Clinical trial results:
Psilocybin vs. escitalopram for major depressive disorder: comparative mechanisms

Summary

EudraCT number	2017-000219-18
Trial protocol	GB
Global end of trial date	17 October 2020

Results information

Result version number	v1 (current)
This version publication date	12 June 2022
First version publication date	12 June 2022

Trial information

Trial identification

Sponsor protocol code	17HH3790

Additional study identifiers

ISRCTN number	ISRCTN10584863
ClinicalTrials.gov id (NCT number)	NCT03429075
WHO universal trial number (UTN)	U1111-1195-4514

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	RGIT Imperial College London, Room 221, Medical School Building, St Marys campus, Norfolk Pl, London, United Kingdom, W2 1PG
Public contact	Carhart-Harris, Robin, Imperial College London, +44 02075946550, r.carhart-harris@imperial.ac.uk
Scientific contact	Carhart-Harris, Robin, Imperial College London, +44 02075946550, r.carhart-harris@imperial.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	17 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 October 2020
Global end of trial reached?	Yes
Global end of trial date	17 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

How effective is a single dose of psilocybin for major depressive disorder against an an active gold-standard medical treatment (6-weeks of escitalopram)?

Protection of trial subjects:

Patients had several hours of in-person and remote preparation sessions with at least one, often two, clinicians (psychiatrists, clinical psychologists or therapists) before receiving psilocybin. The day after their psilocybin sessions they also had several hours (as needed) of 'integration' therapy, a psychological debrief about their psilocybin experience and state of mine. They had a call one week later and could have up to 3 extra calls with their clinical team as required in between visits. They also had a final integration session before the end of the trial to discuss their trial experience, 3 weeks after their second psilocybin dose. They were supported by study psychiatrists, alongside GPs, to come off medication before and after trial (where relevant). There was a 24/7 contact phone number kept by the study psychiatrists.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 November 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 59
Worldwide total number of subjects	59
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)	59
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All enrolled patients were self-referred. We also recruited via the Clinical Research Network.

Pre-assignment

Screening details:

Patients did an initial telephone screening and remote Hamilton Depression Scale (required a score of over 17) with study clinicians. We also required a GP confirmation of their medical history. They then did a face-to-face screening with ECG, blood tests, urine drugs, pregnancy and alcohol breath tests and MINI psychiatric exam, etc.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Baseline - all patients

Arm description:

All patients before they were randomised into arms.

Arm type	Baseline
Investigational medicinal product name	No products in baseline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Unknown use

Dosage and administration details:

No products at baseline.

Number of subjects in period 1	Baseline - all patients
Started	59
Completed	59

Period 2

Period 2 title	6 week trial period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Psilocybin

Arm description:

Patients had two sessions with high doses of psilocybin (25mg), 3 weeks apart. After the first dose, they were given tablets of placebo to take 1 a day for 3 weeks, then 2 a day for another 3 weeks. All other study procedures were the same across arms.

Arm type	Experimental
Investigational medicinal product name	Psilocybin 25mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

5 capsules with 5mg of psilocybin each, 25mg in total

Arm title	Escitalopram

Arm description:

Patients had two sessions with very low (virtually placebo) doses of psilocybin (1mg), 3 weeks apart. After the first dose, they were given tablets of the selective serotonin reuptake inhibitor (SSRI) escitalopram to take 1 a day for 3 weeks (10mg), then 2 a day for another 3 weeks (20mg). All other study procedures were the same across arms.

Arm type	Experimental
Investigational medicinal product name	Escitalopram
Investigational medicinal product code	
Other name	Lexapro, Cipralex
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Daily 10mg capsules of escitalopram for 3 weeks, then daily 20mg (2 capsules) of escitalopram for 3 weeks.

Investigational medicinal product name	Psilocybin 1mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

5 capsules, one with 1mg psilocybin and the others with placebo (made to look identical to the 25mg psilocybin arm)

Number of subjects in period 2	Psilocybin	Escitalopram
Started	30	29
Completed	30	29

Baseline characteristics

Reporting groups	
Reporting group title	Baseline - all patients
Reporting group description:	
All patients before they were randomised into arms.	

Reporting group values	Baseline - all patients	Total	
Number of subjects	59	59	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	59	59	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	20	20	
Male	39	39	

End points

End points reporting groups

Reporting group title	Baseline - all patients
Reporting group description:	
All patients before they were randomised into arms.	
Reporting group title	Psilocybin
Reporting group description:	
Patients had two sessions with high doses of psilocybin (25mg), 3 weeks apart. After the first dose, they were given tablets of placebo to take 1 a day for 3 weeks, then 2 a day for another 3 weeks. All other study procedures were the same across arms.	
Reporting group title	Escitalopram
Reporting group description:	
Patients had two sessions with very low (virtually placebo) doses of psilocybin (1mg), 3 weeks apart. After the first dose, they were given tablets of the selective serotonin reuptake inhibitor (SSRI) escitalopram to take 1 a day for 3 weeks (10mg), then 2 a day for another 3 weeks (20mg). All other study procedures were the same across arms.	

Primary: Quick Inventory of Depressive Symptomatology (QIDS-SR-16)

End point title	Quick Inventory of Depressive Symptomatology (QIDS-SR-16)
End point description:	
End point type	Primary
End point timeframe:	
Change from baseline to 6 weeks after the first psilocybin session.	

End point values	Psilocybin	Escitalopram		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: scale				
arithmetic mean (standard error)				
Depression Symptomatology	-8 (± 1)	-6 (± 1)		

Statistical analyses

Statistical analysis title	ANCOVA
Comparison groups	Escitalopram v Psilocybin
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.17
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	1

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 6 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0
Reporting groups	
Reporting group title	Psilocybin arm
Reporting group description: -	
Reporting group title	Escitalopram arm
Reporting group description: -	

Serious adverse events	Psilocybin arm	Escitalopram arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 29 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Psilocybin arm	Escitalopram arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 30 (86.67%)	24 / 29 (82.76%)	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 30 (3.33%)	3 / 29 (10.34%)	
occurrences (all)	1	3	
Nervous system disorders			
Headache			
subjects affected / exposed	20 / 30 (66.67%)	15 / 29 (51.72%)	
occurrences (all)	78	41	
Migraine			
subjects affected / exposed	3 / 30 (10.00%)	1 / 29 (3.45%)	
occurrences (all)	4	1	
Sleep disorder			

subjects affected / exposed	1 / 30 (3.33%)	3 / 29 (10.34%)	
occurrences (all)	1	3	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 30 (6.67%)	7 / 29 (24.14%)	
occurrences (all)	2	7	
Feeling abnormal			
subjects affected / exposed	0 / 30 (0.00%)	3 / 29 (10.34%)	
occurrences (all)	0	5	
Feeling jittery			
subjects affected / exposed	2 / 30 (6.67%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	8 / 30 (26.67%)	9 / 29 (31.03%)	
occurrences (all)	9	9	
Dry mouth			
subjects affected / exposed	0 / 30 (0.00%)	4 / 29 (13.79%)	
occurrences (all)	0	5	
Diarrhoea			
subjects affected / exposed	1 / 30 (3.33%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
Vomiting			
subjects affected / exposed	2 / 30 (6.67%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 30 (0.00%)	4 / 29 (13.79%)	
occurrences (all)	0	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 November 2017	Various changes to conduct of trial: arm number (3 to 2), patient number (to 50), length of trial, etc.
18 May 2018	Various changes: extra psilocybin dose, primary end-point change from 4 weeks to 6 weeks, extra visit, extra questionnaires, changes required by HRA and MHRA.
13 July 2018	To MHRA: change in escitalopram dosing (all tablets given after first psilocybin dose), addition of Fisher as site of QP certification and Milpharm Limited as MA holder number.
31 July 2018	To REC: changes to adverse event reporting, adding a scale, change in escitalopram dosing (receive all tablets at once after DD1).
08 January 2019	To REC only: poster/flyer/text message templates for recruitment (suggested by Clinical Research Network), addition of press release details, patient contact cards and 2 new questionnaires
22 February 2019	To REC only: new documents (PIS, consent form etc) relating to documentary about trial (patients only see these new documents after they have left trial). Changes to protocol concerning documentary and inclusion of more rescue meds.
19 August 2019	To REC only: increase recruitment goal to 60 completers, new recruitment form and addition of 1m follow-up interview
03 September 2019	To MHRA only: increasing study completers from 50 to 60.

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/33852780