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Safety, blood levels and effects of N,N-dimethyltryptamine [DMT (SPL026)] in healthy participants and participants with major depressive disorder

Submission date
26/07/2023

Recruitment status
No longer recruiting

Registration date
30/08/2023

Overall study status
Completed

Last Edited
30/01/2024

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
This is a study of N, N-dimethyltryptamine (DMT) – a psychedelic substance that occurs naturally in many plants and animals. Psychedelic substances, also known as hallucinogens, act on the brain causing temporary changes to perception, sensations, and emotions, which can be intense. DMT is best known for being the main psychedelic substance in ayahuasca (a hallucinogenic brew that has been used for centuries in religious ceremonies in some South American countries). This study is testing DMT (the study medicine, also known as SPL026, which has been manufactured for this study) as an experimental treatment for major depressive disorder (MDD). The aim is to find out about the effects and blood levels of DMT in healthy volunteers (Part A) and patients with MDD (Part B).
This study aims to answer these questions.
1. Do single doses of DMT improve the symptoms of depression, when given by slow injection into a vein in the arm?
2. Are single doses of DMT safe and well tolerated, when given by slow injection into a vein in the arm?
3. How much DMT gets into the bloodstream, and how long does the body take to get rid of it?
4. What do people experience after a dose of DMT?
5. What are the effects of DMT on mood, feelings, thoughts and beliefs?

Who can participate?
Part A: healthy volunteers aged 25 years or older
Part B: patients aged 18 years or older with major depressive disorder (MDD), also known as ‘depression’

What does the study involve?
In Session 1, participants will receive a dose of DMT or dummy medicine by slow injection into a vein in their arm. In Session 2, they will receive a dose of DMT by slow injection into a vein in their arm. The injections will take 6–11 min. Participants will stay on the ward for 3 days and 2

nights in a row. The researchers will contact them by video call for a check-up at about 7 days after each dose. At about 2 weeks after the last dose, participants come to the ward for a follow-up visit. There will be follow-up phone or video calls at about 1 month and 3 months after the last dose. At follow-ups, participants complete questionnaires to rate their mood, feelings, thoughts and beliefs.

What are the possible risks and benefits of participating?
The highest dose of DMT in this study is predicted to give blood levels no higher than those in previous studies. The dose of DMT is likely to cause a psychedelic experience or 'trip', which is expected to last about 20 min. Participants may experience: visual imagery or hallucinations (seeing colourful patterns, or seeing or hearing things that aren't real); a sense of being detached from their thoughts or feelings; changes in their sense of time and space; out-of-body experiences; disorientation or confusion; anxiety; intense emotions such as happiness or grief. Sometimes people experience unpleasant images and sounds, and may also 'relive' painful memories or traumas. In published research into psychedelic treatments for depression, difficult emotions and upsetting content experienced during the 'trip' are considered therapeutically beneficial, as they can lead to important insights. Participants will have the support and guidance of expert therapists to help them interpret and deal with any experiences they may have during their trip. As with any new medicine, its side effects are not yet known. In any clinical trial, there is a risk of an unexpected, serious reaction to the study medicine, which could be life-threatening.
Participants may get some medical benefit from DMT, but it's not been tested in patients with MDD before, so the researchers can't be sure they will benefit. Participants may benefit from regular conversations with the study psychiatrist and therapist. The screening tests might be of benefit if an important medical problem is found, but they could reveal something participants prefer not to know about.
Participants will be helping with medical research. They can't carry on taking DMT after the study has finished, even if they get some unexpected benefit from it. DMT is a Class A illegal drug – the researchers have a special licence to be able to give it to volunteers in this study.

Where is the study run from?
1. Hammersmith Medicines Research Limited (UK)
2. MAC Clinical Research Liverpool (UK)

When is the study starting and how long is it expected to run for?
August 2020 to December 2022.

Who is funding the study?
Small Pharma Ltd (UK)

Who is the main contact?
Carol Routledge, carol.routledge@smallpharma.co.uk

Contact information

Type(s)
Principal investigator

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT04673383

Clinical Trials Information System (CTIS)
2020-000251-13

Integrated Research Application System (IRAS)
288450

Central Portfolio Management System (CPMS)
52296

Protocol serial number
CT026_001

Study information

Scientific Title
A double-blind, randomized, placebo-controlled study of intravenous doses of SPL026 (DMT fumarate), a serotonergic psychedelic, in healthy subjects (Part A) and patients with major depressive disorder (Part B)

Study objectives
SPL026 is safe and well tolerated and (in participants with MDD) reduces depression scores more than placebo

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 10/12/2020, London - Brent REC (80 London Road, London, SE1 6LH, United Kingdom; +44 (0)20 7104 8137; brent.rec@hra.nhs.net), ref: 20/LO/1035

Study design

Part A: Single ascending dose placebo-controlled double-blinded trial; Part B: Stage 1: Single-dose placebo-controlled double-blinded trial; Stage 2: open-label but blinded to first dose trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Major depressive disorder

Interventions
Subject numbers will be allocated to treatments (active or placebo) according to a randomisation schedule prepared by an independent HMR statistician using a SAS program.

SPL026 (dimethyltryptamine fumarate) by intravenous infusion or matched placebo. Single dose or two single doses, 2 weeks apart.

Part A:
4 cohorts of 8 participants randomised to 6 active, 2 placebo. 3 months follow-up.
Doses: 9 mg, 12 mg, 17 mg, 21.5 mg

Part B:
Stage 1: randomised 1:1 active: placebo.
Stage 2: second active dose 2 weeks after the first dose, open-label but blinded to the first dose.
3 months follow-up following Stage 2.
Doses: 21.5 mg

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
SPL026 (N,N-dimethyltryptamine fumarate; DMT)

Primary outcome(s)
Part A:
Safety and tolerability assessed using adverse events, laboratory values, and tolerability assessments over 3 months

Part B:
Efficacy (depression) assessed using the Montgomery–Åsberg Depression Rating Scale (MADRS) at 2 weeks post first dose

Key secondary outcome(s))
Part A:
1. Pharmacokinetics (PK) measured using frequent blood sampling from pre-dose to 2 hours

post-dose. DMT will be analysed by LC-MS/MS after liquid-liquid extraction of the human plasma sample.
2. Pharmacodynamics (PD) - Wellbeing assessed using the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) from pre-dose to 3 months post-dose
3. PD - Subjective experience assessed using Multidimensional Emotion Questionnaire (MEQ) immediately post-dose

Part B:
1. PK measured using frequent blood sampling from pre-dose to 2 hours post-dose. DMT will be analysed by LC-MS/MS after liquid-liquid extraction of the human plasma sample.
2. Wellbeing assessed using WEMWBS from pre-dose to 3 months post-dose
3. Subjective experience assessed using MEQ immediately post-dose

Part B:
1. Safety and tolerability assessed using adverse events, laboratory values, and tolerability assessments from pre-dose to 3 months post second dose.
2. Efficacy assessed using MADRS from pre-dose to 3 months post second dose.
3. PK measured using frequent blood sampling from pre-dose to 2 hours post-dose. DMT will be analysed by LC-MS/MS after liquid-liquid extraction of the human plasma sample.
4. PD - Wellbeing assessed using WEMWBS from pre-dose to 3 months post-dose
5. PD - Subjective experience assessed using MEQ immediately post-dose

Part B:
1. PK measured using frequent blood sampling from pre-dose to 2 hours post-dose. DMT will be analysed by LC-MS/MS after liquid-liquid extraction of the human plasma sample.
2. PD - Wellbeing assessed using WEMWBS from pre-dose to 3 months post-dose
3. PD - Subjective experience assessed using MEQ immediately post-dose

Completion date
21/12/2022

Eligibility

Key inclusion criteria
1. Normotensive male or female, deemed healthy on the basis of a clinical history, physical examination, ECG, vital signs, laboratory tests of blood and urine, Mini-International Neuropsychiatric Interview (MINI) and Beck Scale for Suicidal Ideation (BSS)
2. Willing to follow the contraception requirements of the trial; willing to refrain from psychedelic drug use (excluding the study drug) during the trial and ≥3 months afterwards
3. Willing to be contacted by email and video call, and have online access; able to give fully informed written consent
4. Part A only: psychedelic-naïve, ie have never taken a serotonergic psychedelic drug, in any form. Must be 25 years or older
5. Part B only: MDD diagnosis (as per DSM-V); not on antidepressant medication or willing to discontinue antidepressant medication (e.g. selective serotonin reuptake inhibitor [SSRI] treatment) for a sufficient time before and during the study
6. No psychedelic drug use in the 6 months before dosing

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
68

Key exclusion criteria
1. Pre-menopausal females who are pregnant or lactating, or who are sexually active and not using a reliable method of contraception
2. Clinically relevant abnormal findings at the screening assessment
3. Acute or chronic illness (other than MDD [Part B only]) or infection; clinically relevant abnormal medical history or concurrent medical condition (other than MDD [Part B only])
4. Positive tests for hepatitis B & C, or HIV
5. Severe adverse reaction to any drug
6. Use of over-the-counter or prescribed medication (excluding oral contraceptives) within the previous 28 days (paracetamol [acetaminophen] permitted up to 7 days, and antidepressant medication must have ceased for at least 14 days; 28 days for MOAIs) before the first dose of trial medication
7. Drug or alcohol abuse; use of cannabis in the 24 h before each study visit
8. Heavy smokers (>10 [Part A] or > 20 cigarettes [Part B] daily)
9. Supine blood pressure, heart rate, or QTcF outside the acceptable ranges
10. Participation in other clinical trials of unlicensed medicines, or loss of more than 400 ml blood, within the previous 3 months
11. Phobia of needles or blood
12. Possibility that the volunteer will not cooperate with the study

Date of first enrolment
10/12/2020

Date of final enrolment
01/09/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

Hammersmith Medicines Research Limited
Cumberland Avenue
London
United Kingdom
NW10 7EW

Study participating centre
MAC Clinical Research Liverpool
11 Tiger Court
King's Business Park
Liverpool
United Kingdom
L34 1BH

Sponsor information

Organisation
Small Pharma Ltd

Funder(s)

Funder type
Industry

Funder Name
Small Pharma 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 due to commercial sensitivity.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Part A results in healthy volunteers	11/01/2024	30/01/2024	Yes	No

Funder report results	version 1		20/06/2023	18/09/2023	No	No