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A study carried out on healthy volunteers to understand how COMP360 can be taken in a safe and well-tolerated way

Submission date
15/05/2024

Recruitment status
No longer recruiting

Registration date
08/08/2024

Overall study status
Completed

Last Edited
16/08/2024

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
COMP360 is being investigated as a drug for depression. This study aims to investigate how safe and well tolerated is the administration of four different doses of COMP360 in healthy volunteers. Also, it aims to investigate whether food intake or or different dosing have an impact on the way the body absorbs, distributes, and gets rid of COM360 as well as on how safe and well tolerated it is. Lastly, this study also wants to look into how the relationship between the concentration of the drug and a heart-related measurement called the QT interval changes as the dose of COMP360 changes.

Who can participate?
People who join the study must be healthy men or women between 18 and 55 years old

What does the study involve?
The single dose part of the study involves giving either a single dose of the drug or a placebo (a harmless pill) to 32 healthy volunteers to find out what happens to the drug or placebo to your body after you take just one dose of it. They won't know if they're getting the real drug or the placebo, and they'll take it on an empty stomach.
The food effect part of the study is an experiment where 12 participants will be randomly assigned to two different sequences of treatments where both the researchers and the participants know which treatment is being given. Each participant will take part in two treatment periods. They'll receive COMP360 (a specific dose of 25 mg) in both periods, once after not eating for a while and once after having a high-fat meal. Everyone will start with an overnight fast. Those in the fasting group will keep fasting, while those in the fed group will eat a meal 30 minutes before taking the dose.
Before participants take the drug on the first day, measurements will be taken and then they'll take the drug. There will be a therapist there to help. Even if they're given a placebo, they'll still have support from the therapist. There will be monitoring of their heart, blood pressure, and blood samples taken through a needle. The session may be recorded on video for training purposes. They'll continue to be monitored for 24 hours after taking the drug, and any assessments will be recorded during this time. They'll also stay overnight at the site. The day

after taking the drug, they'll undergo a safety check, talk about how they're feeling, and have assessments with the Study Clinician and therapist. After this, they'll be allowed to leave. Participants can contact the research team anytime if they have any problems or need help.

What are the possible benefits and risks of participating?
There are no expected benefits as this is a Phase I study in healthy volunteers rather than in participants with depression. Taking part in the study might pose some risks including the possibility of feeling like you want to hurt yourself or having thoughts about suicide. There's also a chance of experiencing heart problems. Some common side effects could include feeling like time and space are different, feeling anxious, feeling disconnected from reality or yourself, experiencing mood changes, having dilated pupils, feeling dizzy, feeling like your mind is foggy or tired, having trouble concentrating, feeling strange sensations in your body, feeling nauseous, feeling nervous, having unusual thoughts, and yawning a lot.

Where is the study run from?
MAC Clinical Research Centre (UK)

When is the study starting and how long is it expected to run for?
November 2020 to October 2022

Who is funding the study?
COMPASS Pathfinder Limited (UK)

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
2021-000011-23

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
COMP 101

Study information

Scientific Title
A pharmacokinetic study with an integrated food effect arm to assess the safety, tolerability and QTcF interval following different strengths of COMP360 in healthy volunteers

Acronym
COMP 101

Study objectives
1. To investigate the safety and tolerability of increasing doses of orally administered COMP360 (1 mg, 10 mg, 25 mg and 50 mg) in healthy volunteers for the single dose pharmacokinetic (PK) and food effect (FE) components.
2. To investigate the PK of increasing doses of orally administered COMP360 (1 mg, 10 mg, 25 mg and 50 mg) in healthy volunteers in the single dose PK component.

3. To investigate the PK of orally administered COMP360 (25 mg), following high-fat food intake relative to fasting conditions in the FE component.
4. To investigate the relationship between the change in QTcF following COMP360 versus placebo and the plasma concentrations of psilocybin and key metabolites (psilocin, 4-HIAA, psilocin-O-glucuronide) following varying doses of orally administered COMP360 (1 mg, 10 mg, 25 mg and 50 mg) in healthy volunteers in the single dose PK component.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 17/03/2021, Wales Research Ethics Committee 1 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 (0)2920 785738; Wales.REC1@wales.nhs.uk), ref: 21/WA/0044

Study design
Single-dose single-centre double-blind randomized placebo-controlled trial (the single dose PK component) followed by an open-label randomized cross-over trial (the food effect component only)

Primary study design
Interventional

Study type(s)
Safety

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

Interventions
In the single dose double-blind PK component of the study, 32 participants will be enrolled into 4 cohorts, with 8 participants each. Each cohort will receive a single dose of either COMP360 or a placebo capsule under fasting conditions. Six participants in each cohort will receive COMP360 (1 mg, 10 mg, 25 mg, or 50 mg), and 2 participants will receive a placebo. The maximum study duration for participants in the single-dose PK component is approximately 7 weeks. The single-dose PK component of the study will be conducted in a double-blinded fashion (investigator- and subject-blinded). The randomisation list will be kept in a secure location until the end of the study. Only the pharmacy staff handling the study drug and laboratory staff responsible for analysing the PK blood samples will be unblinded during the study and will have access to the randomisation list. The planned volume of either COMP360 or placebo will be provided in a blinded dosing container and provided to the dosing staff in the CRU.

For the open-label food effect (FE) component, 12 participants not involved in the single-dose PK component will be enrolled. Each participant will undergo two treatment periods, receiving COMP360 (25 mg) under both fasting and fed (high-fat) conditions following an overnight fast. The maximum study duration for participants in the FE component is approximately 9 weeks.

Day 1 post-dose assessments will be recorded for 24 hours post-dose. Participants will stay at the site overnight for 24 hours post-dose. On day 2 post-dose in the single dose PK component (V3) and day 2 post-dose in each Treatment Period in the FE component (V3 and V5), the day following COMP360 or placebo administration, participants will be seen in person for a safety

check, assessment of suicidality and clinical and self-report assessments by the Study Clinician, and to discuss their experience during the COMP360 session with the Therapist. Following this, participants will be discharged. Participants will have 24-hour access to the research team should they experience difficulty or need support.

The active IMP or matched placebo will be orally administered on day 1 (V3) (and day 1 of Treatment Period 2 [V5] in the FE component). In the single ascending dose PK component and the fasted treatment period of the FE component, the study treatment will be administered following an overnight fast (at least 10 hours fast pre-dose). Each dose will be taken with 240 mL of water at room temperature. Water will be restricted to 1 hour pre-dose and 1-hour post-dose, and breakfast can be eaten 4 hours post-dose. The quantity of food consumed post-dose and the time at which food is consumed post-dose will be recorded. In the fed treatment period of the FE component, a high-fat breakfast will be given 30 minutes prior to COMP360 administration. Dosing will be observed by CRU staff whilst resident in the CRU.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)
The primary safety and tolerability endpoints (single dose PK and FE components) include:
1. Adverse events recorded at Day-1, pre-dose day 1, post-dose day 1, post-dose day 2, and day 7
2. 12-lead electrocardiogram (ECG) measured using cardiac Holter monitoring data extraction at day-35 to day-2 up to post-dose day 2
3. Vital signs measured at pre-dose day 1 to post-dose day 2
4. Clinical laboratory tests including clinical chemistry, haematology and urinalysis measured at Day-1 to post-dose day 2
5. Suicide risk assessed using the Columbia-Suicide Severity Rating Scale (C-SSRS) at Day-1, pre-dose day 1, dosing/post-dose day 1, post-dose day 2, up to follow-up visit day 7

Key secondary outcome(s))
Plasma concentration endpoints (single dose PK and FE components) include:
1. Psilocybin, psilocin, 4-HIAA and psilocin-O-glucuronide plasma concentrations derived from plasma concentration data of psilocybin, psilocin, 4-HIAA and psilocin-Oglucuronide by non-compartmental analysis at pre-dose day 1 to post-dose day 1 for single dose PK. Plasma PK parameters for psilocybin, psilocin, 4-HIAA and psilocin-O-glucuronide derived from plasma concentration data of psilocybin, psilocin, 4-HIAA and psilocin-Oglucuronide by non-compartmental analysis will be calculated in the FE component at pre-dose Day 1, post-dose Day 1, pre-dose day 16 and post-dose day 16.

The secondary safety endpoints (single dose PK component only) include:
2. Change from baseline in QTcF following COMP360 versus placebo and concentration of psilocybin, measured by ECG from screening to post-dose day 2
3. Change from baseline in QTcF following COMP360 versus placebo and concentration of psilocin, measured by ECG from screening to post-dose day 2
4. Change from baseline in QTcF following COMP360 versus placebo and concentration of 4-

HIAA, measured by ECG from screening to post-dose day 2
5. Change from baseline in QTcF following COMP360 versus placebo and concentration of psilocin-O-glucuronide, measured by ECG from screening to post-dose day 2

Completion date
20/10/2022

Eligibility

Key inclusion criteria
1. Signed ICF.
2. Participant is male or female from any ethnic origin.
3. Participant is aged between 18 to 55 years, inclusive, at Screening visit 1 (V1).
4. Participant has a body mass index of 18.5 to 30 kg/m2, inclusive, at Screening (V1) and day 1 (V3).
5. Participant is a non-smoker (including e-cigarettes) for at least 12 months prior to Screening (V1) and day 1 (V3).
6. Negative RT-PCR test for SARS-CoV-2 at Screening (V1) and day -1 (V2).
7. Willing to comply with fasting and food intake requirements.
8. Healthy as determined by a responsible physician, based on medical evaluation including medical history, physical examinations, prior and concomitant medications, vital signs, 12-lead ECG and clinical laboratory evaluations.
9. Male participants must use a condom during the study and for 3 months after their final dose of study medication if their partner is a woman of childbearing potential. In addition, their female partner of childbearing potential must use an additional method of highly protective contraception from first dosing until 3 months following the final dosing.
10. Female participants:
10.1. Of childbearing potential must be established on a highly effective method of contraception prior to dosing until 3 months after the last dose in combination with male partner's use of a condom during the trial and for 3 months after the last dose of trial medication. Participants must have a negative pregnancy test at Screening (V1) and day 1 (V3).
10.2. Of non-childbearing potential i.e., postmenopausal or permanently sterile following hysterectomy, bilateral salpingectomy and bilateral oophorectomy. Postmenopausal is defined as women ≥60 years and having had >12 months of natural (spontaneous) amenorrhea, and a serum follicle-stimulating hormone level in the menopausal range, unless the subject is taking hormone replacement therapy or is using hormonal contraception.
11. In the FE component, the participant is willing to eat a high-fat breakfast, including bacon, in line with Food and Drug Administration guidance.
12. Able to complete all protocol-required assessment tools without any assistance or alteration to the copyrighted assessments, and to comply with all study visits.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit

18 years

Upper age limit
55 years

Sex
All

Total final enrolment
44

Key exclusion criteria
Psychiatric Exclusion Criteria:
1. Current (within the last year) or history of alcohol or substance abuse (including nicotine) as informed by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) at Screening (V1), as determined by self-report or a positive urine drugs of abuse test, alcohol breath test and urine cotinine screen at Screening (V1) or day 1 (V3).
2. Use of pharmacological compounds for psychiatric or neurological conditions acting on the central nervous system within 30 days or 5 half-lives (whichever is longer) prior to Screening (V1).
3. Current or clinically relevant history of schizophrenia, psychotic, bipolar disorder, delusional disorder, paranoid personality disorder, schizoaffective disorder, borderline personality disorder, major depression, panic disorder, generalised anxiety disorder, obsessive-compulsive disorder, eating disorder or body-dysmorphic disorder, as assessed by a structured clinical interview (Mini International Neuropsychiatric Interview [MINI], Version 7.0.2).
4. In first-degree relatives, a history of schizophrenia, psychotic, bipolar disorder, delusional disorder, paranoid personality disorder, schizoaffective disorder, borderline personality disorder, major depression, panic disorder, generalised anxiety disorder, obsessive-compulsive disorder, eating disorder or body-dysmorphic disorder.
5. Significant suicide risk as defined by:
5.1. Suicidal ideation as endorsed on items 4 or 5 on the C-SSRS within 1 year prior to Screening (V1), or on day 1 (V3), or
5.2. Suicidal behaviours within 1 year prior to Screening (V1), or
5.3. Clinical assessment of significant suicidal risk during Participant interview.
6. Other personal circumstances and behaviour that is incompatible with establishment of rapport or safe exposure to psilocybin, as judged by the Investigator.
7. Exposure to psilocybin, or any other psychedelics, such as ayahuasca, mescaline, LSD, or peyote within 1 year prior to Screening (V1).

General Medical Exclusion Criteria:
8. Women of childbearing potential who are pregnant, breastfeeding, or planning to conceive.
9. Clinically relevant history of abnormal physical or mental health (defined as any subject requiring medical, psychological or pharmacotherapeutic intervention for mental illness) interfering with the study as determined by medical history and physical examinations obtained during Screening (V1) as judged by the Investigator (including [but not limited to], thyroid, metabolic, pulmonary, neurological, psychiatric, endocrine, cardiovascular, respiratory, gastrointestinal hepatic or renal disorder, or any other major concurrent illness).
10. Clinically relevant abnormal laboratory results (including hepatic and renal panels, complete blood count, chemistry panel and urinalysis), 12-lead ECG, vital signs, or physical findings at Screening (V1) and/or day -1 (V2) as judged by the Investigator, that in the Investigator's opinion may constitute a risk for an individual who is exposed to psilocybin. In case of uncertain or questionable results, tests performed during Screening (V1) may be repeated once to confirm

eligibility or judged to be clinically irrelevant for healthy participants.
11. Current or previous medical history of any cardiovascular conditions. Participants with a blood pressure ≥140/90 mmHg at Screening (V1) or day 1 (V3), following triplicate readings, will not be eligible to take part in this study.
12. Recent substance use within the last month (excluding alcohol), such as but not limited to, cannabis, cocaine, ketamine, opiates, MDMA, and psilocybin, or a positive urine drugs screen for illicit substances or drugs of abuse test at Screening (V1) and/or day 1 (V3).
13. Current enrolment in any investigational drug or device study, or participation in such within 30 days or 5 half-lives (whichever is longer) of Screening (V1).
14. Current or previous medical history of epilepsy or the presence of other medical conditions associated with seizures or convulsions.
15. Any other concomitant disease or condition that could interfere with, or for which the treatment might interfere with, the conduct of the study as outlined in this Protocol, or that would, in the opinion of the Investigator, pose an unacceptable risk to the participant in this study.
16. Participants with AST, ALT, gamma-glutamyl transferase (GGT) or total bilirubin levels ≥1.5 x the ULN at Screening (V1) or day -1 (V2). These laboratory evaluations may be repeated once at the discretion of the Investigator. If the repeat test is within the reference range, 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.
17. QTcF >450 msec at Screening (V1) or pre-dose on day 1 (V3), following triplicate ECG readings.
18. 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 (V1).
19. Intake of >21 units of alcohol weekly, consumption of alcohol within 48 hours of Screening (V1), or from within 48 hours of day 1 (V3) until the end of the study. One unit is equivalent to a 285 mL glass of full-strength beer or 1 (30 ml) measure of spirits or 1 glass (100 ml) of wine.
20. Habitual and heavy consumption of caffeinated beverages (>8 cups of coffee or equivalent per day) at Screening (V1); and/or unable to refrain from use of (methyl) xanthine (e.g., coffee, tea, cola, chocolate) from 48 hours prior to each clinic visit until the end of the study.
21. Use of any prescription or non-prescription medications, including herbal and nutritional supplements, or over-the-counter (OTC) medications (e.g., ibuprofen, aspirin) within 30 days of first dosing and throughout the study. By exception, the subject may take paracetamol (less or equal 2 g/day) for up to 48 hours prior to first dosing. The Investigator and study team may review medication on a case-by-case basis to determine if its use would compromise subject safety or interfere with study procedures or data interpretation.
22. Strenuous exercise within 48 hours prior to each blood collection for clinical laboratory tests.
23. Donation of blood or plasma of >400 ml within 4 weeks prior to first dosing until 4 weeks after final dosing.
24. Male participant who will not abstain from sperm donation between first dosing and 3 months after final dosing.

Date of first enrolment
03/11/2021

Date of final enrolment
28/09/2022

Locations

Countries of recruitment

United Kingdom

England

Study participating centre
MAC Clinical Research Liverpool
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Sponsor information

Organisation
COMPASS Pathfinder, Ltd

Funder(s)

Funder type
Industry

Funder Name
COMPASS Pathfinder, Ltd

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 as this is a Phase I study.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		10/07/2024	16/08/2024	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes