



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 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 mind. 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 (\pm 1) | -6 (\pm 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 occurrences (all) | 1 / 30 (3.33%) 1 | 3 / 29 (10.34%) 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>