Feasibility Study to Assess the Efficacy and Safety of Psilocybin As a Treatment in Cluster Headaches (PSILOCLEAD study)

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Introduction

The PSILOCLEAD study aims to assess the safety and efficacy of a low dose pulsed Psilocybin regime as a treatment for cluster headaches.

Methods

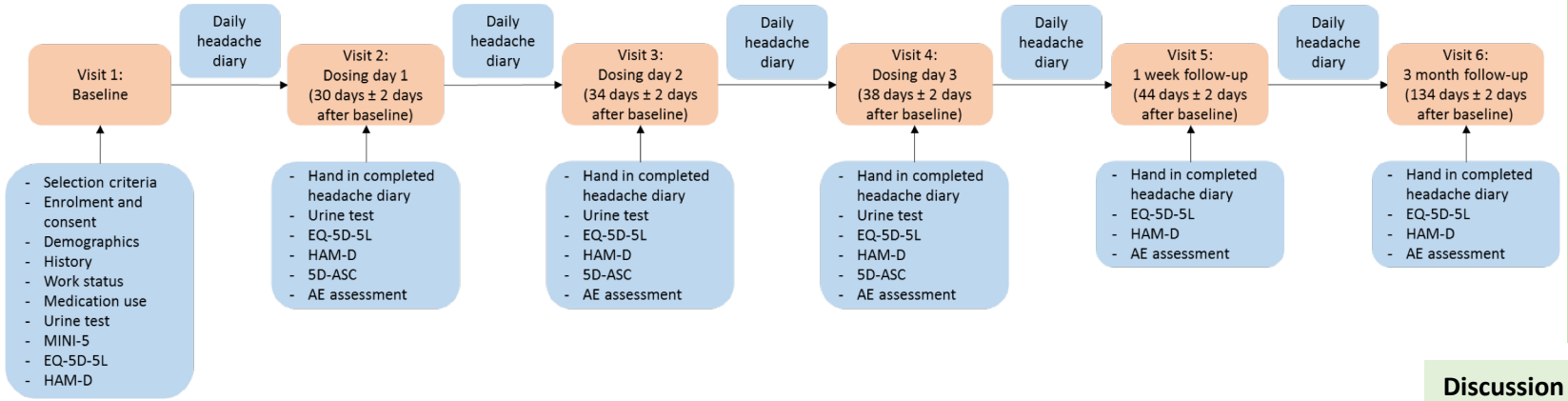
PSILOCLEAD is a prospective single centre feasibility study taking place at Leeds Teaching Hospitals Trust. It is anticipated a total of 20 patients will be consented to take part in the study. Participants will be eligible to enter the study if meeting inclusion/exclusion.

Inclusion criteria:

1. Aged 18-65 years and given written informed consent.
2. In the investigator's opinion has chronic cluster headache with at least one attack every other day and no more than eight attacks each day.
3. In the investigator's opinion has episodic cluster headache (according to IHS criteria) with recurrent predictable episodes that are expected to continue for one month beyond the inclusion.
4. Attacks are managed by no more than twice weekly triptan use (e.g., high-flow oxygen, heat/cold pack).
5. Attacks respond to oxygen.

Exclusion criteria:

1. Current or previous psychotic disorder diagnosis, including in immediate blood-related family members.
2. Other forms of headache attacks.
3. Pregnant, breastfeeding, lack of adequate birth control or a positive pregnancy test at screening or during the study.
4. Use of immunomodulatory agents (i.e. azathioprine) and/or serotonergic antiemetics (i.e. ondansetron) in the past two weeks.
5. Medically significant condition rendering unsuitability for the study (e.g. diabetes, epilepsy, severe cardiovascular disease, hepatic or renal failure etc).
6. History of suicide attempts.
7. Urine toxicology positive to drugs of abuse.
8. Antidepressant use in the last six weeks.
9. Currently using fentanyl, tramadol and MAOIs.
10. Incapable of understanding or responding to the study questionnaires.
11. Current drug or alcohol dependence within the last two years.
12. Use of vasoconstrictive medications (i.e. sumatriptan, pseudoephedrine, midodrine) within five half-lives of test days.
13. History of intolerance to psilocybin, lysergic acid diethylamide (LSD) or related compounds.
14. Participating in a drug or device study within the last 30 days.



Specific objectives

The objectives are to assess the impact of a low-dose pulsed psilocybin regimen on:

- Cluster headache attack frequency, intensity and attack-free time.
- Quality of life (QoL), depression, medication use, satisfaction and states of consciousness.
- Adverse events.

Hypothesis to be tested/research question

We will answer the following research questions:

1. What impact does a low-dose pulsed regimen of psilocybin have on symptoms associated with cluster headache?
2. What is the safety profile of a low-dose pulsed regimen of psilocybin in cluster headache?

Discussion

Since this is a feasibility study, the statistical analysis will be predominantly descriptive (i.e. summary of outcomes at each visit) and will include:

- Mean/median scores plus 95% confidence intervals/interquartile ranges for attack frequency, attack intensity, attack-free time, QoL, depression scores, medication use and patient satisfaction.
- Minimal clinically important difference rates (≥30% reduction in cluster headache attack frequency with psilocybin).
- Response rates (≥50% reduction in cluster headache attack frequency with psilocybin).
- Side-effect types and rates.

It is hoped that findings from this feasibility study will generate the preliminary evidence needed to conduct larger studies, including RCT's.