medication or other medications deemed necessary by the investigator are permitted at the investigator's discretion.
30. 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.
31. Donation of blood or plasma of >400 mL within three months prior to and until four weeks after COMP360 [14C]-psilocybin administration.
32. Participants who do not have suitable veins for multiple venepuncture/cannulation as assessed by the investigator or a delegate at Screening.
33. A confirmed positive alcohol breath test at Screening or Day -1.
34. A confirmed positive urine cotinine test at Screening or Day -1.

35. Participants who are, or are immediate family members of, a study site or sponsor employees.
36. Failure to satisfy the investigator of fitness to participate for any other reason.

Date of first enrolment
12/12/2024

Date of final enrolment
23/01/2025

Locations

Countries of recruitment
United Kingdom

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

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

Data sharing statement to be made available at a later date