



Clinical trial results:

A randomised, placebo controlled trial of psilocybin in treatment resistant depression: A feasibility study

Summary

EudraCT number	2018-003573-97
Trial protocol	GB
Global end of trial date	28 August 2025

Results information

Result version number	v1 (current)
This version publication date	26 September 2026
First version publication date	26 September 2026
Summary attachment (see zip file)	PsiDeR_Clinical_Study Report (PsiDeR_Clinical_Study Report_Docusigned.pdf)

Trial information

Trial identification

Sponsor protocol code	PSIDER
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04959253
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	King's College London
Sponsor organisation address	F16 Guy's Tower, Guy's Hospital, Great Maze Pond,, London , United Kingdom,
Public contact	Prof. Allan Young, King's College London, +44 02078480088, allan.young@kcl.ac.uk
Scientific contact	Prof. Allan Young, King's College London, +44 02078480088, allan.young@kcl.ac.uk
Sponsor organisation name	South London & Maudsley NHS Foundation Trust
Sponsor organisation address	Maudsley Hospital, Denmark Hill, London , United Kingdom,
Public contact	Prof. Allan Young, South London & Maudsley NHS Foundation Trust, 020 78480088, allan.young@kcl.ac.uk
Scientific contact	Prof. Allan Young, South London & Maudsley NHS Foundation Trust, 020 78480088, allan.young@kcl.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 August 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2024
Global end of trial reached?	Yes
Global end of trial date	28 August 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the feasibility of a randomised, controlled trial design, in which a single dose of psilocybin 25mg PO vs placebo, is given to adult participants with treatment resistant major depressive disorder (TRD), under psychologically supportive conditions, with 6 weeks of follow up, by measuring recruitment rates, dropout rates and by estimating the variance of the primary outcome measure (MADRS) to inform upon the design of a phase 3 trial.

Protection of trial subjects:

Participants have the right to withdraw from the study at any time for any reason. The investigator also has the right to withdraw patients from the study drug in the event of inter-current illness, AEs, SAE's, SUSAR's, protocol violations, cure, administrative reasons or other reasons. It is understood by all concerned that an excessive rate of withdrawals can render the study uninterpretable; therefore, unnecessary withdrawal of participants should be avoided. Should a participant decide to withdraw from the study, all efforts will be made to report the reason for withdrawal as thoroughly as possible and efforts will be made to continue to obtain follow-up data, if the participant consents to this. Since the treatment consists of a single dose of psilocybin, it is not practical for participants to withdraw during the Dosing Visit.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 60
Worldwide total number of subjects	60
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	60
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	60
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Number of subjects completed	60
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Period 1

Period 1 title	Overall Trial (overall period)
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Is this the baseline period?	Yes
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Allocation method	Randomised - controlled
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Blinding used	Double blind
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Roles blinded	Subject, Investigator, Monitor, Carer, Assessor
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Blinding implementation details:

Both treatments were delivered in 5 identical opaque HPMC capsules. All participants and members of the study team present during the Dosing Visit were blinded to treatment allocation. Allocation concealment was maintained by the Maudsley Hospital Pharmacy. Emergency unblinding was available 24 hours per day via the on-call pharmacist. MADRS assessments were done by blinded raters who were external and independent to the study team.

Arms

Are arms mutually exclusive?	Yes
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Arm title	Placebo
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Arm description:

To evaluate the feasibility of a randomised, controlled trial design in which a single dose of psilocybin 25mg per os vs placebo is given to adult participants with treatment resistant major depressive disorder (TRD), under psychologically supportive conditions, with 6 weeks of follow up, by measuring recruitment rates, dropout rates and by estimating the variance of the primary outcome measure (MADRS) to inform the design of a Phase 3 trial.

Matching placebo (5 × 5mg HPMC capsules, Starch 1500 only)

Arm type	Placebo
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Investigational medicinal product name	Psilocybin
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Capsule
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Routes of administration	Oral use
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Dosage and administration details:

Psilocybin 25mg, single oral dose (5 × 5mg HPMC capsules)

Arm title	Psilocybin
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Arm description:

Psilocybin 25mg, single oral dose (5 × 5mg HPMC capsules)

Arm type	Experimental
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Investigational medicinal product name	Psilocybin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Psilocybin 25mg, single oral dose (5 × 5mg HPMC capsules)

Number of subjects in period 1	Placebo	Psilocybin
Started	30	30
Completed	29	30
Not completed	1	0
Personal Reasons	1	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
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Reporting group description:

To evaluate the feasibility of a randomised, controlled trial design in which a single dose of psilocybin 25mg per os vs placebo is given to adult participants with treatment resistant major depressive disorder (TRD), under psychologically supportive conditions, with 6 weeks of follow up, by measuring recruitment rates, dropout rates and by estimating the variance of the primary outcome measure (MADRS) to inform the design of a Phase 3 trial.

Matching placebo (5 × 5mg HPMC capsules, Starch 1500 only)

Reporting group title	Psilocybin
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Reporting group description:

Psilocybin 25mg, single oral dose (5 × 5mg HPMC capsules)

Reporting group values	Placebo	Psilocybin	Total
Number of subjects	30	30	60
Age categorical Units: Subjects			
Age 25-59 years	27	27	54
Age >= 60 years	3	3	6
Gender categorical Units: Subjects			
Female	15	15	30
Male	15	15	30

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: To evaluate the feasibility of a randomised, controlled trial design in which a single dose of psilocybin 25mg per os vs placebo is given to adult participants with treatment resistant major depressive disorder (TRD), under psychologically supportive conditions, with 6 weeks of follow up, by measuring recruitment rates, dropout rates and by estimating the variance of the primary outcome measure (MADRS) to inform the design of a Phase 3 trial.	
Matching placebo (5 × 5mg HPMC capsules, Starch 1500 only)	
Reporting group title	Psilocybin
Reporting group description: Psilocybin 25mg, single oral dose (5 × 5mg HPMC capsules)	

Primary: Feasibility Parameters

End point title	Feasibility Parameters ^[1]
End point description:	
End point type	Primary
End point timeframe: Baseline to week 6 follow-up	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Please see uploaded report.	

End point values	Placebo	Psilocybin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	30		
Units: %				
number (confidence interval 95%)				
Retention (MADRS completion at Week 1)	29 (27.3 to 30)	30 (27.3 to 30)		
Retention (MADRS completion at Week 3)	29 (27.3 to 30)	30 (27.3 to 30)		
Retention (MADRS completion at Week 6)	29 (27.3 to 30)	30 (27.3 to 30)		
Attendance at dosing visit (V3)	30 (30 to 30)	30 (30 to 30)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Since the IMP does not have a license or SmPC, all adverse events will be reported. Adverse events will be reported from the start of Dosing Visit (V3) until completion of follow up or until the end of the open label extension if the participant

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Placebo
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Reporting group description: -

Reporting group title	Psilocybin
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Reporting group description: -

Serious adverse events	Placebo	Psilocybin	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 29 (3.45%)	3 / 30 (10.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Reproductive system and breast disorders			
Breast cancer			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychosis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Localised infection			

subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	Psilocybin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 29 (100.00%)	30 / 30 (100.00%)	
Nervous system disorders			
Neurological			
subjects affected / exposed	26 / 29 (89.66%)	29 / 30 (96.67%)	
occurrences (all)	69	75	
General disorders and administration site conditions			
General fatigue/tiredness			
subjects affected / exposed	7 / 29 (24.14%)	11 / 30 (36.67%)	
occurrences (all)	10	13	
Gastrointestinal disorders			
Gastrointestinal			
subjects affected / exposed	16 / 29 (55.17%)	15 / 30 (50.00%)	
occurrences (all)	25	24	
Reproductive system and breast disorders			
Reproductive			
subjects affected / exposed	5 / 29 (17.24%)	4 / 30 (13.33%)	
occurrences (all)	6	6	
Respiratory, thoracic and mediastinal disorders			
Respiratory infection			
subjects affected / exposed	19 / 29 (65.52%)	13 / 30 (43.33%)	
occurrences (all)	41	24	
Skin and subcutaneous tissue disorders			
Skin/ocular			
subjects affected / exposed	5 / 29 (17.24%)	2 / 30 (6.67%)	
occurrences (all)	5	3	
Psychiatric disorders			
Mood/Psychological			

subjects affected / exposed occurrences (all)	18 / 29 (62.07%) 26	19 / 30 (63.33%) 51	
Medication or substance related subjects affected / exposed occurrences (all)	5 / 29 (17.24%) 5	10 / 30 (33.33%) 13	
Musculoskeletal and connective tissue disorders Musculoskeletal/pain subjects affected / exposed occurrences (all)	14 / 29 (48.28%) 19	15 / 30 (50.00%) 22	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 August 2020	MHRA: protocol 1.13 REC/HRA: protocol v1.10 Clinician Info v1.0, PIS Main v1.0, ICF Main v1.0, ICF Neuro v1.0, ICF OLE v1.0, participant advert v1.0, PIS Neuro v1.0, PIS OLE v1.0, On-line screening questionnaire. IB v6.0 27Nov19
12 May 2022	The protocol now clarifies the logistical arrangements between the main trial and the open-label extension. The schedule of visits has been updated to allow a window of up to 5 weeks between visits V7/OLE1 and OLE2, when and where logistically necessary and the allowable window for all follow-up visits is now relative to visit OLE2. Protocol v1.16, PIS Main v1.24, PIS OLE v1.11 & ICF main v1.11, ICF OLE v1.11 (minor changes to all). IB v7.1 05Jan21
12 March 2024	The Investigator Brochure has been updated with administrative and trial-related data revisions. The RSI in the IB has not been altered. No significant new safety findings for COMP360 have been identified. IB v9.0 & IB v10
18 October 2024	The IB was updated with administrative and trial-related data revisions. The RSI in the IB has not been altered but some significant new safety findings for COMP360 have been identified. The protocol was updated with the new sponsor contact details. IB v10.1 & IB v11.0 / Protocol v1.21

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/34853114>